EFFECT OF PALMYTOILETHANOLAMIDE IN 3XTG-AD ASTROCYTES AS AN IN VITRO MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a neurodegenerative disorder whose main features are β-amyloid (Aβ) plaques and neurofibrillary tangles, both responsible for neuronal loss and synapses reduction (DeKosky et al., 1996; Blennow et al., 2006). Recent studies have shifted their focus on another prominent hallmark, characteristic of AD patients, named “reactive gliosis”. Such a phenomenon is sustained by glia (and in particular by astrocytes) and characterized by a marked inflammatory response (Abramov et al., 2004; Heneka et al., 2010). Indeed, these morpho-functional changes can be observed studying cytoskeletal protein responsible for astrocytes functionality such as the glial fibrillary acidic (GFAP) (Verkhratsky and Butt, 2007), astrocyte-derived neurotrophins like S100β (Steiner et al., 2011), or pro-inflammatory mediators, like the cyclooxygenase-2 (COX-2) and the inducible nitric oxide synthase (iNOS) (Koistinaho et al., 2011).

Among the models able to reproduce AD pathology, the 3×Tg-AD one, at present, is considered the most useful since it develops both senile plaques and neurofibrillary tangles (Oddo et al., 2003). Here, we used primary astrocytes obtained from 3xTg-AD and Non-Tg mice to study the effect of palmitoylethanolamide (PEA), an endogenous lipid compound, produced by central nervous system, mainly by glial cells. In the recent past, it has been demonstrated that PEA displays promising pharmacological properties (Calignano et al., 2001; Franklin et al., 2003; Skaper et al., 2014; Scuderi et al., 2012). Among these, the anti-inflammatory and neuroprotective actions, together with the extreme safety in humans (Petrosino and Di Marzo, 2016), seem to indicate it as a promising therapeutic strategy against AD.

Results shown that primary 3×Tg-AD astrocytes are more reactive and produce higher levels of pro-inflammatory markers in comparison with cells deriving from Non-Tg animals. PEA resulted effective in modulating astrocytes reactivity, bringing all hallmarks to physiological values. Our results also confirmed the anti-inflammatory properties of PEA, since its ability to significantly reduce iNOS expression. The positive effects of PEA did not affect cell viability at all concentrations tested.

Our interesting results prompt us to carry on further experiments to demonstrate that this molecule can actually represent a concrete therapeutic tool against AD.

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