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The Role of Autophagy in Neurodegenerative Disease Pathobiology.

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Introduction

Autophagy, a conserved lysosome-mediated degradation pathway, plays a pivotal role in maintaining cellular homeostasis by eliminating damaged organelles, misfolded proteins, and pathogens. In the central nervous system (CNS), proper autophagic activity is essential for neuronal survival and function, given the limited regenerative capacity of neurons. Dysregulation of autophagy has been increasingly recognized as a contributing factor to the pathobiology of various neurodegenerative disorders, including Alzheimer's disease (AD), Parkinson's disease (PD), Huntington's disease (HD), and amyotrophic lateral sclerosis (ALS) [1, 2, 3, 4, 5].

These diseases are often characterized by the accumulation of toxic protein aggregates, such as β-amyloid, α-synuclein, and huntingtin, which overwhelm the cell's proteostasis mechanisms. Impaired autophagy not only fails to clear these aggregates but also exacerbates oxidative stress, mitochondrial dysfunction, and neuroinflammation—further driving disease progression. Recent advances in molecular neuroscience have revealed that modulating autophagy-related signaling pathways, such as mTOR and AMPK, may hold therapeutic potential. Understanding the interplay between autophagy and neurodegeneration can therefore pave the way for innovative treatment strategies targeting the root causes rather than merely alleviating symptoms.

Conclusion

Autophagy is a double-edged sword in neurodegenerative disease pathobiology—while its proper functioning protects neurons from toxic insults, its impairment or dysregulation accelerates neurodegenerative processes. Evidence suggests that therapeutic modulation of autophagy, through pharmacological agents or gene-targeted interventions, could enhance clearance of pathogenic aggregates and restore neuronal health. However, due to the complexity of autophagic regulation and disease-specific mechanisms, a one-size-fits-all approach is unlikely to succeed. Future research should focus on disease-tailored autophagy modulation strategies, precision medicine approaches, and long-term clinical studies to evaluate safety and efficacy. Ultimately, harnessing autophagy as a neuroprotective mechanism may provide a transformative step in the fight against debilitating neurodegenerative disorders.

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