POSTERS

PROTECTIVE ROLE FOR OLEOYLETHANOLAMIDE IN THE HUMAN BRAIN: EFFECTS ON THE MODULATION OF NEUROINFLAMMATION AND INSULIN RESISTANCE IN HUMAN ASTROCYTES

Lucia Sileo[1], Giulia Scanavino[1], Silvana Gaetani[2], Ada MariaTata[1]

[1]Dept. of Biology and Biotechnologies "Charles Darwin", University of Rome "Sapienza", Rome, Italy; [2]Dept. of Physiology and Pharmacology "Vittorio Erspamer", University of Rome "Sapienza", Rome, Italy

Neuroinflammation and insulin resistance are key processes often responsible for neurodegenerative diseases (i.e. Alzheimer's disease) or dementia onset in the elderly. In the present study, normal human astrocytes were used as an in vitro model due to their central role in CNS homeostasis. It is well established that pro-inflammatory stimuli, such as lipopolysaccharide (LPS) and interleukin-1β (IL-1β), induce neuro-inflammation, triggering reactive astrogliosis. In parallel, chronic exposure to insulin in the brain disrupts critical signalling pathways INS-associated, promoting a state of metabolic dysregulation and increasing cellular vulnerability. We have reproduced these experimental conditions in vitro in order to investigate astrocyte responses to inflammatory and metabolic diseases. Based on this rationale, we studied Oleoylethanolamide (OEA), an endogenous lipid mediator and PPARα agonist, whose role in the human brain is still unclear. OEA is known for its anti-inflammatory and insulin-sensitizing effects. The present study aimed to evaluate how OEA modulates astrocyte responses to inflammatory and insulin-related stimuli. Our findings revealed that OEA treatment significantly reduced the expression of pro-inflammatory cytokines (IL-6, TNF-α) and the levels of reactive oxygen species (ROS), while improving insulin sensitivity by enhancing phosphorylation of AKT (Thr308) downstream of the IRS-1 receptor. Moreover, OEA treatment promoted lysosomal biogenesis, as indicated by the upregulation of the lysosomal membrane protein LAMP1, and consequently reduced lipid droplet accumulation, suggesting an improvement in astrocyte lipid metabolism linked to increased lysosomal function. Collectively, these results confirm the potential neuroprotective and anti-inflammatory role of OEA and suggest that a deeper understanding of these mechanisms may open new therapeutic perspectives for preventing the onset of neurodegenerative diseases associated with metabolic and inflammatory dysfunctions.