Table 1 Effect of intracerebral injection of apomorphine and dopamine

Drug		Mean change in core temperature (°C ± s.e. mean) PO/AH	CN	IIIV	LV
Saline		+0.2 ± 0.1	+0.1 ± 0.1	−0.2 ± 0.1	+0.4 ± 0.2
Apomorphine	1.25 μg	−0.3 ± 0.1*	–	−0.3 ± 0.2	–
	5.0 μg	−0.8 ± 0.3**	−0.2 ± 0.1	−0.3 ± 0.1	+0.4 ± 0.1
	10.0 μg	−1.0 ± 0.2**	−0.2 ± 0.2	−0.6 ± 0.1*	+0.3 ± 0.1
	20.0 μg	−0.9 ± 0.2**	−0.6 ± 0.2*	−0.8 ± 0.3	+0.3 ± 0.2
Dopamine	5.0 μg	−0.4 ± 0.1*	–	–	–
	10.0 μg	−0.7 ± 0.2**	–	−0.5 ± 0.1	+0.3 ± 0.1
	20.0 μg	−0.8 ± 0.2**	−0.2 ± 0.1	–	–

Mean of maximum change in core temperature occurring within 40 min of injection into preoptic-anterior hypothalamus (PO/AH), caudate nucleus (CN), third ventricle (IIIV) and lateral ventricle (LV).
n = between 4 and 11 observations, * $P < 0.05$, ** $P < 0.01$.

temperatures were measured. Although a fall in core temperature was always preceded by a rise in skin temperature, the change in core temperature was more consistent and was used in the expression of results (Table 1). Of the sites tested the preoptic-anterior hypothalamus was the most responsive. When equieffective doses of apomorphine were compared, the time for maximum response was significantly shorter after intrahypothalamic injection (5 μg = 7.0 ± 2.0 min) than after either third ventricular (10 μg = 18.5 ± 1.4 min) or intracaudate injection (20 μg = 20.0 ± 5.7 min).

These results suggest that the most likely site of action of dopamine and apomorphine after intracerebral injection is the preoptic-anterior hypothalamus. That dopamine receptors are involved is indicated by the finding that an i.p. injection of pimozide 0.5 mg/kg antagonized the effect of intrahypothalamic injections of each of the agonists.

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Comparison of the effects of dopamine and noradrenaline on single cortical neurones

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Cortical neurones can respond with both excitation and depression to microelectrophoretically applied noradrenaline (NA) (Johnson, Roberts, Sobieszek & Straughan, 1969). We have recently presented evidence that the excitatory responses are mediated by α-adrenoceptors, whereas the depressant responses are mediated by β-adrenoceptors (Bevan, Bradshaw & Szabadi, 1976). Cortical neurones are also sensitive to dopamine (DA), both excitatory and depressant responses having been described (Bevan, Bradshaw & Szabadi, 1975; Stone, 1976). However, it has not yet been established whether DA and NA act at pharmacologically distinct receptors on these cells.

Single spontaneously active neurones were studied in the somatosensory cortices of halothane-anaesthetized rats. All the drugs were applied by microelectrophoresis.

The direction of the responses (excitation or depression) evoked by DA and NA were compared on 46 cells. All these cells responded in the same direction to the two catecholamines, 30 being excited and 16 being depressed by both drugs.

We have compared the effects of the α-adrenoceptor antagonists phentolamine and phenoxybenzamine and the neuroleptic drug haloperidol (a drug which is believed to block DA receptors, see Woodruff, 1971) on excitatory responses to DA and NA. Acetylcholine (ACh) was used as a control agonist. The effects of phentolamine were studied on 4 cells. On all of these cells phentolamine reversibly antagonized excitatory responses to NA and DA without affecting excitatory responses to ACh. On one of the cells the excitatory responses to both NA and DA were reversed into depressant responses in the presence of phentolamine.

The effects of phenoxybenzamine were examined on 8 cells. On all the cells tested phenoxybenzamine reversibly antagonized the response to NA without affecting the response to ACh. On 5 cells the response to DA was also antagonized; however, on the remaining 3, phenoxybenzamine partially discriminated between the responses to NA and DA in that the response to DA was affected to a much lesser degree than was the response to NA.

The effects of haloperidol were tested on 6 cells. On 5 cells, the response to DA was antagonized when the response to ACh was not affected. On 4 of these, the response to NA was affected to a lesser degree than was the response to DA.

The partial selectivity of phenoxybenzamine and haloperidol may indicate that the excitatory responses to the catecholamines are mediated by two populations of receptors. One population (probably α-adrenoceptors; Bevan *et al.*, 1976) may be blocked by phenoxybenzamine, and may be more sensitive to NA than to DA. The other population may be blocked by haloperidol, and may be more sensitive to DA than to NA. It remains to be determined whether there are pharmacologically distinct receptors mediating the depressant effects of DA and NA on cortical neurones.

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On the depressant action of dopamine in rat caudate nucleus and nucleus accumbens

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The putative neurotransmitter dopamine has both inhibitory and excitatory actions on neurones. In our own studies we have found that iontophoretically-applied dopamine causes mainly depression of firing of cells in the rat caudate nucleus and nucleus accumbens; however, several workers have reported excitatory actions of dopamine in the caudate nucleus (for references see Woodruff, McCarthy & Walker, 1976).

Recently, Kitai, Sugimoro & Kocsis (1976) suggested that the depressant action of dopamine in the striatum might be due to an excitation of inhibitory interneurones. If this were so, the depressant action of dopamine should be prevented by antagonists of the inhibitory transmitter involved.

Extracts of rat striatum or nucleus accumbens contain appreciable amounts of γ-aminobutyric acid (GABA), glutamate, glycine, aspartate and taurine. In the present study we have examined the possibility that one of the above amino acids might be involved in the inhibitory actions of dopamine.

Extracellular recordings were made from neurones and drugs were applied microiontophoretically, using techniques described by Crossman, Walker & Woodruff (1974). Neurones were either spontaneously active or were driven by DL-homocysteic acid (100 mM, pH 9.0). Other drugs were applied from 100 mM solutions at pH 3.5, except strychnine (6 mM,