Mechanism of synergistic action following co-treatment with pramipexole and fluoxetine or sertraline in the forced swimming test in rats

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Abstract:
The aim of the present study was to examine the effect of combined treatment of male Wistar rats with pramipexole and fluoxetine or sertraline in the forced swimming test. The obtained results showed that co-treatment with pramipexole (0.1 mg/kg) and fluoxetine (10 mg/kg) or sertraline (5 mg/kg) (in doses inactive per se) exhibited antidepressant-like activity in the forced swimming test. Sulpiride (a dopamine D2/3 receptor antagonist) and WAY 100635 (a 5-HT1A receptor antagonist), either being ineffective in the forced swimming test, inhibited the antidepressant-like effect induced by co-administration of pramipexole and fluoxetine or sertraline. However, SCH 23390 (a dopamine D1 receptor antagonist) did not alter the effect of pramipexole given jointly with antidepressant drugs; on the other hand, S 33084 (a dopamine D3 receptor antagonist) only partly decreased (in a statistically insignificant manner) that effect. Moreover, progesterone and BD 1047 (a σ1 receptor antagonist) counteracted the antidepressant-like effect induced by co-administration of pramipexole and sertraline (but not pramipexole and fluoxetine). In that test, active behavior did not reflect the increases in general activity, since combined administration of pramipexole and fluoxetine or sertraline failed to enhance the locomotor activity of rats. None of the tested drugs (SCH 23390, sulpiride, S 33084, WAY 100635, BD 1047 and progesterone) – alone or in combination with pramipexole and fluoxetine or sertraline – changed locomotor activity. The results described in the present paper indicate that co-administration of pramipexole and fluoxetine or sertraline may induce a more pronounced antidepressive activity than does treatment with pramipexole alone, and that in addition to other mechanisms, dopamine D2/3 and 5-HT1A receptors may contribute to the antidepressant-like activity of pramipexole and fluoxetine or sertraline in the forced swimming test in rats. Moreover, σ1 receptors may constitute one of the possible mechanisms by which co-administration of pramipexole and sertraline induces antidepressant-like activity in that test.

Key words:
pramipexole, fluoxetine, sertraline, forced swimming test, rats