

Galanin and neuropeptide Y interactions linked to neuronal precursor cells of the dentate gyrus in the hippocampus. Role in depression and cognitive impairment.

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Galanin (GAL) interacts with Neuropeptide Y Y1 receptors (NPYY1R) in several regions of the central nervous system associated with mood and motivation, through GAL receptor 2 and NPYY1 receptor 1 (GALR2/NPYY1R) heterodimers. The current work is to evaluate GALR2 and NPYY1R interactions concerning newborn cell proliferation in the ventral and dorsal hippocampal Dentate Gyrus.

Rats (n = 6-8 per group) were randomly assigned to the groups. Each group received i.c.v. injections of artificial Cerebro Spinal Fluid (aCSF), GAL or NPYY1R agonist [Leu31,Pro34]NPY alone or in combination and 24 h later rats were subjected to a 5-min swimming session (test). A different set of rats received ip injections of BrdU 50mg/Kg at 2 and 4 hours after icv injections. 24 hours later brains collected for immunostaining to evaluate cell proliferation.

We observed that the icv injection of GAL and NPYY1R agonist significantly enhanced the decrease in the immobility and the increase in the swimming behavior compared with the NPYY1R agonist alone. Furthermore, GALR2 is involved in this GALR/NPYY1R interaction, since the presence of the GALR2 antagonist M871 counteracted all the parameters. In parallel, coadministration of GAL and NPYY1R agonist increased BrdU-labeled cells located in the SGZ compared with aCSF, GAL and the NPYY1R group. Similar results were observed in dorsal hippocampus.

Our results may provide the basis for the development of heterobivalent agonist pharmacophores, targeting GALR2/NPYY1R heteromers, especially in the neuronal precursor cells of the dentate gyrus in the hippocampus for the novel treatment of depression or cognitive impairments. Study supported by Proyecto UMA18- FEDERJA-100, Proyecto Puente-Universidad de Málaga, proyecto jóvenes investigadores UMA to MNP.