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 $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.005$, $^{d}P < 0.001$.

the first hour after L-DOPA compared with control animals; this was associated with a dose-dependent increase in DA but no significant change in the NA content of whole brain at 45 min after L-DOPA administration. Pre-treatment with FLA-63 caused a dose-dependent suppression of locomotor activity compared with control animals in the second and third hours after L-DOPA; this was associated with a significant decrease in brain NA in the presence of persistent and significant elevations in brain DA, as shown in Table 1.

Further experiments to exclude possible stressful effects of FLA-63 (Moore & Thornburg, 1971) showed that FLA-63 administered in solution by oral intubation did not produce any hypermotility in the first hour after L-DOPA (the Animex counts for high and low dosage levels were 73 and 64% of controls respectively). This was associated with significantly increased DA and decreased NA. In the second time period there was no significant difference between the two routes of FLA-63 administration in either the effect on motor activity or the CA levels. Furthermore, neither corticosterone (3 mg/kg s.c.) nor β-methasone (0.1 mg/kg s.c.) given 15 min before L-DOPA had any significant effect on L-DOPA induced motor activity.

Thus, it appears that the effects of FLA-63, whether administered orally or intraperitoneally, in reducing L-DOPA induced locomotor activity in the reserpinized animal are due primarily to the extent of reduction in cerebral NA, and cannot be explained by stressful effects.

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Dopaminergic and cholinergic interactions in the caudate nucleus in relation to the induction of sleep in the cat

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The onset of sleep is characterized by the appearance of spindles (8-12 Hz activity) in the electroencephalogram. Electrical stimulation of the caudate nucleus elicits similar spindles (Buchwald, Wyers, Okuma & Heuser, 1961). Using a push-pull cannula localized areas of the brain can be perfused and stimulated (Philippu, Przuhtek & Roensberg, 1973). The present study was carried out to examine the effects of perfusions of dopamine and acetylcholine on spontaneous and electrically induced spindles.

Experiments were carried out on *encéphale isolé* cats. A bi-polar stimulating electrode was placed stereotaxically in the head of the caudate nucleus. The anode of the electrode was a tube which was also used for perfusions. Throughout the experiment the nucleus was perfused with artificial cerebro-spinal fluid (c.s.f., 150 μl/min at 38° C). Drugs were added to the c.s.f. as required, and perfused for 15 min intervals, alternating with c.s.f. alone. Cortical activity was recorded from frontal, parietal and occipital lobes and was correlated with behavioural signs of waking or sleeping.

Perfusions of acetylcholine (5.5×10^{-2} or 5.5×10^{-1} M) plus the anticholinesterase physostigmine (2×10^{-9} M) inhibited spontaneous spindling and this effect was atropine sensitive. In some cats perfusions of dopamine (5×10^{-6} M) plus the monoamine oxidase inhibitor tranylcypromine (2×10^{-8} M) increased spontaneous spindling. However, injections of 0.2 μl of dopamine (9.5×10^{-4} mol or 9.5×10^{-3} mol) into the caudate nucleus invariably induced ipsilateral frontal spindles which, in most cats, developed into behavioural and electroencephalographic sleep.

When the caudate nucleus was stimulated electrically, a strength of stimulus (pulse width 0.5 ms) was selected which produced ipsilateral frontal spindles. Repeated stimulation at 5 s intervals for up to 1 min produced similar