



The Impact of Bioenergetic Changes on Brain Growth and Function

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DESCRIPTION

The human brain undergoes an complex and resource-intensive process of development, stretching from prenatal stages through adolescence. This journey, marked by rapid structural and functional changes, demands considerable energy. Bioenergetic changes shifts in the way the brain produces and consumes energy are fundamental to this developmental progression. Understanding these changes gives valuable insight into how the brain's functions emerge, mature and are sustained. These changes also shed light on the potential risks associated with various developmental disorders, allowing for a better comprehension of the metabolic dynamics that govern cognitive and emotional growth.

Brain development relies on a constant supply of energy to support processes such as cellular proliferation, synapse formation, myelination and network integration. In the early stages of life, energy demand surges due to rapid cell division and differentiation. Neurons establish countless connections, forming the essential wiring of the brain's communication networks. This wiring, known as synaptogenesis, requires a significant amount of metabolic fuel, primarily in the form of glucose. Glucose not only fuels these early processes but also serves as a precursor for essential neurotransmitters, which enable neurons to communicate effectively.

The developing brain's metabolism is highly adaptable, as it adjusts to varying energy sources over time. Early brain growth largely relies on glucose; however, as it matures, it increasingly relies on other sources, including ketone bodies and lactate. The brain's ability to adapt its energy sources reflects the changing demands of its structural and functional growth.

During prenatal development, the brain's metabolism is heavily influenced by maternal nutrition, which provides essential nutrients for fetal growth. These nutrients ensure the synthesis of amino acids, lipids and nucleotides necessary for the creation of neural structures. Early in gestation, the brain undergoes a period of rapid expansion, driven by high rates of cell division. This phase is especially sensitive to fluctuations in maternal

health and any disruption to the nutrient supply can impact brain development.

In the postnatal phase, metabolic activity shifts in response to new environmental demands. The infant brain is marked by continued synaptogenesis and myelination, the latter of which strengthens neural connections by insulating axons. This phase, often referred to as the "critical period," relies on an abundant supply of glucose to support energy-intensive processes. Lactate, a metabolite produced during anaerobic glycolysis, is also used by neurons during this phase. Unlike adult brains, which predominantly rely on aerobic metabolism, the infant brain uses both aerobic and anaerobic pathways, allowing it to support rapid growth.

As the brain moves into adolescence, it undergoes structural refinement, known as synaptic pruning, where excess synapses are removed to improve network efficiency. This process, along with the maturation of the prefrontal cortex, requires substantial energy, marking another period of heightened metabolic demand. The adolescent brain shows a shift in fuel utilization, with glucose metabolism becoming more efficient and a rise in the use of fatty acids. During this phase, bioenergetic adjustments align with the brain's need for resources that enhance cognitive functions such as decision-making, impulse control and complex problem-solving.

In addition to glucose, ketone bodies and fatty acids contribute to the adolescent brain's energy supply, particularly during periods of low glucose availability. This shift is thought to provide the brain with additional resilience under different metabolic conditions, supporting cognitive functions that are essential for social and emotional adaptation. The adolescent brain's bioenergetic flexibility allows it to meet these new functional demands effectively, aiding in the maturation of neural networks involved in executive function, emotional regulation and memory formation.

Mitochondria are the powerhouses of cells and their function is essential to the brain's energy supply. They convert nutrients into Adenosine Triphosphate (ATP), which fuels cellular

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activities. Mitochondria also play a key role in regulating oxidative stress, which is the imbalance between free radicals and antioxidants within cells. During brain development, mitochondria support energy production but also manage the production of Reactive Oxygen Species (ROS), a byproduct of cellular respiration that can cause damage if not controlled.

Mitochondrial efficiency is vital for proper neurodevelopment and disruptions in mitochondrial function can lead to various cognitive and developmental disorders. Studies suggest that variations in mitochondrial activity can impact the availability of energy to different brain regions, affecting their growth and function. For example, deficiencies in mitochondrial enzymes have been linked to metabolic conditions that impair motor skills, cognition and emotional stability. Understanding

mitochondrial dynamics in the developing brain provides insights into conditions like mitochondrial encephalopathy, which affects cognitive and physical development.

Both environmental and genetic factors influence brain metabolism during development. Genetic variations can impact enzyme function within metabolic pathways, altering energy production and use. Specific genetic mutations affecting mitochondrial function or nutrient metabolism can predispose individuals to developmental disorders. For instance, Phenylketonuria (PKU), a genetic disorder that hinders the metabolism of the amino acid phenylalanine, can lead to intellectual disabilities if untreated, highlighting the role of metabolic regulation in brain health.