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Theme: F: Nervous System Disorders

Roles of endothelin-1 in beta-amyloid-induced neurotoxicity in hippocampus: An implication for Alzheimer's pathology.

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Alzheimer's disease (AD) is an incurable neurodegenerative disorder. Abnormal levels of endothelin-1 (ET-1) have been demonstrated in parietal white matter(1), cerebral cortex and vessels of the AD brain(2). Neuronal death and accumulation of beta-amyloid (Aβ) are prominent pathological features of AD. Significant neuronal death is found in Aβ-treated primary neurons and Aβ-overexpressing mouse models(3,4). ET-1 is a known vasoconstrictor and neuro-active peptide. ET-1 induces apoptosis in primary retinal neurons(5). In contrary, ET-receptor (ETR) type B agonist can rescue neurons from Aβ-induced apoptosis(6). These findings suggest ET-1 plays dual roles in neurodegeneration and neuroprotection, respectively. This study aims to investigate the effect of ET-1 on Aβ-induced cell death in hippocampal neurons.

Primary hippocampal neurons were pretreated with or without ETR antagonists prior to the treatment of oligomeric form of Aβ1-42, ET-1 or both on 14 DIV. Cell viability was measured by MTT assay. Changes in protein expression in apoptotic and ET-1 signaling pathways were assessed by western-blot analysis. This study shed light on the roles of ET-1 in Aβ1-42-neurotoxicity, building upon which the ET-1 signaling pathway as a potential therapeutic target for AD can be further investigated.

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