Effect of Buspirone, Dizocilpine andAripiprazole on Apomorphine-induced aggression in rats.

Thesis

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Summary

Aggression is one of the most serious problems facing humanity. Today, there are many psychotropic drugs that may abolish aggressive behavior. However, most of them are non-specifically sedative and display many adverse effects limiting their use.

Searching for new specific antiaggresive drugs is needed, but it is complicated because there are only few animal models that can reflect human aggressive behavior. The apomorphine-induced aggressive behavior is effectively antagonized by neuroleptics, D2 receptor blockers, morphine and N-methyl-D-aspartate (NMDA) receptor antagonists. Most of these drugs are also effective antipsychotics in clinical psychopharmacology and thereby this test can be considered as a perfect model for testing aggressive behavior.

Many studies reported that the 5-HT1A receptor partial agonists may abolish the aggressive behavior induced by apomorphine. There is also a growing body of evidence demonstrating a functional interaction between dopamine receptors and NMDA-gated channels. NMDA-gated channels seem to regulate the activity of the dopaminergic system not only at the level of presynaptic mechanisms, but also by affecting postsynaptic dopamine receptors.Aripiprazole is a new antipsychotic drug with

apharmacological profile different from the conventional and atypical antipsychotics. It is a partial agonist at 5-HT1A and antagonist at 5-HT2A receptors, but unlike other antipsychotic, which are potent D2 receptor antagonists aripiprazole has partial agonist activity on these receptors.The drug is effective in different animal models of psychosis as well as in some models of negative symptoms.

In the present study we investigated the possible antiaggressive effect of buspirone, dizocilpine and aripiprazole in apomrphine-induced aggression model in male albino rats.

Fourty male albino rats divided in 5 groups were included in the study. Group 1 was treated with saline and acted as the control group. Group 2 was treated by apomorphine, group 3 was treated by buspirone and apomorphine, group 4 was treated by dizocilpine and apomorphine and group 5 was treated by aripiprazole and apomorphine. Saline and drugs were administered for 12 days.

All rats were tested for aggression score, latency time and locomotor activity at days 1, 4, 8, and 12 of the experiment, and at the last day of the experiment, they were sacrificed by decapitation, frontal areas of the brain were taken and tested by PCR method for expression of $5HT_{1A}$ and D2 receptors expression.

Our results revealed that, buspirone, dizocilpine and aripiprazolehad anantiaggressive effect on apomorphine-induced aggression. Also our results revealed that buspirone and aripiprazole had a hypolocomotor effect, while dizocilpine had a hyperlocomotor effect.

As regards studying 5HT1A and D2 receptors expression, our results revealed that pretreatment of animals with buspirone or dizocilpine before apomorphine administration significantly decreased the level of expression of 5HT1A and D2 receptors in the frontal cortex, compared with apomorphine-treated group. Pretreatment of animals with aripiprazole before apomorphine administration had a non significant effect on receptor expression compared to apomorphine-treated group.