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学位論文の題名	Reduction of glutamatergic activity through cholinergic dysfunction in the hippocampus of hippocampal cholinergic neurostimulating peptide precursor protein knockout mice （HCNP前駆体蛋白ノックアウトマウスの海馬ではコリン作動性神経機能障害を介してグルタミン酸作動性神経活動が低下している） Scientific Reports, 2022 Nov 10;12(1):19161
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Abstract

Cholinergic activation can enhance glutamatergic activity in the hippocampus under pathologic conditions, such as Alzheimer's disease (Sato T, et al. Cell Transplant. 2017). The aim of the present study was to elucidate the relationship between glutamatergic neural functional decline and cholinergic neural dysfunction in the hippocampus. We report the importance of hippocampal cholinergic neurostimulating peptide (HCNP) in inducing acetylcholine synthesis in the medial septal nucleus. Here, we demonstrate that HCNP-precursor protein (pp) knockout (KO) mice electrophysiologically presented with glutamatergic dysfunction in the hippocampus with age. The impairment of cholinergic function via a decrease in vesicular acetylcholine transporter in the pre-synapse with reactive upregulation of the muscarinic M1 receptor may be partly involved in glutamatergic dysfunction in the hippocampus of HCNP-pp KO mice. The results, in combination with our previous reports that show the reduction of hippocampal theta power through a decrease of a region-specifc choline acetyltransferase in the stratum oriens of CA1 and the decrease of acetylcholine concentration in the hippocampus, may indicate the defned cholinergic dysfunction in HCNP-pp KO mice (Madokoro Y, et al. Int J Mol Sci. 2019, Kondo-Takuma Y, et al. Sci Rep. 2021). This may also support that HCNP-pp KO mice are appropriate genetic models for cholinergic functional impairment in septo-hippocampal interactions. Therefore, according to the cholinergic hypothesis, the model mice might are potential partial pathological animal models for Alzheimer's disease.