

Abstract

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Involvement of NMDA receptors and L-arginine-nitric oxide pathway in the antidepressant-like effects of zinc in mice.

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OBJECTIVE: This study investigated the involvement of NMDA receptors and the L-arginine-nitric oxide (NO) pathway in the antidepressant-like effects of zinc in the forced swimming test (FST).

METHODS: The immobility times in the FST and in the tail suspension test (TST) were reduced by zinc chloride (ZnCl₂), 30 and 10-30 mg/kg intraperitoneal (i.p.), respectively).

RESULTS: The doses active in the FST and TST reduced locomotor activity in an open-field. The antidepressant-like effect of ZnCl₂ in the FST was prevented by pre-treatment of animals with guanosine 5'-monophosphate (GMP), ascorbic acid, L-arginine, or S-nitroso-N-acetyl-penicillamine (SNAP), but not with D-arginine, administered at doses that per se produced no anti-immobility effect. The immobility time of mice treated with ZnCl₂+MK-801 was not different from the result obtained with ZnCl₂ or MK-801 alone, but ZnCl₂+imipramine had a greater effect in the FST than administration of either drug alone. Pre-treatment of animals with a sub-threshold dose of ZnCl₂ prevented the anti-immobility effect of MK-801, ketamine, GMP, L-arginine or N(G)-nitro-L-arginine (L-NNA), but did not alter the effect of imipramine or fluoxetine.

CONCLUSION: Taken together, the results demonstrate that zinc produced an antidepressant-like effect that seems to be mediated through its interaction with NMDA receptors and the L-arginine-NO pathway.

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