論 文 要 旨

1,5-Anhydro-D-Fructose Protects against Rotenone-Induced Neuronal Damage In Vitro Through Mitochondrial Biogenesis

笠毛　友揮

Mitochondrial functional abnormalities or quantitative decreases are considered to be one of the most plausible pathogenic mechanisms of Parkinson's disease (PD). Thus, mitochondrial complex inhibitors are often used for the development of experimental PD.

In this study, we used rotenone to create in vitro cell models of PD, then used these models to investigate the effects of 1,5-anhydro-D-fructose (1,5-AF), a monosaccharide with protective effects against a range of cytotoxic substances. Subsequently, we investigated the possible mechanisms of these protective effects in PC12 cells.

The protection of 1,5-AF against rotenone-induced cytotoxicity was confirmed by increased cell viability and longer dendritic lengths in PC12 and primary neuronal cells. Furthermore, in rotenone treated PC12 cells, 1,5-AF upregulated peroxisome proliferator-activated receptor-γ coactivator 1α (PGC-1α) expression and enhanced its deacetylation, while increasing AMP-activated protein kinase (AMPK) phosphorylation. 1,5-AF treatment also increased mitochondrial activity in these cells. Moreover, PGC-1α silencing inhibited the cytoprotective and mitochondrial biogenic effects of 1,5-AF in PC12 cells.

Therefore, 1,5-AF may activate PGC-1α through AMPK activation, thus leading to mitochondrial biogenic and cytoprotective effects. Together, our results suggest that 1,5-AF has therapeutic potential for development as a treatment for PD.

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