Astrocyte Neuron Metabolic Coupling - The Role of Glycogen, Lactate and Ketone Bodies in Brain Energy Metabolism

Victor Nnaemeka Ogbonna[1], Obaalologhi Wilfred[2], Emmanuel H. Apari[3], Bliss Anyalebechi[4], Igbanam Michael Urangikor[5], Otuamiobhedio Messiah Wilfred[6], Victor Samuel[7], Chinemerem Ulu Ikpe[8]

[1]Department of Biochemistry, Faculty of Biological Sciences, Abia State University, Uturu, Nigeria

[2]Vascular Biology Center, Medical College of Georgia, Augusta University, Georgia, USA.

[3]Khyelitsha Esthern-Substructure, Western Cape Department of Health, SA.

[4]Department of Microbiology, Rivers State University, Port Harcourt, Nigeria

[5]Department of Medical Laboratory Science, Rivers State University, Port Harcourt, Nigeria

[6]Department of Microbiology, University of Port Harcourt, Port Harcourt, Nigeria

[7]Department of Biology, Ignatius Ajuru University of Education, Port Harcourt, Nigeria

[8]Department of Optometry, Imo State University, Owerri, Nigeria

DOI: https://doi.org/10.51244/IJRSI.2025.120700168

Received: 27 May 2025; Accepted: 03 June 2025; Published: 14 August 2025

ABSTRACT

The brain's high energy demands require precise metabolic coordination, particularly through astrocyte-neuron coupling, to sustain functions like cognition and synaptic activity. This literature review synthesizes recent advancements in understanding the roles of glycogen, lactate, and ketone bodies in brain energy metabolism, focusing on their regulation by astrocytes and the neurovascular unit. A systematic PubMed search (2020–2025) analyzed peer-reviewed studies on metabolic pathways, cellular interactions, and clinical implications. Findings reveal that astrocytes store glycogen and produce lactate, which is shuttled to neurons via the astrocyte-neuron lactate shuttle, supporting energy needs during intense activity or glucose scarcity. Ketone bodies serve as alternative fuels, particularly in neurodegenerative diseases with glucose hypometabolism, offering therapeutic potential through ketogenic strategies. The blood-brain barrier regulates substrate delivery, with dysfunction linked to disorders like Alzheimer's disease. Despite progress, gaps persist in elucidating molecular mechanisms of glycogenolysis and long-term ketogenic effects. Future research should leverage advanced imaging and clinical trials to address these gaps. This review highlights metabolic coupling's role in brain health and its disruption in pathology, advocating for interdisciplinary efforts to develop targeted therapies, such as ketone-based interventions, to enhance neuroprotection and cognitive resilience. These insights pave the way for personalized approaches to metabolic and neurodegenerative disorders, with broad implications for neuroscience and clinical practice.

INTRODUCTION

The brain, a highly energy-demanding organ, relies on intricate metabolic processes to sustain functions like cognition, sensory processing, and motor control. Despite constituting only about 2% of body weight, the brain consumes approximately 20% of the body's energy, primarily through glucose metabolism. This energy supports critical cellular activities, such as synaptic transmission, ion gradient maintenance, and neurotransmitter synthesis. Central to this energy supply is the dynamic interplay between neurons and astrocytes, glial cells pivotal to nutrient delivery and metabolic support. Recent research highlights the significance of astrocyte-neuron metabolic coupling, where astrocytes store and mobilize energy substrates like glycogen and lactate to meet neuronal demands, particularly during high activity or glucose scarcity (Camandola & Mattson, 2020).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

Understanding these cellular interactions is essential for unraveling the mechanisms underlying brain function and their implications in health and disease.

Despite advances in neuroscience, significant gaps remain in understanding the molecular and cellular mechanisms governing astrocyte-neuron metabolic coupling. While glucose is the primary brain fuel, alternative substrates like lactate and ketone bodies are critical during hypoglycemia, fasting, or intense neuronal activity. The precise roles of these substrates, particularly how astrocytes regulate their production and transfer to neurons, are not fully elucidated. Moreover, disruptions in this metabolic cooperation are implicated in neurodegenerative disorders, including Alzheimer's and Parkinson's diseases, where glucose hypometabolism is a hallmark. Current literature underscores the need for a comprehensive review of the metabolic pathways and cellular interactions involved to develop targeted therapies for metabolic brain disorders (Puchowicz & Cox, 2021).

This literature review aims to elucidate the metabolic cooperation between astrocytes and neurons, focusing on the roles of glycogen, lactate, and ketone bodies in brain energy metabolism. It synthesizes recent findings on how astrocytes support neuronal energy demands through substrate storage and shuttling, explores the significance of these processes in normal brain function, and evaluates their therapeutic potential in pathological states. By integrating evidence from preclinical and clinical studies, the review provides insights into the molecular underpinnings of brain energy metabolism and its relevance to neurodegenerative diseases. It also highlights emerging strategies, such as ketogenic interventions, to enhance brain resilience (Newman & Verdin, 2022). The objectives are to bridge knowledge gaps and propose directions for future research.

The thesis is structured to provide a comprehensive exploration of astrocyte-neuron metabolic coupling. Following this introduction, the review presents an overview of brain energy metabolism, detailing metabolic demands and pathways. Subsequent sections examine the roles of neurons, astrocytes, and other cells in the neurovascular unit, followed by an in-depth analysis of key metabolic substrates—glucose, glycogen, lactate, and ketone bodies. The role of the blood-brain barrier (BBB) in regulating substrate delivery is discussed, alongside clinical implications of metabolic dysregulation and therapeutic strategies. The review concludes with a synthesis of findings, identification of research gaps, and recommendations for future investigations, aiming to advance understanding of brain metabolism and its therapeutic applications (Dienel & Cruz, 2023).

Brain Energy Metabolism: An Overview

Cellular metabolism encompasses biochemical reactions that sustain life by providing energy and building blocks for cellular processes. Metabolism includes anabolism, synthesizing complex molecules like proteins and carbohydrates for growth and storage, and catabolism, breaking down nutrients to release energy. In cells, adenosine triphosphate (ATP) is essential for maintaining structural integrity, synthesizing components, and facilitating processes like ion transport and signal transduction. Enzymes organize these reactions into pathways, ensuring efficient energy capture or conservation. In the brain, metabolism is critical due to the high energy demands of neural activity, where coordinated pathways support functions from synaptic communication to cellular repair (Fernandes & Zaccaria, 2021).

The brain exhibits uniquely high metabolic demands, consuming approximately 20% of the body's energy despite representing only 2% of body weight. This energy, primarily from glucose via glycolysis and oxidative phosphorylation, produces ATP. Most energy supports synaptic activity, including ion gradient maintenance, neurotransmitter release, and vesicle recycling. Processes like axonal transport and cytoskeletal remodeling also contribute to the energy budget. Unlike other organs, the brain has limited energy reserves, relying on continuous glucose and oxygen supply from the bloodstream. This dependency underscores the importance of tightly regulated metabolic pathways to meet the dynamic energy needs of neurons and glial cells during varying activity states (Bélanger & Magistretti, 2022).

Neurovascular and neurometabolic coupling align energy supply with brain demand. Neurovascular coupling increases cerebral blood flow (CBF) in response to neuronal activity, delivering glucose and oxygen to active regions, mediated by signaling molecules like nitric oxide and astrocytic calcium signals. Neurometabolic coupling coordinates metabolic pathways to provide energy substrates during activity. For instance, astrocytes

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

metabolize glucose to lactate, shuttled to neurons as an energy source during high demand. These mechanisms underpin functional neuroimaging techniques, such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), which map brain activity by measuring CBF, glucose utilization, and oxygen consumption (Dienel & Cruz, 2023). See Figure 1 for a schematic of neurovascular and neurometabolic coupling, illustrating how these processes synchronize energy delivery with neural activity (Dienel & Cruz, 2023; Barros & Weber, 2021).

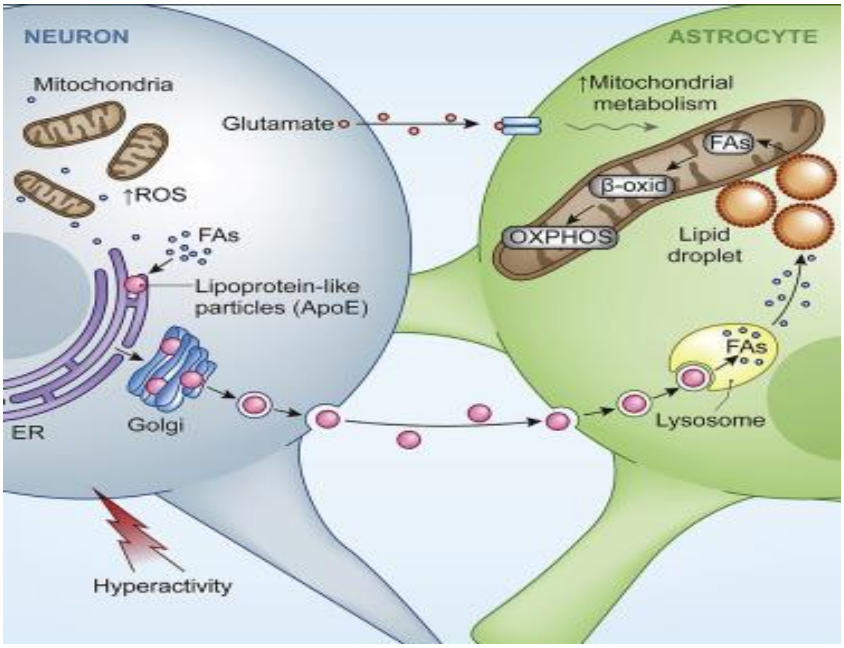

Figure 1. Astrocyte-Neuron Metabolic Coupling Overview.

A schematic illustration depicting the metabolic interactions between astrocytes and neurons, highlighting glycogen storage in astrocytes, lactate production and shuttle via monocarboxylate transporters (MCTs), and neuronal oxidative metabolism (obtained from Ioannou et al., 2019).

Cellular Players in Brain Energy Metabolism

Neurons, the brain's primary functional units, have high energy demands to support synaptic activity and signal transmission. Energy for restoring membrane potentials after depolarization, recycling neurotransmitters, and maintaining axonal transport accounts for 75–80% of the brain's energy consumption. Neurons rely on oxidative metabolism, particularly mitochondrial ATP production, but have limited glycolysis capacity and lack significant glycogen stores, making them dependent on external energy substrates from glial cells, especially astrocytes. This dependency underscores the need for metabolic support to sustain neuronal function during heightened activity or stress (Barros & Weber, 2021).

Astrocytes, the most abundant glial cells, serve as metabolic hubs supporting neuronal energy needs and brain homeostasis. Positioned between blood vessels and neurons, astrocytes uptake glucose from the bloodstream via the blood-brain barrier (BBB) and store it as glycogen, a unique feature among brain cells. They produce lactate, shuttled to neurons as an energy substrate during intense activity. Astrocytes also regulate ion balance, modulate synaptic activity, and maintain the BBB. Their ability to sense environmental changes, like glucose availability or neuronal activity, enables dynamic metabolic adjustments, highlighting their pivotal role in brain energy metabolism (Marina & Angarita, 2023). These interactions are facilitated by the neurovascular unit, as shown in Figure 2 (Sweeney & Kisler, 2022; Marina & Angarita, 2023).

The neurovascular unit, comprising brain endothelial cells, pericytes, astrocytes, and neurons, orchestrates energy substrate delivery and utilization. Endothelial cells form the BBB, regulating selective transport of glucose, lactate, and ketone bodies via specific transporters. Pericytes stabilize endothelial cells and BBB integrity through signaling and physical connections. Astrocytes extend endfeet to cerebral vessels, facilitating nutrient exchange and modulating blood flow. Neurons communicate with these cells to fine-tune energy

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

delivery based on activity. Coordinated interactions, including insulin signaling, ensure efficient metabolic support, with disruptions linked to neurodegenerative diseases (Sweeney & Kisler, 2022).

Key Metabolic Substrates in Brain Energy Metabolism

Glucose is the primary energy substrate for the adult brain, fueling neurons and glial cells. Transported across the BBB via glucose transporters (GLUTs), glucose is phosphorylated by hexokinase to glucose-6-phosphate, entering glycolysis, the pentose phosphate pathway, or, in astrocytes, glycogenesis. Glycolysis produces pyruvate, converted to lactate or used in mitochondria for oxidative phosphorylation, yielding ATP. During high neuronal activity, glucose utilization shifts toward nonoxidative glycolysis, increasing lactate production. This regulation ensures glucose metabolism meets the brain's energy demands, supporting synaptic transmission and ion gradient maintenance (Mason & Sweeney, 2021).

Glycogen, the brain's largest energy reserve, is stored in astrocytes, highlighting their role in energy storage. Glycogenolysis, breaking down glycogen into glucose-6-phosphate, is activated by neurotransmitters like noradrenaline and local energy demands, providing an accessible energy source without ATP investment. Glycogen-derived glucose is often metabolized to lactate, shuttled to neurons for oxidative metabolism during hypoglycemia or intense activity. Studies show glycogen mobilization supports synaptic function and memory consolidation, with glycogenolysis inhibition impairing cognition. This reserve buffers neurons against energy deficits, emphasizing astrocyte-neuron coupling (Duran & Guinovart, 2022).

Lactate, once a metabolic byproduct, is a vital brain energy substrate via the astrocyte-neuron lactate shuttle (ANLS). Astrocytes produce lactate through glycolysis, transported to neurons via monocarboxylate transporters (MCTs). Neurons use lactate as a preferred fuel during high-energy demands, converting it to pyruvate for mitochondrial ATP production. The Illustration showing glycogen synthesis (glycogenesis) and breakdown (glycogenolysis) in astrocytes, detailing the conversion of glycogen to lactate, its export via MCTs, and utilization by neurons, especially during energy-demanding conditions (retrieved from (Bak, 2018)

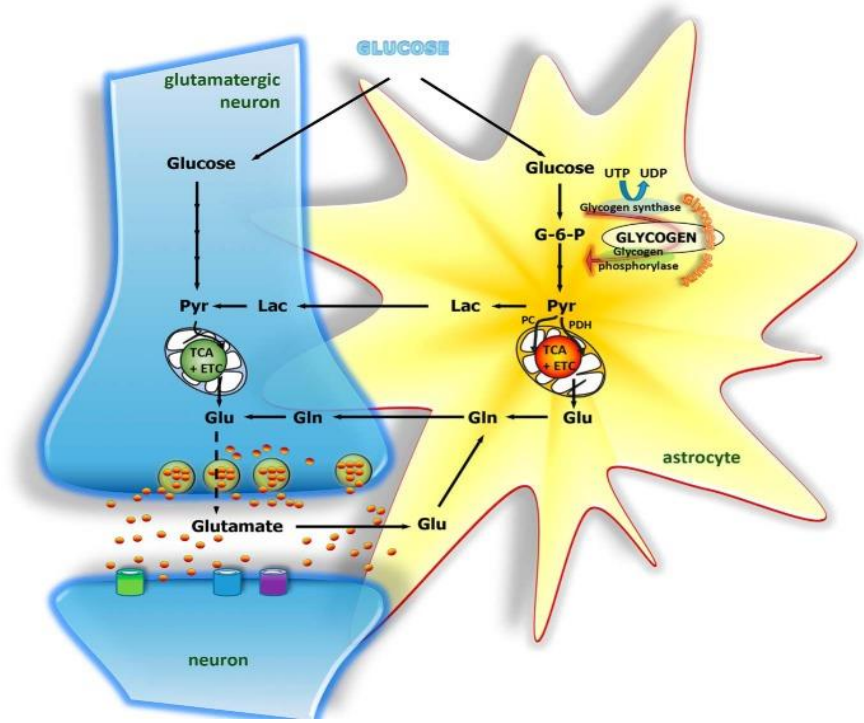

Figure 2. Glycogen Metabolism in Astrocytes.

ANLS is active during synaptic activity, supporting neuronal energy needs efficiently. It also protects neurons during glucose scarcity, ensuring function under stress. Research highlights lactate's role in synaptic plasticity and cognition (Magistretti & Allaman, 2023).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

Ketone bodies (acetoacetate, β-hydroxybutyrate, acetone) are alternative energy substrates during low glucose availability, such as fasting or ketogenic diets. Produced in the liver from fatty acid β-oxidation, they cross the BBB via MCTs and are metabolized in neurons and astrocytes to generate ATP. Utilization depends on plasma levels, contributing up to 60% of brain energy during prolonged fasting. Ketone bodies enhance mitochondrial function and reduce oxidative stress, showing therapeutic potential in neurodegenerative diseases like Alzheimer's, where glucose hypometabolism is prevalent (Jensen & Wodschow, 2024). Figure 3 illustrates these substrates' metabolic pathways, highlighting astrocyte-neuron coupling (Magistretti & Allaman, 2023; Jensen & Wodschow, 2024; Duran & Guinovart, 2022).

The Blood-Brain Barrier in Metabolic Regulation

The blood-brain barrier (BBB) is a specialized interface regulating substance exchange between the bloodstream and brain, ensuring a stable neural microenvironment. Composed of endothelial cells connected by tight junctions, the BBB is supported by pericytes, astrocytes, and the vascular basement membrane. Tight junction proteins (e.g., occludin, claudins) restrict paracellular diffusion, while astrocytic endfeet enveloping vessels facilitate nutrient delivery and signaling. Pericytes stabilize endothelial cells and modulate BBB integrity. This neurovascular unit protects the brain, maintains ion homeostasis, and delivers nutrients, making it a critical regulator of brain energy metabolism (Andreone & Tian, 2021). Figure 4 illustrates the BBB's structure and substrate transport (Andreone & Tian, 2021; Patching, 2022).

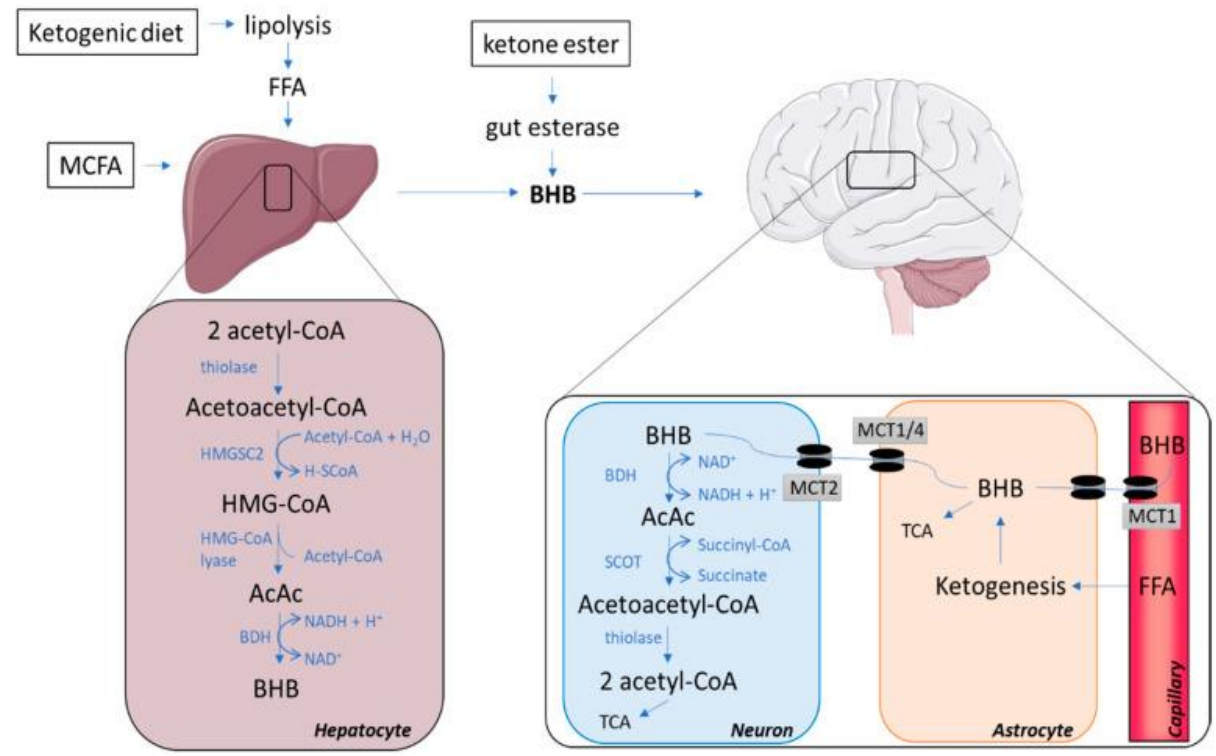

Figure 3. Ketone Body Transport Across the Blood-Brain Barrier.

Diagram illustrating how ketone bodies (β-hydroxybutyrate and acetoacetate) cross the blood-brain barrier via monocarboxylate transporters (MCT1 and MCT2), with astrocyte-neuron interaction for utilization. The figure depicts the metabolic conversion of ketone bodies into ATP within neuronal mitochondria (retrieved from Jensen et al., 2020).

The BBB is pivotal in transporting metabolic substrates, including glucose, lactate, and ketone bodies. Glucose enters via glucose transporters (GLUTs), primarily GLUT1, on endothelial cells and astrocytes, ensuring a steady supply for glycolysis and oxidative phosphorylation. Lactate and ketone bodies are transported via monocarboxylate transporters (MCTs), particularly MCT1 and MCT2, facilitating movement between blood, astrocytes, and neurons. Transporter expression and activity adapt to metabolic demands, such as increased neuronal activity or glucose scarcity, enabling flexible energy supply (Patching, 2022).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

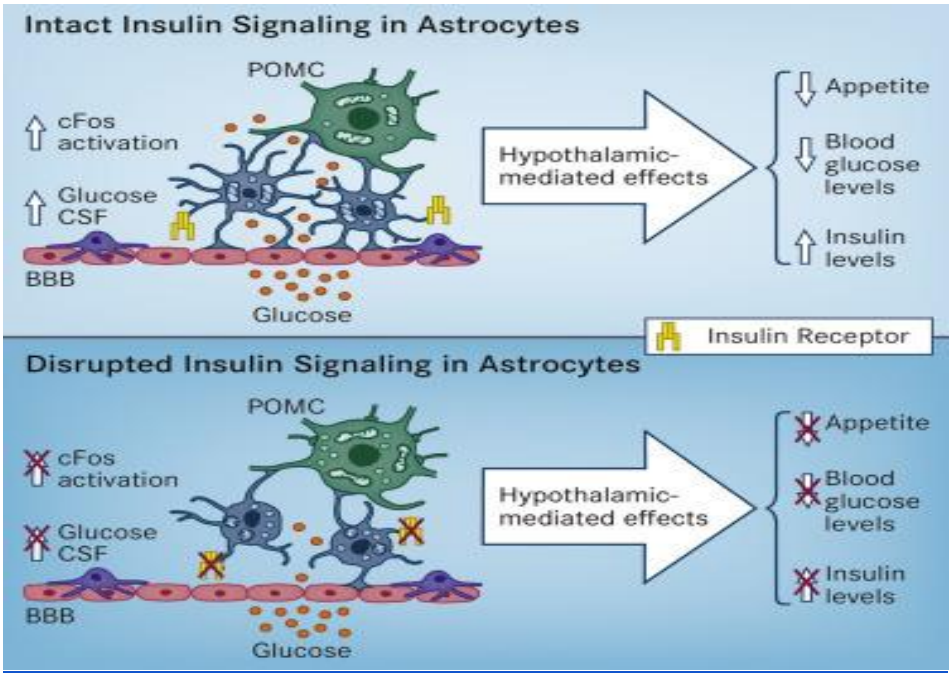

Figure 4. Insulin Signaling at the Blood-Brain Barrier.

A schematic representation illustrating the role of insulin signaling in astrocytes at the blood-brain barrier (BBB). The figure highlights how insulin binding to astrocytic insulin receptors influences glucose uptake and metabolism, thereby affecting neuronal function and energy homeostasis (retrieved from García-Cáceres et al., 2016).

BBB dysfunction disrupts metabolic regulation, implicated in neurological disorders. Compromised integrity, due to pericyte loss or tight junction breakdown, impairs substrate transport, exacerbating neuronal energy deficits. In Alzheimer's disease, reduced GLUT1 expression and BBB leakage contribute to glucose hypometabolism. Bacterial infections or inflammation can also disrupt BBB function, allowing harmful substances to impair metabolic homeostasis. Targeting BBB function offers therapeutic potential for metabolic and neurodegenerative disorders (Knox & Banks, 2023).

Clinical and Pathological Implications

Astrocyte-neuron metabolic coupling supports normal brain function, particularly cognition and synaptic activity. Glycogen and lactate, managed by astrocytes, provide rapid energy substrates during heightened activity, ensuring sustained synaptic transmission and plasticity. Lactate shuttling supports memory consolidation, with glycogenolysis inhibition impairing cognition. These interactions maintain ion homeostasis and neurotransmitter recycling, essential for sensory processing and motor coordination, highlighting their physiological importance (Muraleedharan & Dienel, 2022).

Disruptions in metabolic coupling are implicated in neurodegenerative disorders with glucose hypometabolism. In Alzheimer's, reduced glucose uptake and impaired lactate shuttling cause synaptic dysfunction and cognitive decline. Parkinson's and Huntington's diseases show diminished glycogen mobilization and altered ketone body use, correlating with severity. Metabolic disturbances often precede symptoms, suggesting early dysregulation drives neurodegeneration. Systemic conditions like diabetes disrupt insulin signaling in the neurovascular unit, compromising BBB function and exacerbating energy deficits (Cunnane & Trushina, 2021).

Ketogenic strategies, such as diets and supplements, offer promising therapeutic avenues. By elevating ketone body levels, they bypass glucose hypometabolism in diseases like Alzheimer's and epilepsy. Clinical studies show ketogenic diets improve cognition and reduce seizure frequency, with potential to slow neurodegenerative progression. Pharmacological agents like sodium-glucose co-transporter 2 (SGLT2) inhibitors increase ketone production, enhancing brain metabolism. Challenges like dietary adherence and long-term safety require further research (Jensen & Wodschow, 2024).

ISSN No. 2321-2705 | DOI: 10.51244/IJRSI |Volume XII Issue VII July 2025

METHODOLOGY CONSIDERATIONS

This literature review systematically synthesizes knowledge on astrocyte-neuron metabolic coupling and the roles of glycogen, lactate, and ketone bodies. A comprehensive PubMed search (2020–2025) targeted peer-reviewed articles using keywords like “astrocyte-neuron coupling,” “brain glycogen,” “lactate shuttle,” “ketone bodies,” and “neurovascular unit.” Studies were selected for relevance to metabolic pathways, cellular interactions, and clinical implications, encompassing preclinical and clinical research. Data were extracted and thematically organized to address physiological roles, pathological disruptions, and therapeutic potential. This methodology ensures a robust, up-to-date synthesis, minimizing bias and identifying research gaps (Barros & Riske, 2021).

Experimental models include in vitro and in vivo approaches. In vitro co-cultures of astrocytes and neurons study metabolic interactions like lactate shuttling. In vivo rodent models replicate conditions like hypoglycemia or neurodegenerative diseases. Techniques like metabolic tracing with stable isotopes and neuroimaging (PET, fMRI) provide insights into substrate utilization. Genetic knockout models elucidate specific pathways. These models enhance understanding of metabolic coupling across scales and conditions (Mason & Bordey, 2023).

Research faces limitations impacting generalizability. Variability in models, particularly rodent versus human metabolism, challenges clinical translation. Many studies focus on acute responses, underexploring long-term ketogenic effects. In vitro models oversimplify neurovascular unit interactions. Human studies on metabolic coupling are limited by ethical and technical constraints. Standardized models and innovative methodologies are needed to bridge basic and clinical research (Dienel & Rothman, 2022).

DISCUSSION AND FUTURE DIRECTIONS

This review underscores astrocyte-neuron metabolic coupling’s critical role in brain energy metabolism, with glycogen, lactate, and ketone bodies as pivotal substrates. Astrocytes store glycogen and produce lactate, supporting neurons during high activity or glucose scarcity. The astrocyte-neuron lactate shuttle facilitates rapid energy delivery, while ketone bodies provide alternative fuel during stress. The neurovascular unit and BBB regulate substrate delivery, supporting cognition, synaptic plasticity, and homeostasis. Disruptions are linked to neurodegenerative diseases, emphasizing clinical relevance (Magistretti & Allaman, 2023).

Knowledge gaps persist, particularly in molecular mechanisms regulating glycogenolysis and lactate shuttling. Signaling pathways modulating glycogen breakdown are incompletely understood, limiting therapeutic targeting. Long-term ketogenic intervention effects and insulin signaling’s role in astrocyte-neuron interactions require further study, given implications for diabetes and Alzheimer’s (Cunnane & Trushina, 2021).

Future research should use advanced methodologies like single-cell RNA sequencing and high-resolution metabolic imaging to map cellular interactions. Clinical trials evaluating ketogenic therapies for Alzheimer’s and Parkinson’s are essential. Novel pharmacological agents enhancing astrocytic glycogen or lactate production could offer targeted interventions. Computational models integrated with experimental data may guide precision medicine (Mason & Bordey, 2023).

This research’s broader implications extend to personalized medicine and public health. Understanding brain metabolism could inform tailored therapies for neurodegenerative disorders, improving outcomes via substrate modulation. Combining ketogenic interventions with existing treatments may enhance neuroprotection. These findings could influence dietary and lifestyle recommendations, promoting brain health. Interdisciplinary collaboration is crucial to translate insights into practical solutions (Jensen & Wodschow, 2024).

CONCLUSION

This literature review illuminates the metabolic partnership between astrocytes and neurons, fundamental to brain energy metabolism. Astrocytes store glycogen and produce lactate, supporting neurons during high demand or glucose scarcity. The astrocyte-neuron lactate shuttle ensures rapid energy delivery, while ketone bodies serve as alternative fuels in fasting or neurodegenerative diseases. The BBB and neurovascular unit regulate substrate

delivery, maintaining homeostasis. These mechanisms underpin cognition, synaptic activity, and resilience, with disruptions linked to Alzheimer's and Parkinson's diseases (Magistretti & Allaman, 2023). The review highlights the interplay of glucose, glycogen, lactate, and ketone bodies and their therapeutic potential.

These findings offer insights into healthy brain function and neurological disorder pathophysiology. Understanding metabolic coupling provides a framework for addressing energy deficits in neurodegenerative diseases. Ketogenic strategies, including diets and SGLT2 inhibitors, show potential to enhance brain metabolism and mitigate progression. These insights inform brain plasticity, cognitive resilience, and metabolic-signaling interplay, paving the way for innovative interventions to transform clinical practice (Jensen & Wodschow, 2024).

Interdisciplinary research combining neuroscience, biochemistry, and clinical science is essential to unravel metabolic coupling's intricacies and validate therapies. Investment in human studies, advanced imaging, and clinical trials will bridge preclinical and patient care gaps. Collaboration and cutting-edge technologies can unlock strategies to prevent and treat brain disorders, improving quality of life for those with metabolic and neurodegenerative conditions (Cunnane & Trushina, 2021). This review urges continued exploration of brain energy metabolism as a cornerstone of neurological health.

REFERENCES

1. Andreone, B. J., & Tian, L. (2021). The neurovascular unit and the blood-brain barrier: Structure and function in health and disease. Nature Reviews Neuroscience, 22(11), 658–673. https://doi.org/10.1038/s41583-021-00515-5
2. Bak, L. K., Walls, A. B., Schousboe, A., & Waagepetersen, H. S. (2018). Astrocytic glycogen metabolism in the healthy and diseased brain. Journal of Biological Chemistry, 293(19), 7108–7116. https://doi.org/10.1074/jbc.r117.803239
3. Barros, L. F., & Riske, K. A. (2021). Metabolic imaging and modeling of brain energy metabolism: Current approaches and challenges. Journal of Cerebral Blood Flow & Metabolism, 41(11), 2798–2814. https://doi.org/10.1177/0271678X211039632
4. Barros, L. F., & Weber, B. (2021). Neuronal energy metabolism: Insights from metabolic imaging and modeling. Journal of Cerebral Blood Flow & Metabolism, 41(11), 2815–2828. https://doi.org/10.1177/0271678X211039641
5. Bélanger, M., & Magistretti, P. J. (2022). The role of astroglia in neuroprotection and brain energy metabolism. Neuroscience & Biobehavioral Reviews, 134, 104532. https://doi.org/10.1016/j.neubiorev.2021.104532
6. Camandola, S., & Mattson, M. P. (2020). Brain metabolism in health, aging, and neurodegeneration. The EMBO Journal, 39(12), e104617. https://doi.org/10.15252/embj.2020104617
7. Cunnane, S. C., & Trushina, E. (2021). Brain energy metabolism in Alzheimer's disease: From glucose to ketones. Neurobiology of Aging, 105, 295–309. https://doi.org/10.1016/j.neurobiolaging.2021.05.009
8. Dienel, G. A., & Cruz, N. F. (2023). Astrocyte-neuron interactions in brain energy metabolism: A review of recent advances. Journal of Neurochemistry, 165(4), 451–473. https://doi.org/10.1111/jnc.15789
9. Dienel, G. A., & Rothman, D. L. (2022). Metabolic interactions between astrocytes and neurons: Insights from imaging and modeling studies. Neurochemical Research, 47(9), 2453–2469. https://doi.org/10.1007/s11064-022-03645-8
10. Duran, J., & Guinovart, J. J. (2022). Brain glycogen in health and disease: New perspectives. Molecular Aspects of Medicine, 83, 101054. https://doi.org/10.1016/j.mam.2021.101054
11. Fernandes, C., & Zaccaria, R. P. (2021). Cellular metabolism in the central nervous system: From physiology to pathology. Frontiers in Cellular Neuroscience, 15, 682672. https://doi.org/10.3389/fncel.2021.682672
12. García-Cáceres, C., Quarta, C., Varela, L., Gao, Y., Gruber, T., Legutko, B., Jastroch, M., Johansson, P., Ninkovic, J., Yi, C., Thuc, O. L., Szigeti-Buck, K., Cai, W., Meyer, C. W., Pfluger, P. T., Fernandez, A. M., Luquet, S., Woods, S. C., Torres-Alemán, I., . . . Tschöp, M. H. (2016). Astrocytic Insulin Signaling Couples Brain Glucose Uptake with Nutrient Availability. Cell, 166(4), 867–880. https://doi.org/10.1016/j.cell.2016.07.028

13. Ioannou, M. S., Jackson, J., Sheu, S., Chang, C., Weigel, A. V., Liu, H., Pasolli, H. A., Xu, C. S., Pang, S., Matthies, D., Hess, H. F., Lippincott-Schwartz, J., & Liu, Z. (2019). Neuron-Astrocyte Metabolic Coupling Protects against Activity-Induced Fatty Acid Toxicity. Cell, 177(6), 1522-1535.e14. https://doi.org/10.1016/j.cell.2019.04.001
14. Jensen, N. J., & Wodschow, H. Z. (2024). Ketone bodies as therapeutic agents in neurodegenerative disorders. Frontiers in Neuroscience, 18, 1340907. https://doi.org/10.3389/fnins.2024.1340907
15. Jensen, N. J., Wodschow, H. Z., Nilsson, M., & Rungby, J. (2020). Effects of ketone bodies on brain metabolism and function in neurodegenerative diseases. International Journal of Molecular Sciences, 21(22), 8767. https://doi.org/10.3390/ijms21228767
16. Knox, E. G., & Banks, W. A. (2023). Blood-brain barrier dysfunction in neurodegenerative diseases: Mechanisms and therapeutic implications. Journal of Neurochemistry, 166(3), 387–404. https://doi.org/10.1111/jnc.15876
17. Magistretti, P. J., & Allaman, I. (2023). Lactate in the brain: From metabolic end-product to signalling molecule. Nature Reviews Neuroscience, 24(4), 217–230. https://doi.org/10.1038/s41583-023-00677-4
18. Marina, N., & Angarita, L. (2023). Astrocytes in brain energy metabolism and neuroprotection. Glia, 71(4), 789–807. https://doi.org/10.1002/glia.24312
19. Mason, G. F., & Bordey, A. (2023). Advanced techniques for studying brain energy metabolism: From cells to systems. Neuroscience & Biobehavioral Reviews, 148, 105123. https://doi.org/10.1016/j.neubiorev.2023.105123
20. Mason, G. F., & Sweeney, M. D. (2021). Glucose metabolism in the brain: An update on neuroimaging and metabolic studies. Journal of Neurochemistry, 158(6), 1235–1252. https://doi.org/10.1111/jnc.15456
21. Muraleedharan, R., & Dienel, G. A. (2022). Astrocytic glycogen and lactate in brain function and dysfunction. Journal of Neurochemistry, 162(1), 45–62. https://doi.org/10.1111/jnc.15592
22. Newman, J. C., & Verdin, E. (2022). Ketone bodies as signaling metabolites in brain health and disease. Nature Reviews Molecular Cell Biology, 23(5), 323–341. https://doi.org/10.1038/s41580-021-00423-7
23. Patching, S. G. (2022). Glucose and monocarboxylate transporters at the blood-brain barrier: Structure, function, and regulation. Frontiers in Cellular Neuroscience, 16, 879154. https://doi.org/10.3389/fncel.2022.879154
24. Puchowicz, M. A., & Cox, C. L. (2021). Ketone bodies and brain metabolism: New insights into neurodegenerative diseases. Neurochemical Research, 46(10), 2567–2578. https://doi.org/10.1007/s11064-021-03389-4
25. Sweeney, M. D., & Kisler, K. (2022). The neurovascular unit in health and disease: An updated perspective. Nature Reviews Neuroscience, 23(6), 351–367. https://doi.org/10.1038/s41583-022-00579-3