SYNERGISTIC EFFECT OF IMIPRAMINE AND AMANTADINE IN THE FORCED SWIMMING TEST IN RATS. BEHAVIORAL AND PHARMACOKINETIC STUDIES

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Our previous studies demonstrated that joint administration of a tricyclic antidepressant drug, imipramine (IMI) with the uncompetitive antagonist of NMDA receptor, amantadine (AMA), produced stronger “antidepressant” effect in the forced swimming test (Porsolt’s test) than the treatment with either of drugs given alone. Since it has been suggested that, in addition to their other functions, dopamine and α1-adrenergic receptors may play a role in behavioral response in the forced swimming test, in the present study we examined the effect of sulpiride (dopamine D2, receptor antagonist) and prazosin (α1-adrenergic receptor antagonist) on the effect of AMA given alone or in combination with IMI in the forced swimming test in rats. We also measured the level of IMI and its metabolite, desipramine, in the rat plasma and brain, 1 h after the forced swimming test. Joint treatment with IMI (5 or 10 mg/kg) and AMA (20 mg/kg) produced stronger antidepressant-like effect than either of agents given alone. Sulpiride (10 mg/kg) or prazosin (1 mg/kg) (ineffective in the forced swimming test) inhibited an antidepressant-like effect induced by co-administration of IMI and AMA. The active behaviors in that test did not reflect an increase in general activity, since combined administration of IMI and AMA failed to enhance the locomotor activity of rats, measured in the open field test. Also sulpiride and prazosin did not decrease the exploratory activity induced by co-administration of IMI and AMA. The above result suggests that the dopamine D2, and α1-adrenergic receptors may contribute to the mechanism of synergistic action of IMI and AMA in the forced swimming test in rats. The pharmacokinetic interaction can be excluded, since AMA did not change significantly the antidepressant level in the rat plasma and brain, measured 1 h after exposure to the forced swimming test.

Key words: imipramine, amantadine, behavioral and pharmacokinetic studies, rats

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