

Abstract 3289

Intranasal Delivery of Galanin 2 and Neuropeptide Y1 Agonists Enhanced Spatial Memory Performance and antidepressant effects through Neuronal Precursor Cells Proliferation in the hippocampus

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Abstract Body

Neuropeptide Y(NPY) Y1 receptor (Y1R) and galanin (GAL) receptor 2 (GALR2) interact in brain regions responsible for learning and memory processes, emphasizing the hippocampus. The current study assesses the sustained memory performance and antidepressive-like effects induced by GALR2 and NPYY1R agonists intranasal coadministration and their neurochemical hippocampal correlates. Object-in-place task and forced swimming test were conducted together with in situ proximity ligation assay (PLA) to manifest the formation of GALR2/Y1R heteroreceptor complexes. We evaluated cell proliferation through a 5-Bromo-2'-deoxyuridine (BrdU) expression study within the hippocampus. The GalR2 agonist M1145 was demonstrated to act with the Y1R agonist to improve memory retrieval and antidepressive-like actions at 24 hours in both tasks, enhancing the cell proliferation in the DG of the hippocampus through BrdU expression and the GALR2/Y1R heteroreceptor complexes upon agonist coactivation. Our results may provide the basis for developing heterobivalent agonist pharmacophores targeting GALR2-Y1R heterocomplexes. It involves especially the neuronal precursor cells of the dentate gyrus in the hippocampus for the novel treatment of Alzheimer's disease or depression. The work was supported by the UMA18-FEDERJA-100 and Proyecto Jovenes Investigadores (B1-2019_04) and Proyecto Puente (B4-2021) UMA , Spain to MN. Special mention to Grupo Vithas.

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