

Cerebroprotein Hydrolysate Can Activate the Nrf2/ARE Signaling Pathway, Improve the Cognitive Function Deficits of Rats with Vascular Dementia, and Alleviate the Autophagic Response

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Abstract

Vascular dementia (VD) is a common neurodegenerative disease that severely affects the quality of life of patients. Current treatments are limited and have unsatisfactory effects. Cerebroprotein hydrolysate (CH) have potential neuroprotective effects, however, the mechanism by which they improve cognitive function in VD model rats is unclear. In this study, the cognitive function of VD model rats treated with different CH concentrations was detected using the Morris water maze and novel object recognition methods. The autophagy status of hippocampal neurons was observed by transmission electron microscopy, and hippocampal expression of autophagy markers was determined by immunohistochemistry and western blotting. The effects were further verified by adding the nuclear factor erythroid 2-related factor 2/antioxidant response element (Nrf2/ARE) pathway inhibitor brusatol. Compared with that of sham-operated rats, the cognitive function of rats treated with normal saline was significantly reduced. However, the learning and memory abilities of the CH-treated rats improved, indicating enhanced cognitive function. CH treatment optimized the cellular state and reduced autophagy damage. Ubiquitin expression increased in the hippocampal neurons of VD model rats, and CH treatment alleviated this change. Furthermore, CH partially reversed the enhanced autophagic activity in the hippocampus of VD model rats. In a cellular oxygen–glucose deprivation model of VD, CH treatment increased Nrf2/ARE signaling pathway activity and reduced autophagic activity, and brusatol addition reversed this effect. CH application in VD may effectively alleviate cognitive decline and reduce autophagy in hippocampal neurons. This effect may be related to enhanced Nrf2/ARE signaling pathway activity.

Keywords

Cerebroprotein Hydrolysate, Autophagy, Vascular Dementia, Cognitive Dysfunction