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The role of N-acetylglucosaminyltransferase III in Alzheimer's disease progression

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The pathogenic mechanism of Alzheimer's disease (AD) has not been clearly defined, and many factors have been discovered to explain this multifactorial disorder. The alteration of glycoprotein glycans in AD has been highlighted recently. It has been reported that the bisecting N-acetylglucosamine (GlcNAc) levels were higher in the cerebrospinal fluid of most AD patients, which indicates that N-acetylglucosaminyltransferase III (GnT-III), a glycosyltransferase responsible for synthesizing a bisecting GlcNAc residue, may play an important role in the development of AD. In our previous studies, we demonstrated that the levels of GnT-III and bisecting GlcNAc were increased in AD models, and glucagon-like peptide-1 (GLP-1) receptor agonists could downregulate aberrant expression of GnT-III through the Akt/GSK-3β/β-catenin signaling pathway in neurons. Here, we further explored the role of GnT-III in AD progression. We overexpressed GnT-III in PC12 cells and found that the intracellular reactive oxygen species (ROS) was increased significantly in GnT-III overexpressing cells. The mitochondrial structure was damaged and the mitochondrial membrane potential ($\Delta\psi m$) tested by JC-1 probe was lower in GnT-III overexpressing cells, which indicated that the mitochondrial function might be damaged by aberrant GnT-III expression. Besides, we also tested the GLP-1 receptor signaling mediated by GLP-1 and found that overexpression of GnT-III disrupted the normal GLP-1 receptor signaling in neurons. In conclusion, our findings reveal that GnT-III could be a potential therapeutic target for AD.

Recent Publications

1. Wang Y, Chen S, Xu Z, Chen S T, Yao W B, et al. (2018) GLP-1 receptor agonists downregulate aberrant GnT-III expression in Alzheimer's disease models through the Akt/GSK-3β/β-catenin signaling. Neuropharmacology 131:190–199.
2. Chen S, Yin L, Xu Z, An F M, Liu A R, et al. (2016) Inhibiting receptor for advanced glycation end product (AGE) and oxidative stress involved in the protective effect mediated by glucagon-like peptide-1 receptor on AGE induced neuronal apoptosis. Neurosci Lett. 612:193–198.
3. An F M, Chen S, Xu Z, Yin L, Wang Y, et al. (2015) Glucagon-like peptide-1 regulates mitochondrial biogenesis and tau phosphorylation against advanced glycation end product-induced neuronal insult: Studies in vivo and in vitro. Neuroscience 300:75–84.

Biograpy

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