A neuroprotective role of aquaporin-4 against other than amyloid β deposition or neuroinflammation in the 5xFAD transgenic mice model.

Yoichiro Abe[1], Natsumi Ikegawa[2], Minetaka Murakami[2], Takumi Tanaka[2], Takako Niikura[2], Kyosuke Muramatsu[3], Kaoru Yamada[3], Tadafumo Hashimoto[3], Motohito Goto[4], Taichi Yamamoto[4], Kenji Kawai[4], Wakami Goda[1], Keitaro Yoshida[5], Satoko Hattori[6], Tsuyoshi Miyakawa[6], Kenji Tanaka[5], Masaru Mimura[5], Takeshi Iwatsubo[3], Jun-Ichi Hata[4], Masato Yasui[1]

[1]Dept. Pharmacol., Keio Univ. Sch. Med., [2]Dept. Information and Communication Sci., Sophia Univ., [3]Dept. Neuropathol., Grad. Sch. Med., Univ. of Tokyo, [4]CIEA, [5]Dept. Neuropsychiatry, Keio. Univ. Sch. Med., [6]Div. Syst. Med.; Sci., Inst. Comp. Med. Sci., Fujita Health Univ,

Aquaporin-4 (AQP4) is the most abundant water channel in the CNS specifically expressed in the astrocytic end-feet around blood vessels and is thought to contribute to water and ion homeostasis in the brain. AQP4 has been suggested to be involved in the pathogenesis of neurodegenerative diseases including Alzheimer's disease (AD), which may be due to the modulation of neuroinflammation or the impairment of interstitial fluid bulk flow system in the central nervous system. In this study, to investigate the implication of AQP4 in AD pathology, we crossed an AD model, 5xFAD with AQP4 knockout mice. We demonstrate that deleting AQP4 from 5xFAD resulted in acceleration of behavioral abnormality, namely an age-dependent reduction of nighttime activity, associated with aggravation of epileptiform neuronal activity as well as convulsions. Importantly, these symptoms occurred independently of accumulation of amyloid plaques or neuroinflammatory responses of glial cells, since in this model, AQP4 deficiency did not affect age-dependent increase in amyloid deposition in parenchyma or neuroinflammation. Our results provide an important perspective for developing new diagnostic methods and treatments for Alzheimer's disease.