Astrocytic nitric oxide triggers tau hyperphosphorylation in hippocampal neurons

Saez, Estefanía T.

Pehar, Mariana

Vargas, Marcelo

Barbeito, Luis

Maccioni, Ricardo B.

Production of nitric oxide (NO) by glial cells has been proposed to mediate cytotoxic effects on neighboring neurons. Although extensive genetic data implicate the beta amyloid peptide (A?) in the neurodegenerative cascade of Alzheimer's disease (AD), the molecular mechanisms underlying its effects on neurons and glia and the relationship between glial activation and neuronal death are not well understood. In AD, A? is sufficient to induce glial activation and promote the generation of inflammatory mediators including NO. We examined whether A? stimulated astrocytes to express nitric oxide synthase and produce NO. Also, we investigated whether astrocytic NO contributes to degenerative changes occurring in co-cocultured hippocampal neurons. We found that the treatment of rat hippocampal astrocyte cultures with A?(25-35) fragment upregulated the mRNA and protein levels of both the inducible and neuronal forms of nitric oxide synthase (iNOS and nNOS, respectively) and increased the produc