ROLE OF 5-HT1A RECEPTORS IN THE EFFECT OF GALANIN(1-15) ON FLUOXETINE-MEDIATED ACTION IN THE FORCED SWIMMING TEST

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Galanin N-terminal fragment (1-15) [GAL(1-15)] modulates the antidepressant effects induced by the 5-HT1A receptor (5-HT1AR) agonist in the forced swimming test (FST) and the binding characteristics and mRNA levels of 5-HT1AR in the dorsal hippocampus and dorsal raphe (DR).

Recently, we observed that GAL(1-15) enhanced the antidepressant-like effects induced by Fluoxetine (FLX) in the FST. In this work, we have studied whether the effects of GAL(1–15) on FLX action were mediated via 5-HT1AR, analyzing the effect of the 5-HT1AR antagonist WAY100635 in this effect and if the binding characteristics and mRNA levels of 5-HT1AR in the DR and dorsal hippocampus are modified by GAL(1-15)+FLX.

Groups of rats (n=6-8) received three injections of sc FLX(10mg/kg) and 15 minutes before the FST a single icv injection of GAL(1-15) (1nmol) and 5HT1AR antagonist WAY100635(6nmol) icv alone or in combination.
We also analyzed the effects of GAL(1-15)+FLX in the binding characteristics of the 5-HT1AR agonist [H^3]-8-OH-DPAT and 5-HT1A mRNA levels in the DR, CA1 and Dentate Gyrus (DG).

WAY100635 significantly blocked the reduction in immobility time ($p<0.05$), and the increase in swimming time ($p<0.01$) induced by GAL(1-15)+FLX in the FST.
GAL(1-15)+FLX produced a significant increase in the 5HT1AR mRNA levels in CA1 ($p<0.05$) and DG ($p<0.05$). This effect was not observed in the DR. Moreover, GAL(1-15)+FLX produced a significant decrease in the Kd value ($p<0.01$) and in the Bmax value ($p<0.05$) of [^{3}H]-8-OH-DPAT in the DG. These effects were not observed in the CA1 or in the DR.
These results indicate that 5HT1AR participates in the GAL(1-15)/FLX interactions in the FST and the mechanism underlying affected the binding characteristics and the mRNA levels of 5-HT1AR specifically in the dorsal hippocampus. The heteroreceptor 5-HT1AR-GALR1-GALR2 located in the dorsal hippocampus may be the target for GAL(1-15).

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