Betaine attenuates Alzheimer-like pathological changes and memory deficits induced by homocysteine.


Abstract

Hyperhomocysteinemia (Hhcy) may induce memory deficits with β-amyloid (Aβ) accumulation and tau hyperphosphorylation. Simultaneous supplement of folate and vitamin B12 partially restored the plasma homocysteine level and attenuated tau hyperphosphorylation, Aβ accumulation and memory impairments induced by Hhcy. However, folate and vitamin B12 treatment have no effects on Hhcy which has the methylenetetrahydrofolate reductase genotype mutation. In this study, we investigated the effects of simultaneous supplement of betaine on Alzheimer-like pathological changes and memory deficits in hyperhomocysteinemic rats after a 2-week induction by vena caudalis injection of homocysteine (Hcy). We found that supplementation of betaine could ameliorate the Hcy-induced memory deficits, enhance long-term potentiation (LTP) and increase dendritic branches numbers and the density of the dendritic spines, with up-regulation of NR1, NR2A, synaptotagmin, synaptophysin, and phosphorylated synapsin I protein levels. Supplementation of betaine also attenuated the Hcy-induced tau hyperphosphorylation at multiple AD-related sites through activation protein phosphatase-2A (PP2A) with decreased inhibitory demethylated PP2A(C) at Leu309 and phosphorylated PP2A(C) at Tyr307. In addition, supplementation of betaine also decreased Aβ production with decreased presenilin-1 protein levels. Our data suggest that betaine could be a promising candidate for arresting Hcy-induced AD-like pathological changes and memory deficits.

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