

HYPOTHERMIC ACTION OF BROMOCRIPTINE

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The body temperature of rats has been studied in a cold environment. In this setting, bromocriptine induced hypothermia. This fall in core temperature was inhibited by pimozide. It was concluded that bromocriptine has a dopamine-like action in areas of the brain concerned with the control of body temperature, as has previously been shown for apomorphine and amphetamine.

Introduction Drugs such as amphetamine and apomorphine reduce the core temperature of rats placed in a cold (4-15°C) ambient temperature. This hypothermic action is produced by dopaminergic mechanisms in the central nervous system (Kruk, 1972; Yehuda & Wurtman, 1972). It has recently been suggested that bromocriptine (2-brom- α -ergocryptine; CB 154 Sandoz) stimulates dopaminergic neurones (Corrodi, Fuxe, Hokfelt, Lidbrink & Ungerstedt, 1973). We have investigated the effect of bromocriptine on the colonic temperature of rats in an attempt to establish further evidence of the dopaminergic activity of this compound in the central nervous system.

Methods Drugs were administered intraperitoneally to male Wistar rats weighing 150-200 g. In each series of observations 5-13 animals were placed in individual perspex cages (20 x 10 x 10 cm) in a refrigerated room 1 h before starting observations. The intracolonic temperature was recorded every 10 min with a thermistor (Yellow Spring International Co., Yellow Springs, Ohio, U.S.A.) inserted 5-6 cm into the rectum. Ambient temperature in the cold room was maintained at 5-6°C. Observations were made following administration of bromocriptine 5-20 mg/kg. Bromocriptine was dissolved in a minimum volume of ethanol and appropriate dilutions in 0.9% w/v NaCl solution (saline) were made to allow the dose to be administered in a total volume of 0.7-1.0 ml. The effect of the ethanol saline vehicle alone was

observed. Temperatures were also recorded following blockade of dopamine receptors with pimozide, which was dissolved in a minimum volume of glacial acetic acid, and then diluted.

Results The colonic temperature began to fall 10 min after intraperitoneal injection of bromocriptine 5-20 mg/kg. This hypothermic response was sustained for the full 1.5 h over which the

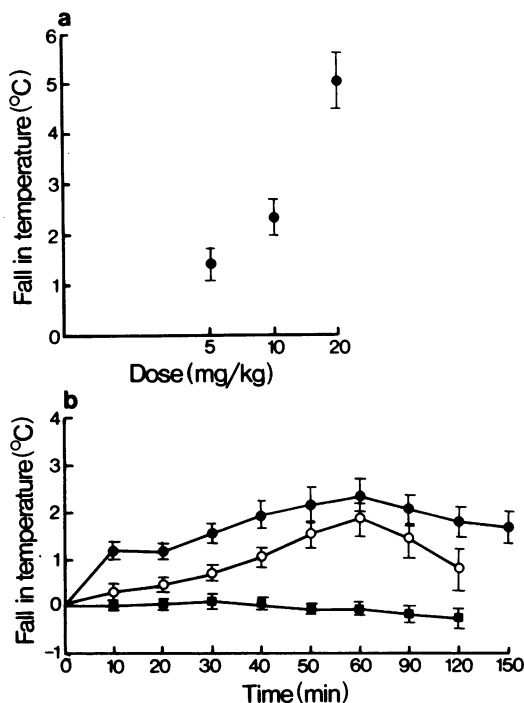


Figure 1 (a) Dose-response relationship for the maximum fall in colonic temperature induced by bromocriptine. The vertical bars show s.e. mean. (b) Inhibition of the hypothermic action of bromocriptine by pimozide. (●) Bromocriptine 10 mg/kg; (○) bromocriptine 10 mg/kg, 1 h after pretreatment with intraperitoneal pimozide, 1 mg/kg; (■) vehicle without drugs. The vertical bars show s.e. mean.

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temperature was recorded. The hypothermia was dose-dependent, 20 mg/kg of bromocriptine producing a fall in temperature of 5°C (Figure 1a).

The dopamine receptor blocking drug pimozide (Andén, Butcher, Corrodi, Fuxe & Ungerstedt, 1970) was administered 1 h before bromocriptine in order to establish whether the fall in temperature could be modified by inhibition of dopamine receptors. Pimozide reduced the hypothermic action of bromocriptine (Figure 1b).

Administration of the ethanol saline vehicle intraperitoneally caused short-lasting, 10-15 min sedation but had no effect on colonic temperature (Figure 1b).

Discussion Bromocriptine decreases prolactin secretion (Del Pozo, Brun, Varga & Friesen, 1972) and has been employed to decrease lactation (Varga, Lutterbeck, Pryor, Wenner & Erb, 1972). The mechanism of prolactin suppression is thought

to be a dopaminergic effect on the hypothalamic pathways concerned with secretion of prolactin inhibitory factor into the portal circulation of the anterior pituitary. Bromocriptine has been found to induce rotational behaviour in rats with unilateral nigrostriatal lesions induced by 6-hydroxydopamine (Corrodi *et al.*, 1973), in the same way as levodopa and dopamine agonists such as apomorphine and piribedil (Ungerstedt, 1971; Corrodi, Fuxe & Ungerstedt, 1971). There is substantial evidence that dopamine mediates hypothermia in rats placed in a cold ambient temperature (Kruk, 1972; Yehuda & Wurtman, 1972), so the findings reported here provide further support for the view that bromocriptine is a dopamine receptor agonist.

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