Hyperforin prevents beta-amyloid neurotoxicity and spatial memory impairments by disaggregation of Alzheimer's amyloid-beta-deposits

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Abstract

The major protein constituent of amyloid deposits in Alzheimer's disease (AD) is the amyloid beta-peptide (Abeta). In the present work, we have determined the effect of hyperforin an acylphloroglucinol compound isolated from Hypericum perforatum (St John's Wort), on Abeta-induced spatial memory impairments and on Abeta neurotoxicity. We report here that hyperforin: (1) decreases amyloid deposit formation in rats injected with amyloid fibrils in the hippocampus; (2) decreases the neuropathological changes and behavioral impairments in a rat model of amyloidosis; (3) prevents Abeta-induced neurotoxicity in hippocampal neurons both from amyloid fibrils and Abeta oligomers, avoiding the increase in reactive oxidative species associated with amyloid toxicity. Both effects could be explained by the capacity of hyperforin to disaggregate amyloid deposits in a dose and time-dependent manner and to decrease Abeta aggregation and amyloid formation. Altogether these evidences suggest that hyperforin may be useful to decrease amyloid burden and toxicity in AD patients, and may be a putative therapeutic agent to fight the disease.