1. No.

FP01912186

2. Title

Reduction of NAA in the Brain of Alzheimer Disease Patients; the Relationship between their Onset and *Chrna7*

3. Period

2016-2020

4. Summary

The purpose of the study is to clarify the significance of the reduction of N-acetyl aspartate (NAA) in the hippocampus of Alzheimer's disease (AD) patients in its pathology. Shati, which was identified by our group, is a responsive enzyme to NAA biosynthesis. We analyzed the cognitive impact of the regulation of NAA synthesis using Shati-deficient mice (Shati-KO). Shati-KO exhibited cognitive decline in female, while hippocampal long-term potentiation (LTP) was observed in both gender of Shati-KO mice. Recovery of Shati gene expression in hippocampus of female Shati-KO mice improved cognitive function and synaptic LTP. In consistent, hippocampus-specific knockdown of Shati (Shati-cKD) impaired cognitive function and synaptic LTP. Interestingly, the expression of *Chrna7*, encoding nicotinic acetylcholine receptor a7, was reduced in female Shati-KO mice. Administration of donepezil, which was reported to increase *Chrna7*, recovered suppression of hippocampal LTP in female Shati-KO mice. Taken together, hippocampal NAA reduction observed in AD patients is suggested to contribute to the cognitive dysfunction mediated by the reduction of *Chrna7*.