

HALOPERIDOL BOTH PREVENTS AND REVERSES QUINPIROLE-INDUCED NON REGULATORY WATER INTAKE, A PUTATIVE ANIMAL MODEL OF PSYCHOGENIC POLYDIPSIA

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Rationale: There is extensive evidence that catecholamine and in particular dopamine is determinant in drinking behaviour. Repeated injections of the D_{2/3} agonist quinpirole induce polydipsia via an unknown mechanism of action. It has been reported that the D₂ antagonist haloperidol, and D₁ antagonist SCH-23390, partially reduce the hyperdipsic response to the amphetamine, an indirect dopamine agonist.

Objectives: The aim of this study was to determine the potential activity of compounds with different affinity for D₂ receptors in preventing and/or reversing QNP-induced polydipsia.

Methods: Male Sprague-Dawley rats were injected (-)-Quinpirole HCl (0.5 mg/kg, QNP) intraperitoneally (ip) once daily for five days to induce polydipsia. The oral effect of haloperidol, olanzapine, clozapine and ST2472 on QNP-induced polydipsia was analyzed in two schedules. In polydipsia prevention schedule (PPS), haloperidol (0.2, 0.4 and 0.8 mg/kg), olanzapine (1.5, 3 and 6 mg/kg) and ST2472 (1 and 2 mg/kg), were administered before QNP from the first to the last day of the experiment (5 days). In polydipsia reversal schedule (PRS), rats which were polydipsic on the third day were administered haloperidol (0.4 mg/kg), olanzapine (1.5 and 3 mg/kg), clozapine (10, 20 and 40 mg/kg) and ST2472 (1, 2, 5 and 10 mg/kg) before QNP on the fourth and fifth day of the experiment. **Results:** QNP (0.5 mg/kg) induced polydipsia. In PPS, only haloperidol (0.4, 0.8 mg/kg) prevented polydipsia. Moreover, haloperidol (0.8 mg/kg) and olanzapine (6.0 mg/kg) showed a trend of reduction in drinking behavior per se. In PRS, haloperidol (0.4 mg/kg), olanzapine (3.0 mg/kg) and ST2472 (1 mg/kg) reversed polydipsia only after the second administration. Differently from the other antipsychotics, ST2472 (5 and 10 mg/kg) reversed polydipsia from the first administration. Finally, clozapine could not reverse QNP-induced polydipsia.

Conclusions: It is suggested that the dopaminergic pathway is probably the major component in the establishment of polydipsia (allowing the sensitization). Instead, when the phenomenon is established, the dopamine-induced water intake involves other neurobiological pathways that concur to keep up the drinking behaviour.

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