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AN EFFECT OF HALOPERIDOL ON THE INCREASED FOOD AND WATER INTAKE INDUCED IN RABBITS BY 2-DEOXY-D-GLUCOSE

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Rabbits treated with 2-deoxy-D-glucose (2DG) (300 mg/kg) show an increased intake of food and water. Pretreatment with haloperidol (1 mg/kg) abolishes the increase in water intake but does not prevent the increase in food intake.

Introduction The effects of 2-deoxy-D-glucose (2DG) on carbohydrate metabolism have been reviewed by Brown (1962). Under the stimulus of insulin, 2DG moves into cells and is converted to 2DG-6-phosphate. This substance inhibits the hexose phosphate isomerase reaction and the membrane transport system which normally carries glucose into the cell. 2DG-6-phosphate is not further metabolized inside the cell (Horton, Meldrum & Bachelard, 1973). 2DG, consequently, decreases glucose utilization throughout the body tissues. It increases food intake in the rat, rabbit and monkey (Smith & Epstein, 1969; Russel & Mogenson, 1975) and has been observed to increase drinking in the rat (Russel & Mogenson, 1975).

Antelman, Szechtman, Chin & Fisher (1975) demonstrated that eating induced by tail-pinch in the rat appeared to involve cerebral dopaminergic neuronal systems. Since 2DG causes an increase in food and water intake, the possibility arises that the mechanisms by which 2DG acts also involve the dopaminergic neuronal systems in the brain. This was tested by studying the effects on food and water intake produced by 2DG following the administration of haloperidol, a drug thought to block central dopamine receptors (Andén, Butcher, Corrodi, Fuxe & Ungerstedt, 1973).

Methods Female New Zealand White rabbits weighing 2.0 to 3.5 kg were used. The animals were housed in cages in a laboratory where the daytime temperature ranged between 17 and 22°C. There was natural illumination. They were fed 'Oxoid' Laboratory Diet SGI. Both food and water were available *ad libitum*.

A 5% (w/v) solution of 2DG made up in pyrogen-free distilled water was given subcutaneously. Haloperidol was dissolved in 0.1 M lactic acid to produce a 2 mg/ml solution. The animals were injected with haloperidol (1 mg/kg), or an equivalent volume of the lactic acid vehicle. One h later, they were injected with 2DG (300 mg/kg). Food and water intake were estimated by weighing the food present in the cage and by measuring the volume of water in the water bottle at the beginning and end of the experimental period. The food and water intake were measured from the time halfway between the two injections.

Results Table 1 shows that 2DG increased both food and water intake in rabbits pretreated with the lactic acid vehicle. Pretreatment with haloperidol at a concentration of 1 mg/kg one hour before 2DG injection prevented the increase in water intake. However, there was no effect on food intake.

Discussion The results demonstrate that, following 2DG injections, haloperidol suppresses the increase in water intake but not the increase in food intake, under the conditions of these experiments. This suggests that the two responses to 2DG involve different pathways in respect of the mechanisms controlling hunger and thirst.

Haloperidol has been shown to have some affinity for β-adrenoceptors in the brain (Bylund & Snyder, 1976) and since propranolol is known to block the increase in water intake that is induced by isoprenaline injections in rats, probably because of β-adrenoceptor blockade (Katovitch & Fregly, 1978), the possibility that haloperidol is blocking the same receptors cannot be discounted. However, the increased water intake induced by the intracranial injection of angiotensin in rats can be antagonized by haloperidol or spiperone (Fitzsimons & Setler, 1975). These authors also showed that haloperidol reduced the water intake following water deprivation.

The mechanism by which 2DG increases water intake in rabbits remains to be elucidated but the present results are further evidence for the involvement of cerebral dopaminergic neurones in thirst. The possibility that dopaminergic neurones are also involved in the control of food intake cannot be excluded because only one dose of haloperidol was used in these experiments.

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Table 1 The effect of haloperidol on the increases in food and water intake caused by 2-deoxy-D-glucose (2DG)

Water intake	*Mean water intake (ml/6 h) for 2 days before experiment*	*Mean water intake (ml/6 h) after lactic acid vehicle and 2DG*	*Mean water intake (ml/6 h) after haloperidol and 2DG*
Expt 1	86.3 ± 15.0 (6)	151.7 ± 8.3 (6)*	—
	67.9 ± 11.2 (6)	—	62.5 ± 16.6 (6)
Expt 2	77.3 ± 3.5 (12)	142.8 ± 10.6 (12)**	—
	81.3 ± 4.7 (12)	—	85.1 ± 3.8 (12)
Food intake	*Mean food intake (g/6 h) for 2 days before experiment*	*Mean food intake (g/6 h) after lactic acid vehicle and 2DG*	*Mean food intake (g/6 h) after haloperidol and 2DG*
Expt 1	34.5 ± 3.5 (6)	70.8 ± 6.0 (6)**	—
	31.0 ± 3.1 (6)	—	64.2 ± 22.6 (6)
Expt 2	29.3 ± 2.5 (12)	53.9 ± 5.0 (12)**	—
	30.8 ± 1.7 (12)	—	55.7 ± 5.4 (12)**

Values are mean ± s.e. mean; number of observations given in parentheses. Different animals used for each observation in experiment 1. Each animal used for both treatments in experiment 2 with an interval of 7 days between tests.
Statistical analysis: difference from means of observations on two days before experiment $*P < 0.02$; $**P < 0.01$.

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