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

responses and in some cats induced sleep. Perfusion of c.s.f. containing dopamine plus tranylcypromine potentiated the effects of stimulation. This was observed as a spread of spindles into the contra-lateral frontal, and non-frontal cortices. In some animals, stimulation which did not produce sleep during control perfusions of c.s.f., induced sleep during perfusions of dopamine plus tranylcypromine. Perfusion of acetylcholine plus physostigmine reduced or abolished the spindling induced by electrical stimulation.

These results suggest that dopaminergic and cholinergic mechanisms in the caudate nucleus are involved in the control of cortical spindling.

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Hypotensive action of α-methyldopamine

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It is generally agreed that α-methyldopa exerts a hypotensive action via interference with the sympathetic nervous system, and that α-methyldopa must undergo decarboxylation to form α-methyldopamine and α-methylnoradrenaline in order to exert this effect (Davis, Drain, Horlington, Lazare & Urbanska, 1963). Carlsson & Lindqvist (1962) suggested that these decarboxylation products of α-methyldopa may take over the functions of monoamines in the brain, and Day & Rand (1964) extended this hypothesis to peripheral adrenergic nerves.

Most of the studies on α-methyldopa have concentrated on α-methylnoradrenaline as a false transmitter in the periphery although recent evidence suggests a central locus of action of α-methyldopa (Henning & Van Zwieten, 1968; Finch & Haeusler, 1973).

In this study we have examined the activity of α-methyldopamine which has been largely neglected, although Farmer (1965) has shown that it impairs peripheral sympathetic nerve activity and Heise & Kroneberg (1973) have demonstrated a central hypotensive action when α-methyldopamine was infused intraventricularly into the chloralose anaesthetized cat.

α-Methyldopamine (50-200 μg i.c.v.) caused a dose-related fall in blood pressure in conscious spontaneous hypertensive rats. Pretreatment with intraventricular 6-hydroxydopamine (3 x 250 μg) prevented this hypotensive effect of α-methyldopamine (150 μg i.c.v.). Intraventricular administration of phentolamine (200 μg) or desmethylimipramine (200 μg), but not haloperidol (0.5 mg/kg i.p.) prevented the hypotensive action of α-methyldopamine (150 μg i.c.v.). Pretreatment with U-14, 624 (200 mg/kg i.p.), a selective central dopamine-β-hydroxylase inhibitor also prevented the hypotensive effect of α-methyldopamine (150 μ i.c.v.).

In the chloralose anaesthetized cat pressor responses elicited by stimulation of the midbrain reticular formation (Finch & Haeusler, 1973) were reduced after intraventricular injection of α-methyldopamine (1 mg) and completely abolished with 5 mg.

Intraventricular administration of α-methylnoradrenaline (20-100 μg) to the chloralose anaesthetized cat caused dose related pressor responses.

Intravenous α-methyldopamine was considerably less potent than noradrenaline as a pressor agent in the pithed rat, but noradrenaline and α-methylnoradrenaline were found to be equipotent.

These results suggest that the hypotensive effect of α-methyldopamine may be mediated via central action of α-methylnoradrenaline on α-adrenoceptors. As a prerequisite α-methyldopamine must be taken up into adrenergic neurones to produce this effect. However, α-methylnoradrenaline (i.c.v.) in chloralose-anaesthetized cats caused a dose related rise in blood pressure which does not support this hypothesis.

Since α-methyldopamine is considerably less potent than noradrenaline as a pressor agent in the pithed rat, it is possible that this might reflect partially, a false transmitter action of α-methyl-