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Investigation of the Therapeutic Effect of O-GlcNAc Modification on Cognitive Impairment Associated with Excessive Dietary Salt Intake

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Summary

Phosphorylation of tau due to excessive salt intake leads to cognitive decline. Phosphorylated tau aggregates and accumulates in the brain, causing neurodegeneration. Antibody drugs are being developed to reduce phosphorylated tau by reducing tau protein itself. However, tau knockout mice show impairments in the reward system, feeding behavior abnormalities, age-dependent short-term memory impairment, hyperactivity, synaptic plasticity, and other disorders, so long-term tau inhibition may have side effects. In this study, we aimed to clarify whether cognitive function can be improved by controlling O-GlcNAc modification and suppressing excessive phosphorylation, rather than reducing tau itself, in response to cognitive decline caused by excessive salt intake.

In this experiment, the drug was administered intranasally through the nasal cavity to efficiently deliver the drug to the brain. O-GlcNAcylation of brain proteins by intranasal administration of Thiamet G tended to reduce phosphorylated tau in mice with high salt intake. Cognitive function evaluation using a novel object recognition test tended to suppress cognitive decline. In the future, it is necessary to increase the reliability of the results by adding more samples and evaluating other batteries such as the Morris water maze test.

In addition, the relationship between hypertension, for which salt intake is a risk factor, and Alzheimer's disease was analyzed using the National Alzheimer’s Coodinating Center (NACC) database. It is suggested that hypertension in old age may delay the age at which cognitive decline begins and suppress the pathological changes seen in Alzheimer's disease.