Differential Effects of Palmitoylethanolamide Against Amyloid-β Induced Toxicity in Cortical Neuronal and Astrocytic Primary Cultures from Wild-Type and 3xTg-AD Mice

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Considering the heterogeneity of pathological changes occurring in Alzheimer's disease (AD), a therapeutic approach aimed both to neuroprotection and to neuroinflammation reduction may prove effective. Palmitoylethanolamide (PEA) has attracted attention for its anti-inflammatory/neuroprotective properties observed in AD animal models. In the present study, we evaluated the protective role of PEA against amyloid-β_{42} ($A\beta_{42}$) toxicity on cell viability and glutamatergic transmission in primary cultures of cerebral cortex neurons and astrocytes from the triple-transgenic murine model of AD (3xTg-AD) and their wild-type littermates (non-Tg) mice. Furthermore , an astrocyte-neuron coculture model has been used to determine whether the exposure of astrocytes to $A\beta_{42}$ could influence the viability of neurons.
$A\beta_{42}$ (0.5 μM; 24 hours) affects the cell viability in cultured cortical neurons and astrocytes from non-Tg mice, but not in those from 3xTg-AD mice. These effects were counteracted by the pretreatment with PEA (0.1 μM). Basal glutamate levels in cultured neurons and astrocytes from 3xTg-AD mice were lower than those observed in cultured cells from non-Tg mice. $A\beta_{42}$-exposure reduced and increased glutamate levels in non-Tg mouse cortical neurons and astrocytes, respectively. These effects were counteracted by the pretreatment with PEA. By itself, PEA did not affect cell viability and glutamate levels in cultured cortical neuron and astrocytes from non-Tg or 3xTg-AD mice. In astrocyte-neuron cocultures obtained from non-Tg mice, the presence of astrocytes pre-exposed to $A\beta_{42}$ (0.5 μM; 24 hours) significantly reduced the neuronal viability. This effect was counteracted by the pretreatment with PEA (0.1 μM).
The exposure to $A\beta_{42}$ induced toxic effects on cultured cortical neurons and astrocytes from non-Tg mice, but not in those from 3xTg-AD mice. Furthermore, PEA exerts differential effects against $A\beta_{42}$-induced toxicity in primary cultures of cortical neurons and astrocytes from non-Tg and 3xTg-AD mice. In particular, PEA displays protective properties in non-Tg but not in 3xTg-AD mouse neuronal cultured cells overexpressing Aβ.