Investigation of GABA A receptor modulation in the antidepressant- and anxiolytic-like effect of zinc

MAUREN KRUGER, MAURICIO PEÑA CUNHA, ANDRÉ ROBERTO COLLA, ANA LÚCIA S. RODRIGUES.

Universidade Federal de Santa Catarina, Bioquímica, Santa Catarina - Brasil

Abstract:

Zinc is a transition metal that has multiple biological and neuropharmacological effects, including antidepressant and anxiolytic properties (Samardzic et al, 2013; Joshi et al., 2012). Taken into account that anxiety disorders are often associated with depressive symptoms and that GABAergic system plays a crucial role in mood regulation, this study investigated the role of GABAergic system in the effect of zinc administration in anxiety and depression models in mice. The experimental protocols were approved by Institution Ethics Committee (PP00795). Male Swiss mice were administered with zinc (1-30 mg/kg, ip), diazepam (1-10 mg/kg, ip, positive control) or fluoxetine (20 mg/kg, ip, positive control) and subjected to the behavioral paradigms. Zinc chloride (30 mg/kg), similar to fluoxetine (20 mg/kg) decreased the immobility time in the forced swimming test (FST) and, similarly to diazepam (5-10 mg/kg, ip) also decreased the marble buried in the marble burying test (MBT). Considering that GABA A receptor is implicated in the pathophysiology of anxiety and depression, the effect of muscimol (0.5-1 mg/kg, ip, a selective GABA receptor agonist) in FST and MBT was investigated. Muscimol (1 mg/kg) reduced the immobility time in the FST, and the marble buried in the MBT. The anti-immobility effect of zinc (30 mg/kg) and muscimol (1 mg/kg) in the FST was prevented by pretreatment of mice with bicuculline (1 mg/kg, ip, GABA A receptor antagonist). Although bicuculline (1 mg/kg, ip) was able to prevent the anxiolytic effect of muscimol (1 mg/kg), it did not abolish the anxiolytic-like effect of zinc in the MBT. Overall the results suggest that the antidepressant-like effect of zinc, but not its anxiolytic-like effect, is dependent, at least in part, on GABA A receptor activation.

Keywords: Anxiety, Depression, Forced swimming test; GABA A Receptor; Marble burying test; Zinc.

References: