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

synthesis, despite the rate of 5-HT accumulation being the same in both groups. (Total movements in the 90 min following L-tryptophan, control 8680 ± 1102, experimental 3468 ± 166, 3 observations each, $P < 0.01$). The hyperactivity response to the suggested 5-HT agonist, 5-methoxy *N,N*-dimethyl tryptamine was also inhibited in these animals indicating an interference with the mechanisms by which 5-HT brings about the hyperactivity syndrome (see Green & Grahame-Smith, 1976).

The locomotor response of iron-deficient rats to tranylcypromine (20 mg/kg) and L-dopa (100 mg/kg) was also inhibited although there was no difference in the accumulation of DA and NA from controls.

The response to methamphetamine (2 mg/kg) and apomorphine (2 mg/kg) was also decreased. This suggests that DA responses were inhibited in the iron deficient-group.

The DA and 5-HT mediated responses became normal after feeding the iron-deficient group with the iron-plus diet for 7 days. At this time the haemoglobin values approached normal (12.2 ± 0.42 g/dl (6)).

These results will be discussed in relation to the role of iron in the mechanisms of monoamine neurotransmission.

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Ultrastructural changes in the coronary vascular system following prolonged emotional stress. An experimental model for the study of coronary vascular disease?

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Following exposure of the rat to a variety of stressful situations there occurs an elevation of circulating corticosterone (11-OHCS). Work from this laboratory indicates that the elevation can be quantitated, in that rats exposed to signalled regular footshock (2 s of 2 mA scrambled footshock every 88 s for 45 min, i.e. 30 trials) show an intermediate (45–55 μg/100 ml blood plasma), and that rats exposed to irregular signalled footshock with the possibility of escape (7 shock exposures randomly placed in a 35 min session) show extreme (85–95 μg/100 ml blood plasma) (Bassett, Cairncross & King, 1973) steroid elevation. Intermediate 11-OHCS elevation is independent of the physical intensity of the stressor, and the extreme 11-OHCS elevation occurs only with unpredictability of stress. The contention is made therefore, that extreme steroid elevation contains a psychological component which when superimposed on the physical stress response produces an increment in 11-OHCS output (Cairncross & Bassett, 1975).

The 'psychological increment' of the stress response appears to be linked with unpredictability in the timing of the stressor, and might be considered of emotional derivation. Such a derivation has long been implicated in the pathogenesis of cardiovascular disease. It seemed not unreasonable therefore to expose male rats to the irregular signalled footshock regimen over a prolonged period of time (70 days) and to examine during and at the end of that period, not only the degree of 11-OHCS elevation, but also the morphological changes which could predictably occur within the cardiovascular system and within other physiological systems.

The morphological changes obtained with light microscopy were largely confined to the microcirculation of the coronary vasculature, and included, at 70 days, a significant degree of congestion and