Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that leads to cognitive decline, memory loss, and reduced daily functioning, with a rising global prevalence within aging populations. Current understanding of AD is limited to characterizing AD with amyloid-β accumulation, tau pathology, neuroinflammation, and synaptic dysfunction, with treatment options that are limited to addressing these issues. This study investigated the effects of Mg supplementation on the expression of AD-associated genes and compared the findings with publicly available human transcriptomic datasets.

RT-qPCR analysis revealed modest AD-associated increase in BACE1 and reduction in GSK3β, IL-1β, and BDNF expression relative to WT. The results were statistically not significant, but WTMg sim showed the most consistent normalization, particularly for BDNF and IL-1β. Cross-species comparison showed that BACE1 had the strongest directional concordance, whereas other genes revealed regional-dependent variations across different datasets. GSEA KEGG analyses consistently showed enrichment in processes related to mitochondrial dysfunction, oxidative phosphorylation abnormalities, ubiquitin-proteasome system disruption, axonal transport defects, and dysregulated Wnt signaling. BACE1 and GSK3β showed no substantial changes transcriptionally despite extensive dysregulation on upstream regulatory networks, suggesting potential dysregulation happen at protein level.

Findings suggest magnesium potential neuroprotective effects primarily take place within the upstream stress response regulation, rather than directly altering the transcription of BACE1, BDNF, GSK3β, and IL-1β. Comparative study between mice qPCR analysis and human datasets highlights magnesium potential influence within mitochondrial dysfunction, oxidative stress, and impaired cellular transport mechanisms.

Keywords: Alzheimer's disease, magnesium, amyloid processing, tau phosphorylation, neuroinflammation, synaptic dysfunction