Inhibition of PKA attenuates memory deficits induced by β-amyloid (١-٤٢), and decreases oxidative stress and NF-κB transcription factors.

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Source

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Abstract

Alzheimer's disease (AD), the most relevant cause of dementia in elderly, is characterized by amyloid β (Aβ) containing plaques and neurofibrillatory tangles, synaptic and neuronal loss, along with progressive cognitive impairment in short-term memory. However, mechanistic links between protein kinase A (PKA), oxidative stress and memory loss in response to Aβ remain elusive. In the present study, we examined the effects of post-training bilateral intra-hippocampal infusions of the specific protein kinase AII inhibitor, H-٨٩, on memory deficits induced by Aβ (١-٤٢) in Aβ-pretreated rats. H-٨٩ and Aβ were administered immediately after completion of training. All animals were trained for ٤ consecutive days and tested ٩ and ١٩ days after the infusions. Significant differences were observed in the time and distance of finding the hidden platform in Aβ treated animals after ١٩ days. Interestingly, intra-hippocampal infusion of H-٨٩ (٥μM/side) significantly prevented the Aβ-induced memory impairment. Furthermore, evaluation of NFκB (nuclear factor-κB), and antioxidant enzymes, such as γ-GCS (glutamylcysteine synthetase), HO-١ (hemeoxygenase-١), GSH (glutathione), and SOD (superoxide dismutase) confirmed the protective effect of H-٨٩. Given the possible neuroprotective effects of H-٨٩ on Aβ-induced memory impairment, our results may open a new avenue for the prevention of AD by PKAII signaling pathway inhibitor.