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# Exploring The Molecular Mechanisms Underlying Neurodegenerative Disorders: Biochemical Insights and Pathophysiology

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## ABSTRACT

Neurodegenerative disorders (NDs), including Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis, are characterized by progressive neuronal loss and cognitive and motor dysfunction. These disorders impose a significant global health burden due to their increasing prevalence, lack of definitive cures, and complex pathophysiology. Central to their development are molecular and biochemical perturbations that disrupt neuronal homeostasis and trigger cell death pathways. This review investigates the molecular mechanisms underpinning neurodegeneration, emphasizing biochemical insights and the underlying pathophysiological processes.

At the molecular level, protein misfolding and aggregation are hallmark features of many NDs. For instance, amyloid-beta and tau protein aggregates in Alzheimer's disease, alpha-synuclein inclusions in Parkinson's disease, and huntingtin protein aggregates in Huntington's disease disrupt synaptic function, impair cellular trafficking, and provoke oxidative stress. These proteinopathies are often associated with dysregulation of the ubiquitin-proteasome system and autophagy, highlighting the crucial role of cellular clearance mechanisms in neuronal survival.

Mitochondrial dysfunction is another critical contributor to neurodegeneration. Impaired mitochondrial bioenergetics reduce ATP production, elevate reactive oxygen species (ROS), and activate apoptotic pathways. Coupled with calcium dyshomeostasis, these alterations precipitate excitotoxic neuronal injury, particularly in energy-demanding regions such as the hippocampus and substantia nigra. Additionally, neuroinflammation, mediated by microglial activation and pro-inflammatory cytokine release, amplifies neuronal damage and contributes to disease progression.




Dysregulated signaling pathways, including MAPK, PI3K/Akt, and NF-κB, further modulate apoptosis, synaptic plasticity, and neuronal survival, integrating biochemical alterations with functional outcomes.

Advances in molecular biology and biochemical techniques have facilitated the identification of potential biomarkers for early diagnosis and monitoring disease progression. Metabolomic and proteomic profiling reveal distinct biochemical signatures associated with specific NDs, offering avenues for targeted therapeutic interventions. Current therapeutic strategies aim to modulate protein aggregation, enhance mitochondrial function, mitigate oxidative stress, and reduce neuroinflammation. Despite these advances, effective disease-modifying treatments remain limited, underscoring the necessity for continued mechanistic investigations.