NOOTROPIC EFFECTS OF ALPHA-GLYCERYL-PHOSPHORYL-ETHANOLAMINE IN HUMAN HIPPOCAMPAL CELLS

Giorgina Mangano[1], Simona Daniele[2], Lucia Durando[1], Claudia Martini[2]

[1]Angelini RR&D (Research, Regulatory & Development) - Angelini S.p.A., S. Palomba-Pomezia (Rome) - Italy, [2]Dept. of Pharmacy, University of Pisa, Pisa - Italy

Brain aging involves changes in the lipid membrane composition that lead to a decrease in membrane excitability and neurotransmitter release. These membrane modifications have been identified as contributing factors in age-related memory decline. In this sense, precursors of phospholipids (PLs) can restore the physiological composition of cellular membranes and produce valuable therapeutic effects in brain ageing. Among drugs showing nootropic properties, alpha-glyceryl-phosphoryl-ethanolamine (GPE) has demonstrated protective effects in amyloid-injured astrocytes and in an aging model of human neural stem cells. However, the compound properties on mature neuronal cells remain unexplored.

Herein, GPE was tested in human adult hippocampal neurons, which are involved in cognition, learning and memory and are characterised by a functional cholinergic transmission, thus representing a valuable cellular model to explore the neurotrophic properties of GPE.

Adult human hippocampal neurons were assayed in basal conditions for release of membrane precursors and neurotransmitters (phosphatidylcholine (PC), phosphatidylethanolamine (PE) and acetylcholine (Ach)), and for some markers of well-being of neuronal cell (lipid peroxidation, membrane fluidity and autophagy) by fluorometric methods and western blot analysis. Moreover, DNA damage and neuronal viability were assayed in a neuronal physiological aging model by cytofluorimetric and MTS viability assay respectively. GPE treatments were performed at 5, 50 and 500 μM.

GPE was proved to induce dose-dependently the release of the neurotransmitter acetylcholine and, when tested at 500 μM it doubled levels of the main membrane phospholipids. Moreover, the compound reduced lipid peroxidation and enhanced membrane fluidity of human brain cells. GPE protected in vitro aged neurons against DNA damage and viability decrease in a dose-dependent manner. Among GPE treatment effects, the induction of autophagy was demonstrated.

Overall, these results confirm the beneficial effects of GPE treatment and suggest the compound as a promising agent to preserve hippocampal neurons and virtually memory performances.