ACUTE BUT NOT CHRONIC TREATMENT WITH OLANZAPINE REDUCES EXPERIMENTAL ANXIETY IN RATS: POSSIBLE MECHANISMS

Locchi Federica, Rimondini Roberto, Dall'Olio Rossella, Gandolfi Ottavio

Department of Pharmacology, University of Bologna, 40128 Bologna, Italy

Olanzapine is an atypical antipsychotic whose particular action is due to the blockade of both dopaminergic (namely D_2/D_4 type) and serotonergic receptors (namely $5HT_2$ type). Previous studies from our laboratory demonstrated that the pharmacological effects of olanzapine could involve the glutamatergic system. Furthermore, olanzapine administration increases plasma and brain concentration of progesterone and of its metabolite allopregnanolone. It is notable that clinical studies have recently reported that olanzapine is effective in treatment –resistent depression (TRD) and in panic disorder (PD). Additionally, recent studies have shown that glutamatergic antagonist may have potential anxiolytic action.
These experimental and clinical evidences might indicate a possible use of olanzapine in the treatment for anxiety disorders.
The aim of this study is to confirm the anxiolytic and antidepressant effects of olanzapine in animals and to clarify the underlying mechanisms.
To examine this hypothesis, we used the elevated plus-maze test (EPM) either in basal condition or after restrain stress and the forced swim test (FST) in rats acutely or chronically (21 days) treated with a dose of olanzapine (0.5 mg/Kg i.p.) alone or in combination with DCS, an agonist at the glycine site on NMDA receptor, or the 5-alpha-reductase inhibitor finasteride.
The results showed an anxiolytic effect of the acute but not of the chronic treatment with olanzapine. Furthermore, this anxiolytic effect was counteracted by the co-administration of olanzapine and DCS or finasteride. No antidepressant effect could be observed after either an acute or chronic treatment with olanzapine.
The anxiolytic effect of olanzapine might be due to possible actions of olanzapine on glutamatergic and corticosteroid pathways.