Influence of zinc supplementation on imipramine effect in a chronic unpredictable stress (CUS) model in rats

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Abstract:
Zinc is an endogenous modulator of neuronal activity and may play an important role in the pathogenesis of depression. Recent studies have shown that zinc exhibits antidepressant-like activity in some models of depression in rodents. Our previous studies have shown that the footshock-induced fighting behavior was reduced in the rats subjected to chronic unpredictable stress (CUS). This test is used as the new experimental model of depression. Various antidepressant drugs given repeatedly prevented this kind of behavioral depression.

The aim of the present study was to evaluate the effect of prolonged treatment with zinc hydroaspartate and to examine if zinc supplementation could modulate the imipramine effect in CUS model of behavioral depression in rats. The experiments were carried out on male Wistar rats. Chronic stress (persisting for 16 days) was induced by the modified method described by Katz et al. Zinc hydroaspartate at the dose of 30 mg/kg/day or 15 mg/kg/day and imipramine at the dose of 5 mg/kg/day were administered once daily for 14 days. Imipramine was given (ip) 1 h before every stress session and zinc hydroaspartate (ip) 1 h before the antidepressant.

The footshock-induced fighting behavior test was performed 48 h after the last session of the chronic stress. It was demonstrated that in chronically stressed rats the number of fighting attacks was significantly reduced (by about 75%). Zinc hydroaspartate at the dose of 30 mg/kg/day, given alone, prevented the deficit in fighting behavior in chronically stressed rats. Neither imipramine at the dose of 5 mg/kg/day nor zinc hydroaspartate (15 mg/kg/day) administered alone changed the intensity of fighting behavior in chronically stressed rats. However, when imipramine was given at the same dose in the rats pretreated with zinc hydroaspartate (15 mg/kg/day) the deficit of fighting behavior was not observed. The present results indicate that zinc similarly to antidepressants protects the rats against the CUS-induced behavioral depression. Moreover, our findings suggest that zinc supplementation could potentiate the antidepressant effect of imipramine.

Key words:
imipramine, zinc, chronic unpredictable stress (CUS), electric footshock-induced fighting behavior, rats