EFFECT OF PHARMACOLOGICAL BLOCKADE ON LITHIUM-INDUCED WATER DRINKING

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Administration of lithium chloride (40 mg/kg i.p.) led to a significant increase in 24 h water intake of rats. Prior administration of propranolol and haloperidol blocked the effect of lithium while atropine failed to show such an effect. The dipsogenic effect of lithium is probably exerted through β-adrenergic and dopaminergic pathways.

Fitzsimons (1972) reviewing the dipsogenic actions of drugs suggested that three neuronal mechanisms, cholinergic, β-adrenergic and possibly dopaminergic, may be involved in drinking. Lithium causes increased water drinking (Davies & Fann, 1971; Gutman, Benzakein & Livineh, 1971). The present investigation was aimed at finding out the neuronal mechanism involved in lithium-induced polydipsia.

Methods Albino rats (190-280 g wt) housed in individual cages were maintained on rat feed (supplied by Hindustan Lever, India). The 24 h water intake of each rat was measured every morning at 10 h 00 minutes. The experiments were started only after the 24 h water intake was reasonably well stabilized in each rat, which generally took about 10 days after placing the rats in individual cages. The rats were divided into four groups with four animals in each group. The 24 h water intake of each animal in all groups was measured for three days and the values obtained served as controls for the group. The following drugs were administered intraperitoneally daily for the next three days: distilled water (group A), atropine 3 mg/kg (group B), propranolol 0.5 mg/kg (group C) haloperidol 0.04 mg/kg (group D). Haloperidol at this dose was shown to be sufficient to block dopaminergic transmission in rat brain (Bunney, Walters, Roth & Aghajanian, 1973). During the next four days the rats received lithium chloride 40 mg/kg intraperitoneally along with the respective drugs and the 24 h water intake of the last three days was measured. Since there was a wide variation in the individual values (27-87 ml), the responses of each animal are expressed as a percentage of its control value. The food intake of the rats measured every day over this period (18-30 g) did not show any significant variation.

Results Table 1 summarizes the results obtained which confirm the effect of lithium on water intake and indicate that both haloperidol and propranolol decreased excessive water intake caused by lithium administration, whereas atropine showed no such effect.

Discussion The results suggest that the dipsogenic action of lithium probably involves pathways with β-adrenergic and dopaminergic transmission and blockade of these by propranolol and haloperidol leads to inhibition of the action of lithium.

According to Gutman *et al.* (1971) polydipsia induced by lithium may be due to liberation of

Table 1 Water intake of rats during 24 h expressed as percentage of controls

Treatment	*Group A (Water)*	*Group B (Atropine)*	*Group C (Propranolol)*	*Group D (Haloperidol)*
Control	100 ± 4.5	100 ± 3.5	100 ± 4.0	100 ± 4.0
Drug alone	99 ± 6.5	104 ± 6.5	97 ± 5.0	106 ± 6.0
Drug + lithium	169 ± 11.5*	154 ± 22.5	119 ± 8.5†	111 ± 5.5†

Values expressed as mean with s.e. of mean.
† Differ significantly ($P < 0.05$) from *.

renin from the kidney which leads to the production of angiotensin. Angiotensin is one of the most potent dipsogens known (Fitzsimons, 1972). Fitzsimons & Setler (1971) have shown that haloperidol injected into the hypothalamus through a cannula prevents the thirst induced by similarly administered angiotensin. This idea is supported by our finding that haloperidol can block the thirst induced by lithium.

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