PRELIMINARY COMMUNICATION

EFFECT OF ANTIDEPRESSANT DRUGS ON THE HUMAN CORTICOTROPIN-RELEASING-HORMONE GENE PROMOTER ACTIVITY IN NEURO-2A CELLS

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In order to test if antidepressant drugs can directly influence corticotropin-releasing hormone (CRH) gene expression, their effect on CRH gene promoter activity was evaluated in neuro-2A cells stably transfected with a human CRH – chloramphenicol acetyltransferase plasmid. Forskolin (an activator of adenylate cyclase), but not phorbol 12-myristate 13-acetate (an activator of protein kinase C), ca. 3-fold increased reporter gene activity, which confirms the critical role of the cAMP-responsive element in regulation of the CRH gene. Imipramine and fluoxetine present in the medium for 5 days, in a concentration-dependent manner (3–30 µM) inhibited the basal activity of CRH gene promoter, while tianeptine was inactive. The obtained results indicate that inhibition of the human CRH gene promoter activity by imipramine and fluoxetine, but not tianeptine, may play a role in a mechanism by which the former drugs attenuate HPA axis activity.

Key words: imipramine, fluoxetine, tianeptine, corticotropin-releasing hormone, gene promoter activity, neuro-2A cells

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