

Dysregulated Crosstalk Between AMPK And PI3K-AKT Signaling In Alzheimer's Disease Drives Metabolic Neurodegeneration

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TAKE HOME MESSAGE

Targeting the metabolic convergence of AMPK and PI3K–AKT pathways offers a promising approach to restore neuronal homeostasis, enhance bioenergetics and slow or halt the progression of Alzheimer's disease

INTRODUCTION

- Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by cognitive decline, amyloid- β (A β) accumulation, tau hyperphosphorylation and synaptic loss. Metabolic dysfunction and impaired intracellular signaling are central drivers of neuronal dysfunction.
- AMPK is the master energy sensor that maintains cellular energy homeostasis, promotes autophagy and mitochondrial integrity.
- PI3K–AKT signaling regulates cell survival, growth and metabolism through mTOR activation.
- Emerging evidence suggests aberrant crosstalk between AMPK and PI3K–AKT pathways contributes to key pathological hallmarks of AD.

Study Objective

Evaluate AMPK–PI3K/AKT signaling crosstalk and metabolic dysregulation in Alzheimer's disease.

METHODS

Experimental Models

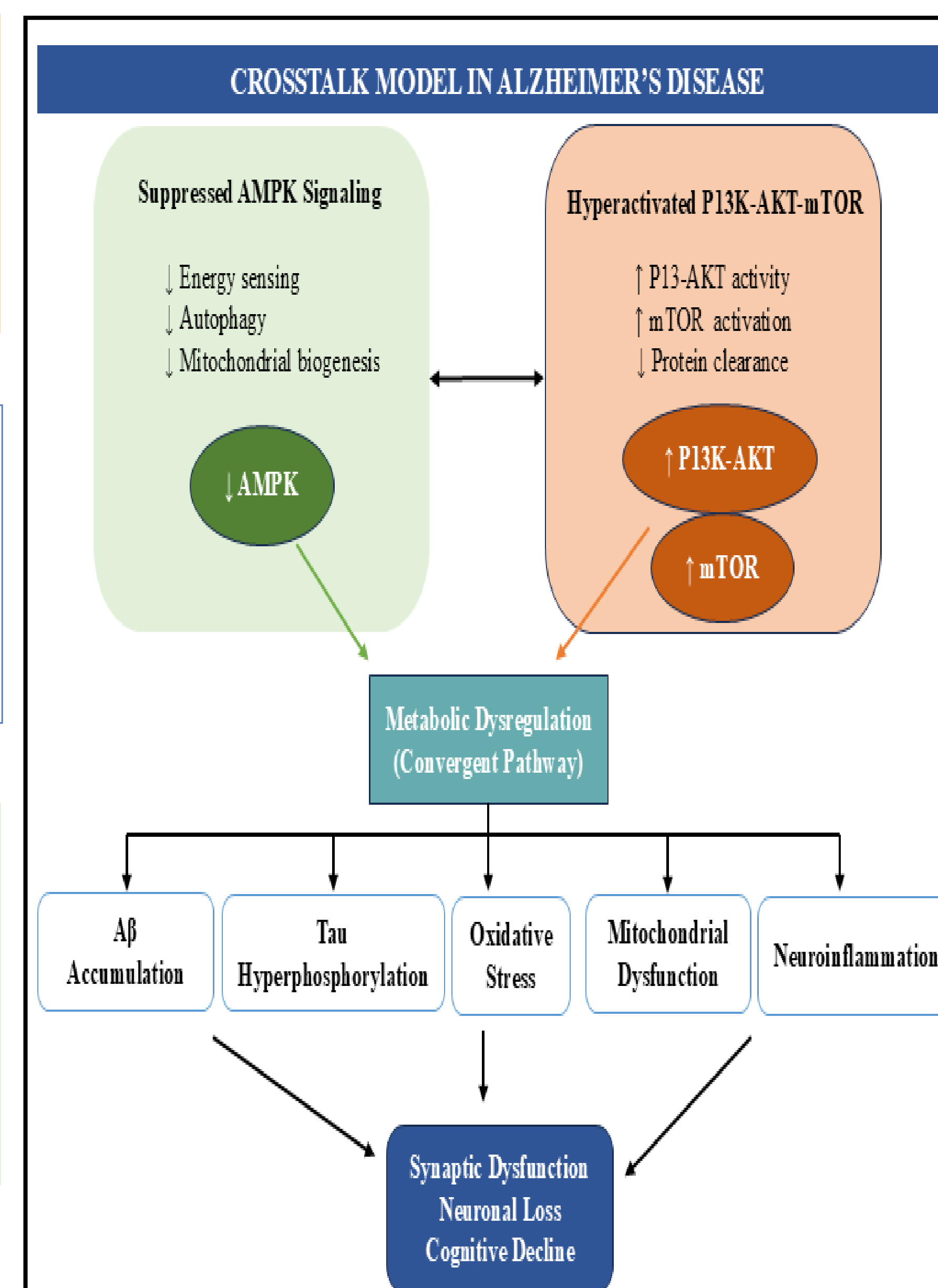
- In vitro neuronal cultures
- In vivo transgenic AD model

Molecular Techniques

- Western blotting
- Immunofluorescence
- Kinase activity assay

Data Analysis

Statistical and bioinformatic analyses were performed to identify signaling convergence and pathway interactions



RESULTS

- Reduced AMPK activity and enhanced PI3K–AKT signaling are consistently associated with Alzheimer's disease.
- An inverse regulatory relationship between these pathways contributes to metabolic imbalance and increased neuronal vulnerability.
- Dysregulated AMPK–PI3K/AKT crosstalk promotes oxidative stress, defective autophagy, and mitochondrial dysfunction and A β /Tau accumulation, leading to progressive neuronal loss.

CONCLUSION

Restoring the balance between AMPK and PI3K–AKT signaling represents a promising therapeutic strategy to re-establish neuronal homeostasis, enhance bioenergetic function, and slow or halt the progression of Alzheimer's disease.

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