Anxiolytic action of group II and III metabotropic glutamate receptors agonists involves neuropeptide Y in the amygdala

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Abstract:
Several lines of evidence indicate that activation of group II and III metabotropic glutamate (mGlu) receptors produces anxiolytic-like effects in rodents. On the other hand neuropeptide Y (NPY) induces an anxiolytic effect in mts after intraventricular or intramygdalar administration. Therefore, in the present study we investigated whether the anxiolytic action of (2S,3S,4S)-(carboxycycloproplyl)glycine (L-CCG-I), an mGlu2/3 receptor agonist, and (1S,3R,4S)-1-aminocyclopentane-1,3,4-tricarboxylic acid (ACPT-I), an mGluR4/6/7/8 receptor agonist, was mediated by a mechanism involving NPY receptor.

In behavioral studies, the anxiolytic activity of L-CCG-I (10 µg/0.5 µl/site) and ACPT-I (1.5 µg/0.5 µl/site) was examined using plus-maze tests. The Y1 receptor antagonist BIBO 3304 was given at a dose of 128 ng/0.5 µl/site. All the compounds tested were injected bilaterally into the amygdala, BIBO 40 min and mGluR agonists 30 min before the test. It was found that the anxiolytic effects of mGluR agonists were abolished by BIBO 3304 (1,1)-N-[4-(aminocarbonylaminomethyl) phenyl] methyl]-N2-(diphenylacetyl)-argininamide trifluoracetate (3304) administration. Immunohistochemical studies showed a moderate density of mGlu2/3 receptor immunoreactivity (IR) in the amygdala. The effect of L-CCG-I and ACPT-I on NPY expression in the amygdala was studied using immunohistochemistry (IH). While NPY mRNA expression was studied using in situ hybridization. We showed a diminution in NPY-IR after L-CCG-I administration and decrease in NPYmRNA expression after both L-CCG-I and ACPT-I treatment, to about 77% (IH) or 32-41% (mRNA) of the control level 18 h after injection of these mGluR agonists. Our results indicate that the anxiolytic action of both compounds is conveyed by NPY neurons with the involvement of Y1 receptors in the amygdala, and that NPY neurons seem to be regulated by the glutamatergic system.

Key words: metabotropic glutamate receptors, neuropeptide Y, anxiety, immunohistochemistry