

Galanin and Neuropeptide Y Interaction Enhances Proliferation of Granule Precursor Cells and Expression of Neuroprotective Factors in the Rat Hippocampus: Role in depression and memory

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Neuropeptide Y(NPY) Y1 receptor (Y1R) and galanin (GAL) receptor 2 (GALR2) interact in brain regions responsible for mood control and 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 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) and PCNA expression study within the hippocampus. The GalR2 agonist M1145 and GAL were 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 and PCNA expression and the GALR2/Y1R heteroreceptor complexes upon agonist coactivation. Our results may provide the basis for developing heterobivalent agonist pharmacophores targeting Y1R-GALR2 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.

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