paratyrosine methyl ester in saline; 10 mg/kg reserpine suspended in Tween 80.

For the acute experiments animals were anaesthetized with 1-1.25 g/kg urethane, and the frontoparietal cerebral cortex was exposed. To compare responses in normal and amine-depleted animals only one type of cell was studied. These were pyramidal tract cells with antidromic latencies of less than 3.0 ms. Five-barrelled micropipettes filled with 200 mM solutions of the various drugs were used for microiontophoresis. Ejecting currents of 60 nA were applied for 15 s in all cases. Three parameters of the neuronal response were measured to allow comparison of the normal and treated animals. These were *h*, the maximum change of firing rate produced, *t*, the time taken to reach that maximum, and *d*, the total duration of the response.

The reduction of amine levels was confirmed by fluorimetric estimation of noradrenaline and dopamine in the cortex.

Dopamine responses were unchanged in the amine depleted animals when compared to controls. Responses to amphetamine and amantadine were significantly reduced in amplitude *h*, but were not abolished. The parameters *t* and *d* were unchanged.

Failure to abolish amphetamine responses by amine depletion has been reported in the cerebellum (Kostopoulos & Yarborough, 1974) and caudate nucleus (Feltz & de Champlain, 1972) and seems to indicate an important difference in the action of amphetamine in these areas and in the brain stem (Boakes, Bradley & Candy, 1972).

The present experiments suggest that on pyramidal tract cells amphetamine and amantadine do not act solely by releasing stored catecholamines.

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Effect of dopamine-β-hydroxylase inhibitors and centrally administered noradrenaline on (+)-amphetamine anorexia in mice.

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Whilst the finding that α-methyl p-tyrosine antagonizes (+)-amphetamine anorexia in mice (Abdallah, 1971) implied possible involvement of catecholamines in the production of (+)-amphetamine anorexia in this species, resolution of the individual function of dopamine and noradrenaline in this capacity has not been attempted. Consequently, we have undertaken a preliminary study of the interactions between (+)-amphetamine, noradrenaline and centrally acting dopamine-β-hydroxylase inhibitors in mice.

Male albino mice of an ICI strain, weighing 20-25 g were housed in groups of 8 at an environmental temperature of 25 ± 1°C and trained over 10 days to adapt to a daily 3 h period of a 41B cube diet consumption. Water was given *ad libitum*. In trained mice, (+)-amphetamine injected subcutaneously, 15 min before feeding, produced a dose related depression of food intake during the first hour of feeding, and 2 mg/kg which produced a submaximal response, was subsequently used as the standard anorexic dose.

Intracerebroventricular (icv) injection of noradrenaline (4 and 8 μg in 5 μl saline) 25 min before feeding, potentiated (+)-amphetamine anorexia significantly ($P < 0.01$) only at the higher dose level. At doses of 250 and 500 mg/kg both disulfiram given orally 3 h before food and sodium diethyldithiocarbamate (DDC) given intraperitoneally 2 h before food markedly potentiated (+)-amphetamine anorexia ($P < 0.001$, $P < 0.001$). Neither noradrenaline nor the dopamine-β-hydroxylase inhibitors significantly influenced feeding when given alone at these dose levels. However, the potentiation of (+)-amphetamine anorexia by DDC was partially, though significantly reversed by noradrenaline (4 and 8 μg icv ($P < 0.05$, $P < 0.001$), although noradrenaline and DDC in combination did not significantly alter feeding compared with saline controls.

The potentiation of (+)-amphetamine anorexia by dopamine-β-hydroxylase inhibitors in mice differs from the antagonism seen in rats (Frey & Schulz, 1973) and this discrepancy may reflect species variation in the mechanism of action of (+)-amphetamine and/or DDC. In addition, although the potentiation of (+)-amphetamine anorexia by icv noradrenaline appears consistent with an involvement of noradrenaline in the mediation of (+)-amphetamine anorexia, this finding is difficult to reconcile with the potentiation of (+)-amphetamine anorexia brought about by DDC and disulfiram and the partial reversal by icv noradrenaline of the intense anorexia following DDC pretreatment. Nevertheless, both sets of results remain compatible with an influence of the noradrenergic component of the central action of (+)-amphetamine on the anorexia produced by this drug in mice although the exact nature of this role requires further study.

However, the conflicting nature of these results leads us to suspect that the mechanisms underlying (+)-amphetamine anorexia in mice cannot be interpreted solely in terms of noradrenergic systems and in spite of the lack of direct evidence, when considered in conjunction with the results of Abdallah (1971), they appear to indicate the possibility of a significant dopaminergic component in the production of anorexia by (+)-amphetamine in the mouse.

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The mechanism of the effect of dopamine-β-hydroxylase inhibitor FLA-63 on the L-DOPA reversal of reserpine akinesia

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The effects of dopamine-β-hydroxylase inhibitors (DBHI) on behaviour are thought to result from their ability to deplete cerebral noradrenaline (NA) (Svensson & Waldeck, 1969). The pattern of motor activity produced by L-DOPA in reserpinized animals is attenuated by pre-treatment with the DBHI bis-(4-methyl-1-homopiperazinylthiocarbonyl)disulphide (FLA-63) (Ahlenius & Engel, 1971; Marsden, Dolphin, Duvoisin, Jenner & Tansy, 1974).

We have therefore compared the effect of pre-treatment with FLA-63 on the reversal of reserpine akinesia by L-DOPA with changes in brain catecholamine content.

Pre-treatment with i.p. FLA-63 caused a dose-dependent increase in locomotor activity in

Table 1 Effect of L-DOPA (200 mg/kg i.p. plus the peripheral decarboxylase inhibitor α-methyldopa hydrazine 25 mg/kg i.p.) on motor activity and whole brain catecholamine content in mice reserpinized (10 mg/kg i.p.) 18-24 hours previously. Animals are given either saline or FLA-63 one hour prior to L-DOPA.

Pretreatment	*Animex Counts 1st hour after L-DOPA*	*DA ng/g 45 mins after L-DOPA*	*NA ng/g 45 mins after L-DOPA*
Saline (0.1 ml i.p.)	2520.5 ± 294.4 (45)	972.8 ± 117.6 (12)	52.1 ± 12.4 (14)
FLA-63 (10-25 mg/kg i.p.)	2729.3 ± 322.9 (24)	1667.9 ± 208.8^{c} (8)	31.8 ± 11.4 (8)
FLA-63 (40-50 mg/kg i.p.)	3704.6 ± 400.0^{b} (14)	2166.8 ± 372.9^{c} (11)	49.2 ± 8.9 (11)
	2nd and 3rd hour after L-DOPA	*120 mins after L-DOPA*	*120 mins after L-DOPA*
Saline (0.1 ml i.p.)	10641.5 ± 505.6 (41)	2109.9 ± 199.1 (10)	67.5 ± 17.4 (12)
FLA-63 (10-25 mg/kg i.p.)	7210.3 ± 713.0^{d} (23)	3792.4 ± 595.8^{d} (8)	15.0 ± 2.6^{a} (8)
FLA-63 (40-50 mg/kg i.p.)	5134.9 ± 1108.1^{d} (9)	3026.3 ± 453.4^{a} (11)	19.3 ± 1.9^{a} (9)

The results are given ± s.e.mean and the number of experiments is indicated in brackets. Significant differences from control values are given by superscripts $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.005$, $^{d}P < 0.001$.