Brain hypothyroidism leads to immune tolerance of microglia in Alzheimer's disease

Genomic Medicine Institute, Medical Research Center

Seoul National University

Hyunjung Choi

Abstract

Hypothyroidism is one of the most common cause of dementia with cognitive decline. It is also widely known that the imbalance of thyroid hormones in the blood could be a risk factor for the onset of Alzheimer's disease (AD). However, the precise causal relationship between thyroid hormones and AD pathophysiology is still elusive. In this study, using a ADLP^{APT} transgenic mice showing both brain amyloidosis and severe tauopathy along with memory deficits, we investigated the etiology of hypothyroidism in AD and the role of thyroid hormone in the pathogenesis. ADLP^{APT} mice showed a localized hypothyroidism in the hippocampus, which precedes the changes in thyroid hormones in the blood and is attributed to neurological pathology in ADLP^{APT} mice. It could be a new phenotype related to thyroid hormones that characterizes AD. In particular, the hypothyroidism due to a decreased expression in the enzyme involved in T4 metabolism provided evidence that T3 may be effective as a thyroid hormone therapy (thyromimetics) to relieve AD pathologies. Furthermore, we uncovered a novel mechanism by which immune tolerance of microglia, corresponding to the deficiency of T3 in the hippocampus, could be detrimental to AD pathogenesis. Thus, supplementing the T3 concentration may have positive effects on AD treatment by restoring the function of microglia.