Abstract

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Marginal vitamin A deficiency facilitates Alzheimer's pathogenesis.

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BACKGROUND AND OBJECTIVE: Deposition of amyloid β protein (Aβ) to form neuritic plaques in the brain is the unique pathological hallmark of Alzheimer's disease (AD). Aβ is derived from amyloid β precursor protein (APP) by β- and γ-secretase cleavages and turned over by glia in the central nervous system (CNS). Vitamin A deficiency (VAD) has been shown to affect cognitive functions. Marginal vitamin A deficiency (MVAD) is a serious and widespread public health problem among pregnant women and children in developing countries. However, the role of MVAD in the pathogenesis of AD remains elusive.

METHODS AND FINDINGS: Our study showed that MVAD is approximately twofold more prevalent than VAD in the elderly, and increased cognitive decline is positively correlated with lower VA levels. We found that MVAD, mostly prenatal MVAD, promotes beta-site APP cleaving enzyme 1 (BACE1)-mediated Aβ production and neuritic plaque formation, and significantly exacerbates memory deficits in AD model mice. Supplementing a therapeutic dose of VA rescued the MVAD-induced memory deficits.

CONCLUSION: Taken together, our study demonstrates that MVAD facilitates AD pathogenesis and VA supplementation improves cognitive deficits. These results suggest that VA supplementation might be a potential approach for AD prevention and treatment.

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