Chronic imipramine treatment reduces inhibitory properties of group II mGlu receptors without affecting their density or affinity

Agnieszka Pałucha, Piotr Brański, Kinga Klak, Magdalena Sowa

Department of Neurobiology, Institute of Pharmacology Polish Academy of Sciences, Smętna 12, PL 31-043 Krakow, Poland

Correspondence: Agnieszka Pałucha, e-mail: npalucha@cyf-kr.edu.pl

Abstract:
An increasing body of evidence indicates an important role of the glutamatergic system in the pathophysiology of depression. Not only ionotropic but also metabotropic glutamate receptors (mGlu receptors) have been suggested to be involved in the mechanism of action of antidepressant drugs. Moreover, several mGlu receptor ligands possess a great antidepressant potential. Group II mGlu receptor antagonists have been shown to induce antidepressant-like effects in rodents. An influence of chronic antidepressant treatment on group II mGlu receptors has also been suggested. In our studies, we examined an influence of repeated (21-day) imipramine treatment on the density of group II mGlu receptors and affinity of mGlu2 and mGlu3 receptor radioligand [3H]-LY341495 for group II mGlu receptors in the rat brain hippocampus and frontal cortex. Moreover, we analyzed an influence of chronic imipramine administration on the ability of group II mGlu receptor agonist, 2R,4R-APDC, to inhibit forskolin-stimulated cAMP accumulation in the rat brain cortical slices. We found that inhibitory properties of group II mGlu receptors were diminished after chronic, but not acute imipramine administration. However, no changes in the density or affinity of the mGlu2 and mGlu3 receptor ligand for group II mGlu receptors were observed.

Key words: cAMP, imipramine, group II mGlu receptors