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,

pH 3.5), picrotoxin (saturated solution in 150 mM NaCl), glutamate and aspartate (each 100 mM, pH 9.0) and α-flupenthixol (200 mM, pH 2.0).

The activity of neurones in both the nucleus accumbens and caudate nucleus was consistently depressed by GABA (10–30 nA), glycine (10–30 nA), dopamine (10–50 nA) or taurine (10–50 nA). Glutamate and aspartate caused excitation of all cells tested. Strychnine (60 nA for 4 min) reversibly blocked the depression produced by glycine (24 neurones), but had no effect on responses to GABA or dopamine in either the nucleus accumbens (12 cells) or caudate nucleus (8 cells). In both regions of the brain picrotoxin (70 nA for 5 min) reversibly antagonized the inhibitory actions of GABA and taurine, but had no effect on responses to glycine (14 cells) or dopamine (16 cells). α-Flupenthixol selectively blocked the depressant action of dopamine on 9 out of 20 neurones in the caudate nucleus and on 12 out of 22 cells tested in the nucleus accumbens. α-Flupenthixol has been shown to have a similar action in cat putamen and amygdala (Ben-Ari & Kelly, 1976).

Our results suggest that, although GABA, taurine and glycine might be inhibitory transmitters in the nucleus accumbens and caudate nucleus, it is unlikely that they are involved in mediating the depressant actions of dopamine in these regions of the brain.

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The effect of iron deficiency on brain monoamine metabolism and the behavioural responses to increased brain 5-hydroxytryptamine and dopamine synthesis

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Iron has been suggested to be a co-factor for monoamine oxidase (see Youdim, 1976), tryptophan and tyrosine hydroxylase. It has been shown that iron deficiency anaemia lowers the activity of monoamine oxidase both in rat liver (Symes, Sourkes, Youdim, Gregoriadis & Birnbaum, 1969; Symes, Missala & Sourkes, 1971) and human platelets (Youdim, Woods, Mitchell, Grahame-Smith & Callender, 1975). In the brain these enzymes are involved in the synthesis and catabolism of the monoamine neurotransmitters. However there has been little investigation of the effects of iron deficiency anaemia on the metabolism and function of 5-hydroxytryptamine (5-HT), dopamine (DA) or noradrenaline (NA). We have now investigated the effect of iron deficiency anaemia in rats on various enzymes involved in central monoamine metabolism and on the functional activity of 5-HT and DA.

Rats were fed a semi-synthetic diet lacking in iron (McCall, Newman, O'Brien, Valberg & Witts, 1962) and distilled water. Control rats were given the same diet with iron added and tap water. After approximately 5 weeks when the rats were iron-deficient (haemoglobin (g/dl); control 14.2 ± 0.44 (16) experimental: 5.55 ± 0.42 (22), $P < 0.001$) it was found that brain non-haem iron stores were decreased by 60%. At this time the activities of tryptophan hydroxylase, aldehyde dehydrogenase and monoamine oxidase were unaltered in the brain.

The concentration of brain 5-HT was somewhat decreased (control 0.38 ± 0.02 μg 5-HT/g brain (wet wt) (6); experimental 0.31 ± 0.02 (9), $P < 0.01$) possibly because of decreased 5-HT binding at the nerve ending, since Fe^{++} has been implicated in this process (Tamir, Klein & Rapport, 1976). However, DA and NA concentrations were unaltered, as was the rate of 5-HT synthesis.

The iron-deficient rats showed inhibition of the hyperactivity response following administration of tranylcypromine (20 mg/kg) and L-tryptophan (100 mg/kg) a procedure which increases brain 5-HT