Analysis of astrocyte and microglia in Alzheimer's disease model mouse with higher uric acid level

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Several epidemiological studies suggest that uric acid exerts a neuroprotective effect in neurodegenerative disease such as Parkinson's disease and Alzheimer's disease (AD). However, the molecular mechanism how uric acid affect the pathology and/or cognitive function in Alzheimer's disease remains unclear. In this study, we developed a combined mouse model by cross-breeding App^{NL-G-F} knock-in mouse (App-KI) which carries humanized amyloid β protein (Aβ) sequence with familiar AD-associated mutations, and uricase knockout mouse (Uox-KO) which shows increased level of uric acid. To prevent renal failure caused by elevated uricnary excretion of uric acid, App-KI-Uox-KO mice were treated with allopurinol by dietary administration. We performed immunohistochemical staining for Aβ with anti-Aβ, astrocytes with anti-GFAP, and micloglia with anti-Iba1 using brain sections from 8 month-old mice. Aβ accumulation was increased in App-KI-UOX-KO mice in comparison with App-KI mouse. However, App-KI-Uox-KO mice displayed reduced astrocytosis and microgliosis in the cortex. Further studies are required to determine whether the glial changes are the cause or consequence of increased Aβ accumulation under higher uric acid level.