FUNDAMENTAL BASIS OF NEUROVASCULAR INTERACTION IN PEDIATRIC STROKE

Jumayeva Mahliyo Jahongir qizi

Assistant of the Department of Propaedeutics of

Childhood Diseases and Pediatric Neurology

Bukhara State Medical Institute

Abstract

Pediatric stroke represents a significant cause of long-term neurological disability in children and is increasingly recognized as a condition with unique pathophysiological mechanisms distinct from adult stroke. Unlike the mature brain, the developing nervous system demonstrates heightened vulnerability to disturbances in cerebral blood flow and altered neurovascular coupling. This article examines the fundamental mechanisms underlying neurovascular interaction in pediatric stroke, focusing on vascular pathology, neuronal injury cascades, inflammation, oxidative stress, and developmental differences in cerebrovascular regulation. Understanding these mechanisms is essential for designing age-specific diagnostic, therapeutic, and rehabilitation approaches for affected children.

Keywords: pediatric stroke, neurovascular unit, cerebral blood flow, neuronal injury, inflammation, neurodevelopment, ischemia.

Джумаева Махлиё Жахонгир кизи

Ассистент кафедра пропедевтики детских

болезней и детской неврологии

Бухарский государственный медицинский институт

Аннотация

Инсульт у детей является одной из ведущих причин длительной неврологической инвалидизации и характеризуется патофизиологическими механизмами, существенно отличающимися от инсульта у взрослых. Незрелость нейроваскулярного юнита делает детский мозг особенно

уязвимым к ишемии, нарушению целостности гематоэнцефалического барьера, воспалительным процессам и оксидативному стрессу. В данной статье рассматриваются фундаментальные основы нейроваскулярного взаимодействия при детском инсульте, включая эндотелиальную дисфункцию, функциональную незрелость астроцитов, нейрональную эксайтотоксичность и возрастные особенности церебральной ауторегуляции. Понимание этих механизмов имеет ключевое значение для совершенствования диагностики, разработки возраст-специфических терапевтических подходов и улучшения долгосрочных исходов у детей.

Ключевые слова: детский инсульт, нейроваскулярный юнит, ишемия, ГЭБ, нейровоспаление, повреждение нейронов, мозговой кровоток.

1. Introduction

Stroke in children, though less common than in adults, is a major cause of morbidity, lifelong disability, and cognitive impairment. The incidence of pediatric stroke ranges from 2 to 13 per 100,000 children annually, with neonates being the most vulnerable subgroup due to ongoing cerebral development. Unlike adults, in whom stroke is primarily associated with atherosclerosis, pediatric stroke is driven by congenital heart disease, infections, hematologic disorders, trauma, and genetic vasculopathies.

The neurovascular unit (NVU)—comprising neurons, endothelial cells, astrocytes, pericytes, and extracellular matrix—plays a vital role in regulating cerebral blood flow and maintaining blood–brain barrier integrity. In children, the NVU is structurally and functionally immature, making it more susceptible to ischemic injury. This article analyzes the fundamental biological interactions between neuronal and vascular components during pediatric stroke and highlights how these age-dependent mechanisms shape the clinical course and outcomes.

2. Neurovascular Unit in the Developing Brain

The neurovascular unit undergoes significant maturation during early childhood. Each component contributes uniquely to neurovascular coupling:

2.1. Endothelial Cells

In infants, endothelial cells express immature tight junctions, resulting in a more permeable blood–brain barrier (BBB). This increases the risk of cerebral edema and inflammatory infiltration during ischemia.

2.2. Astrocytes

Astrocyte end-feet, which regulate blood flow and metabolic support, are not fully developed in neonates. Their reduced ability to buffer glutamate predisposes the immature brain to excitotoxic neuronal injury.

2.3. Pericytes

Pericytes, crucial for vessel stabilization and BBB integrity, are reduced in number in early neurodevelopment, making cerebral microvasculature more fragile.

2.4. Neurons

Developing neurons exhibit high metabolic demand and low resistance to oxidative stress. Their susceptibility to ischemic injury is significantly greater compared with adults.

3. Pathophysiology of Pediatric Stroke

3.1. Vascular Factors

Pediatric stroke is predominantly driven by:

congenital heart defects (e.g., single ventricle physiology), arteriopathies (e.g., Moyamoya disease), sickle-cell anemia, infections (e.g., varicella vasculopathy),

trauma-related dissections.

These conditions lead to disrupted blood flow, vessel stenosis, or thromboembolism, causing cerebral ischemia.

3.2. Neuronal Injury Mechanisms

During ischemia, oxygen and glucose deprivation trigger:

ATP depletion, membrane depolarization, calcium influx, glutamate-mediated excitotoxicity, activation of proteases and lipases.

Because the neonatal NVU is immature, these cascades progress more rapidly than in adults.

3.3. Inflammation and Oxidative Stress

Microglial activation occurs early in the ischemic response in children. Excessive inflammatory cytokines (IL-1β, TNF-α) increase BBB permeability, aggravating neuronal death.

Immature antioxidant systems (e.g., low superoxide dismutase activity) elevate susceptibility to oxidative damage.

4. Neurovascular Interaction During Ischemia

The neurovascular response to ischemia in children includes:

4.1. Impaired Neurovascular Coupling

Developing astrocytes cannot efficiently regulate blood flow in response to neuronal activity, worsening ischemic vulnerability.

4.2. BBB Breakdown

Due to immature tight junctions and astrocytic support, the BBB is prone to early breakdown, allowing infiltration of leukocytes and plasma proteins.

4.3. Cerebral Blood Flow Dysregulation

Autoregulation mechanisms are underdeveloped in young children. Even small reductions in systemic blood pressure significantly decrease cerebral perfusion.

4.4. Mitochondrial Dysfunction

Developing neurons rely heavily on mitochondrial energy production, making ischemic mitochondrial failure particularly damaging.

5. Clinical Implications

5.1. Diagnostic Considerations

MRI remains the gold standard for diagnosing pediatric stroke. Age-adjusted biomarkers and neurovascular imaging are essential due to the unique pathophysiology of the immature NVU.

5.2. Therapeutic Approaches

While thrombolysis is rarely used in children, treatment options include:

correction of underlying disorders (e.g., heart defects),

anticoagulation or antiplatelet therapy,

aggressive management of inflammation and edema,

neuroprotective strategies targeting excitotoxicity and oxidative stress.

5.3. Rehabilitation

Children demonstrate greater neuroplasticity than adults. Early, intensive neurorehabilitation significantly improves long-term motor and cognitive outcomes.

6. Conclusion

Pediatric stroke is fundamentally different from adult stroke due to the unique characteristics of the developing neurovascular unit. Immaturity of endothelial cells, astrocytes, neurons, and autoregulatory mechanisms increases vulnerability to ischemia and shapes the clinical presentation and prognosis. Understanding these fundamental neurovascular interactions is crucial for optimizing early diagnosis, designing age-specific treatments, and improving long-term functional outcomes in affected children.

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