EFFECT OF ULTRAMICRONIZED-PALMYTOILETHANOLAMIDE ON ASTROCYTE DYSFUNCTION IN A TRIPLE TRANSGENIC MODEL OF ALZHEIMER'S DISEASE

1)Facchinetti R.. 2)Bronzuoli MR. 3)Letizia A.. 4)Cassano T.. 5)Steardo L.. 6)Scuderi C..

Department of Physiology and Pharmacology "V. Erspamer"

Alzheimer's disease (AD) is one of the most economically burdensome health conditions in current society that leads patients to functional disabilities. The main features of the disease are β-amyloid plaques (SPs) and neurofibrillary tangles (NFTs) creation which causes neuronal and synaptic loss (Braak et al., 1988; Merz et al., 1983). During last decades, also astrocyte dysfunction and the presence of an intense inflammatory state have been considered further hallmarks of AD. Indeed, abnormally activated microglia and dysfunctional astrocytes are closely associated with amyloid deposits in brain parenchyma (Akiyama et al., 2000). According to these events, it is reasonable to assume that a combination of neuroprotective and anti-inflammatory treatments may represent an appropriate approach to tackle AD. In this context, the endogenous lipid mediator palmitoylethanolamide (PEA), abundant in the central nervous system and produced also by glial cells, seems to fulfill the criteria of a multi-factorial approach. The aim of this work was to investigate the effect of a chronic treatment with ultramicronized (um)-PEA (subcutaneously administered by a depot delivery system) in 6-month-old 3xTg-AD mice. In particular, we investigated the effect of um-PEA on glial dysfunction and neuroinflammation during the mild stage of AD pathology. We studied both glial fibrillary acidic protein (GFAP) and S100B as markers for astrocyte functioning, and cyclooxygenase (COX)-2, inducible nitric oxide synthase (iNOS), NF-kB transcriptional factor, and the main proinflammatory cytokines to explore the inflammatory state. Results revealed a mild astrocyte dysfunction in the 3xTg-AD mice when compared with their Non-Tg littermates. Such a dysfunction was rescued by um-PEA chronic treatment. Moreover, we found that 6-month-old 3xTg-AD mice are characterized by an intense pro-inflammatory state. Um-PEA chronic treatment was able to normalize these alterations. By virtue of its high tolerability and safety (Petrosino et al., 2016), also demonstrated in humans, in their entirety, these results suggest um-PEA as a valid tool in the therapeutic strategy against AD.

Braak et al. (1988). Neuropathol Appl Neurobiol. 14: 39–44.

Merz et al. (1983). Acta Neuropathol. 60: 113–24.

Akiyama et al. (2000). Neurobiol Aging 21(3): 383–421.

Petrosino et al. (2016) Br J Pharmacol. 173(7):1154-62.