



Influence of serotonin 5-HT₇ receptor blockade on the behavioral and neurochemical effects of imipramine in rats

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Abstract:

The aim of the present study was to examine the effect of the selective 5-HT₇ receptor antagonist (2R)-1-[(3-hydroxyphenyl)sulfonyl]-2-[2-(4-methyl-1-piperidiny)ethyl]pyrrolidine (SB-269970), administered alone or in combination with imipramine, on the immobility time of rats in the forced swim test as well as on the extracellular levels of dopamine (DA), noradrenaline (NA), serotonin (5-HT) and their metabolites in the prefrontal cortex of freely moving rats. Both compounds were administered intraperitoneally (*ip*). Like imipramine (30 mg/kg, but not 20 mg/kg), SB-269970 (1.25 and 2.5 mg/kg, but not 0.625 mg/kg) significantly shortened the immobility time of rats without affecting their exploratory locomotor activity measured in the open field test. SB-269970 (0.625 and 1.25 mg/kg) raised the extracellular levels of DA, NA, 5-HT and their metabolites in rat prefrontal cortex. In that structure, imipramine (20 mg/kg) produced an increase in all the neurotransmitters measured, but failed to affect the levels of their metabolites. A combination of the inactive doses of SB-269970 (0.625 mg/kg) and imipramine (20 mg/kg) found in the forced swim test produced antidepressant-like effect, which did not stem from the increased exploratory locomotor activity. At the same time, that combination evoked a vast increase in the output of NA – but not DA and 5-HT – compared to the effects of both those drugs given alone. These results open up a possibility that the stimulating effect of SB-269970 on DA, NA and 5-HT transmission in the prefrontal cortex plays some role in the antidepressant-like activity of this compound. Moreover, these findings suggest that the increase in cortical NA level seems to account for the anti-immobility action observed after joint administration of the selective 5-HT₇ receptor antagonist and imipramine in rats.

Key words:

5-HT₇ receptor antagonist, SB-269970, imipramine, forced swim test, microdialysis, rats
