clopramide (IC_{50} 5×10^{-4} M and EC_{50} 2×10^{-5} M respectively), but was unaffected by sulpiride. Clebopride did not inhibit dopamine uptake, but had a marked effect on release (EC_{50} 1×10^{-7} M). These values compare with an uptake IC_{50} value of 9×10^{-9}M for nomifensine and a release EC_{50} value of 1×10^{-8} for amphetamine.

These data suggest that the substituted benzamides investigated do interact *in vitro* with dopamine receptors, although they have no consistent effect on dopamine-sensitive adenylate cyclase, nor do they consistently influence presynaptic dopamine uptake or release. They do cause an increase in cerebral dopamine metabolites, which is dependent on nerve impulse flow as judged by the effects of GOBA. Such an increase in HVA is sensitive to atropine in the case of sulpiride, but not in the case of metoclopramide and clebopride. Thus, substituted benzamides resemble classical neuroleptics in some respects, but differ in others.

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Antipodal central effects of dopamine and apomorphine

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Cohen & Berkowitz (1975) suggested there were two types of dopamine receptor, based on the response of rat aortic strips to dopamine and to apomorphine. Cools & van Rossum (1976) postulated that there were 'two types of dopamine site' in the central nervous system. Clear-cut differences (Table 1) in the effects of dopamine and apomorphine infused into the hypothalamus and the third cerebral ventricle were observed in young and adult chickens (*Gallus domesticus*).

Thus dopamine (0.1 μmol) infused into the hypothalamus of young chicks pretreated with mebanazine (10 μmol/100 g i.v. 18 h and 1 h previously) induced behavioural and electrocortical sleep, suppressed vocalization, body temperature declining up to 6°C at thermoneutrality and mean CO_2 elimination falling 55%, effects lasting 4–6 hours. In contrast, apomorphine (0.05 μmol) infused into the identical site evoked behavioural and electrocortical arousal, vocalization and pecking, accompanied by an 0.5°–1°C increase in body temperature at thermoneutrality, and a mean increase in CO_2 elimination of 70%. The effects on body temperature lasted about 40 min, and 20–30 min for other variables. Apomorphine (0.025 μmol/100 g i.v.) evoked behavioural and electrocortical arousal in chicken encéphale isolé preparations. Similar effects to the doses infused into the hypothalamus were elicited by dopamine (0.5 μmol) and apomorphine (0.25 μmol) given into the third cerebral ventricle of adult fowls at thermoneutrality.

Table 1 Effects of dopamine and apomorphine infused into the hypothalamus and third cerebral ventricle of chickens

	Dopamine	*Apomorphine*
Behaviour	Sleep	Arousal
Electrocortical activity	Slow wave, large amplitude	Fast frequency, small amplitude
Posture	Standing or squatting, wings lowered	Standing (wing abduction in adult only)
Vocalization	Decreased	Increased
Body temperature	Decreased	Increased
CO_2 elimination	Decreased	Increased
Effective antagonists	Phenoxybenzamine	Spiroperidol (encéphale isolé)
Ineffective antagonists	Spiroperidol, propranolol	Phenoxybenzamine, propranolol
Effects of amphetamines	Dissimilar to those of dopamine	Resembled those of apomorphine

The effects of dopamine but not apomorphine were attenuated by phenoxybenzamine (0.1 μmol) given previously into the hypothalamus. In contrast, the effects of apomorphine were attenuated by spiroperidol (0.0025 μmol/100 g i.v.). Phentolamine, even in doses as small as 0.005 μmol given centrally, elevated body temperature 1°C for 4–5 h, so precluding testing with an adequate dose-ratio against the agonists. Propranolol was ineffective against both substances. Whereas the effects of apomorphine resembled those of dexamphetamine, doses of methysergide (0.01 μmol/100 g i.v.) that prevented arousal with dexamphetamine did not affect response to apomorphine. The results are compatible with the existence of two types of central dopamine receptor in chickens.

B.A.K. is an MRC Student.

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Origin of dopaminergic afferents to the rat frontal cortex

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Dopamine is present in two areas of the rat frontal cortex, the medial prefrontal and cingulate cortex, where it is believed to be contained in nerve fibres (Thierry, Stinus, Blanc & Glowinski, 1973; Lindvall, Björklund, Moore & Stenevi, 1974). Using a sensitive radioenzymatic assay for dopamine (DA) and noradrenaline (NA) (Cuello, Hiley & Iversen, 1973) we have mapped the distribution of these two catecholamines in the areas and layers of the prefrontal and cingulate cortex. In particular, we investigated the response of these two catecholamines to lesions designed to deplete selectively either DA or NA in the frontal cortex.

The quantities of DA and NA in the dorsal, and medial prefrontal and cingulate cortical areas are indicated in Table 1. The unilateral injection of 6-hydroxydopamine (6OHDA) 8 μg in 2 μl saline (ascorbic acid 1 mg/ml) into the ascending NA projections in the central tegmental tract (Mason & Iversen, 1975) resulted in an almost complete depletion of the frontal cortex NA. In contrast the content of DA was increased in those areas of frontal cortex believed to contain DA terminals and reduced in areas which contain mainly NA. Thus in the dorsal prefrontal cortex area DA is probably a precursor of

Table 1 The effects of various lesions on the catecholamine content of the rat frontal cortex

	Cortical area assayed	*Dopamine content ng/g*	*% change relative to control*	*Noradrenaline content ng/g*	*% change relative to control*
Control samples	+DPFC	24.6 ± 3.7 (6)	—	134 ± 21 (6)	—
	+MPFC	74.5 ± 11.6 (6)	—	137 ± 23 (6)	—
	+CgFC	48.0 ± 6.4 (5)	—	114 ± 29 (6)	—
6-hydroxydopamine (8 μg/2 μl saline) into ascending noradrenaline bundle	DPFC	14.5 ± 5.6 (7)	−41%	3.2 ± 3.3* (7)	−97.2%
	MPFC	104 ± 25* (7)	+39%	8.2 ± 3.6* (7)	−95.4%
	CgFC	72.4 ± 22.3* (7)	+50%	14.8 ± 7.1* (7)	−87.0%
Electrolytic lesion in ventral tegmental area	DPFC	20.3 ± 14.4 (6)	−6.7%	146 ± 7 (6)	+8.9%
	MPFC	24.8 ± 13.4* (6)	−63%	136 ± 19 (6)	+0.7%
	CgFC	32.2 ± 3.9* (6)	−33%	125 ± 14 (6)	+9.6%
6-hydroxydopamine (4 μg/μl saline) into lateral substantia nigra	DPFC	23.1 ± 3.9 (6)	−7%	138 ± 21 (6)	+2.1%
	MPFC	76.3 ± 41.4 (6)	+3%	120 ± 19 (6)	−13.5%
	CgFC	36.3 ± 2.5* (6)	−25%	109 ± 22 (6)	−4.4%

+ DPFC—Dorsal prefrontal cortex, MPFC—Medial prefrontal cortex, CgFC—Cingulate cortex. Numbers of determinations given in brackets. Statistical analysis by paired *t*-test. Significance (*) taken at $P < 0.05$.