

THE DOPAMINERGIC MESOLIMBIC SYSTEM ARE INVOLVED IN THE ANHEDONIC-LIKE EFFECTS PRODUCED BY GALANIN (1-15) IN RATS.

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Galanin (1-15)[GAL(1-15)] induces depressant- and anxiogenic-like actions in several behavioural tests. Recently, we described that GAL(1-15) induces an anhedonic-like effect in saccharine self-administration and sucrose preference test in rats. In order to investigate whether the effect of GAL(1-15) in anhedonia was associated with the reward circuit, we have studied the GAL(1-15) actions over the mesolimbic system by PET for in vivo imaging and in the expression of the C-Fos, Dat, Vmat2 and Dopamine and Galanin receptors genes in VTA and NAc.

In the PET experiments, the [¹⁸F]FDG at 30, 60 and 90min after GAL(1-15) administration was measure as indicative of brain glucose metabolism. In the qPCR experiments, groups of rats (n=5-6) were killed 1h after i.c.v. GAL(1-15) 3nmol or vehicle. The VTA and NAc were dissected and the mRNA expression of C-Fos, Dat, Vmat2 and D1, D2, D3, D5, GALR1, and GALR2 receptors were measured by RT-qPCR.

The GAL(1-15) induced a decrease in [¹⁸F]FDG uptake in the hippocampus and thalamus at 30, 60 and 90min, and in the striatum at 30min, however, in the prefrontal cortex, an increase in [¹⁸F]FDG uptake was observed after 30 and 60min. GAL(1-15) at a dose of 3 nmol produced a significant decrease in the mRNA levels of Dat and Vmat2 (p<0.05) and an increase in the D3 receptor (p<0.05) in VTA. In the NAc, GAL(1-15) induced a significant decrease in the expression of C-Fos (p<0.05) mRNA and a significantly increased the mRNA expression of D1 (p<0.05), D2 (p<0.05) and D3 (p<0.05).

These results suggest the involvement of the dopaminergic mesolimbic system, a key region for the reward system, in GAL(1-15)-mediated action on anhedonia. These results may give the basis for the development of novel therapeutic strategies using GAL(1-15) for treatment of depression and reward-related diseases.

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