



Repeated co-treatment with fluoxetine and amantadine induces brain-derived neurotrophic factor gene expression in rats

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Abstract:

In the present study, we investigated the influence of repeated treatment with fluoxetine (FLU, 5 or 10 mg/kg) and amantadine (AMA, 10 mg/kg), given separately or jointly (twice daily for 14 day), at the mRNA level (the Northern blot) in the hippocampus and cerebral cortex. The experiment was carried out on male Wistar rats. The tissue for biochemical assays was dissected 24 h after the last dose of drug. We also studied the effect of repeated treatment with FLU and AMA on the action of 5-hydroksytryptamine (5-HT)_{1A}- and 5-HT₂ receptor agonists (±)-8-hydroxy-2-(di-*n*-propylamino)-tetralin (8-OH-DPAT) and (±)-1-(4-iodo-2,5-dimethoxy-phenyl)-2-aminopropane ((±)DOI), respectively, in behavioral tests. The obtained results showed that FLU (10 mg/kg) in the hippocampus, and FLU (5 and 10 mg/kg) and AMA (10 mg/kg) in the cerebral cortex, significantly elevated BDNF mRNA levels. Joint administration of FLU (5 or 10 mg/kg) and AMA (10 mg/kg) induced a more substantial increase in BDNF gene expression in the cerebral cortex (but not in the hippocampus), and inhibited the behavioral syndrome induced by 8-OH-DPAT or (±)DOI (compared to treatment with either drug alone). The obtained results suggest that the enhancement of BDNF gene expression may be essential for the therapeutic effect of the co-administration of FLU and AMA in drug-resistant depressed patients, and that among other mechanisms, 5-HT_{1A} and 5-HT₂ receptors may play some role in this effect.

Key words:

repeated treatment, fluoxetine, amantadine, mRNA BDNF, 5-HT_{1A} and 5-HT₂ syndrome, rats
