Fatty acid acyl ethanolamines and PPAR-alpha in neurodegenerative and neurological diseases. Cellular models of neurodegeneration: preliminary data

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Palmitoylethanolamide (PEA) is the amide between palmitic acid and ethanolamine. It belongs to the family of the fatty acid acyl ethanolamines (FAEs) and, when used as a drug, it displays anti-inflammatory and analgesic pharmacological properties by activating peroxisome proliferator-activated receptor-α (PPAR-α; Fu et al., 2003; Lo Verme et al., 2005).
Although PEA is present in the brain with its putative receptor PPAR-α, little evidence exists about its neuroprotective potential (Skaper et al., 1996; Cimini et al., 2009). We have tested the neuroprotective potential of PEA in different cellular models of neuronal damage and degeneration, by using the SHSY5Y neuroblastoma cell line (Xie et al, 2010). These cells posses many biochemical and functional properties of neurons. SHSY5Y express functional neuronal enzymes such as tyrosine and dopamine-β-hydroxylases, α3, α5, α7, β2, β4 subunits of cholinergic receptor and dopamine transporter (DAT).
By means of molecular biology and immunocytochemical analysis we verified the expression and functionality of PPAR-α receptor at different stages of cell differentiation. We then exposed SHSY5Y to a number of cellular stressors, such as 6-hydroxydopamine (6-OHDA), rotenone, hydrogen peroxide (H_2O_2), 3-hydroxykynurenine (3-HK), N-methyl-D-aspartic acid (NMDA). Cell death was evaluated using MTT (3-[4, 5-dimethylthiazol-2-yl]-2, 5-diphenyltetrazolium bromide) and automated trypan blue exclusion assays.
We have found that PEA is particularly effective in reducing neuronal cell death induced by 6-OHDA. This effect is mediated by PPAR-α receptor and mimicked by a synthetic PPAR-α agonist, GW7647. The neuroprotective effect of PPAR-α agonists was fully retained in SHSY5Y cells differentiated toward a dopaminergic phenotype by retinoic acid incubation. Moreover PPAR-α activation protected neuroblastoma cells from neuronal damage induced by tunicamycin (TM), an endoplasmic reticulum (ER) stressor. Since ER stress commonly causes neuronal damage in a lot of neurodegenerative diseases (Forloni et al, 2002), this gives a further indication for the neuroprotective potential of this nuclear receptor.

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