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-

dopa in the periphery, but the present observations still support a central hypotensive action.

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The potentiation of certain effects of amphetamine by inhibitors of prostaglandin synthesis

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Sever & Trelinski (1974) have shown that indomethacin, a prostaglandin synthesis inhibitor (PGSI), potentiates the hyperthermic effect of amphetamine in the rat.

We now report other studies in which we show that other PGSIs (mefenamic acid, flufenamic acid and antipyrine) also potentiate the amphetamine-induced hyperthermia in rats, and alter the pattern of behavioural stimulation in rats and mice.

Female Wistar rats (150-200 g body weight) were used, and the hyperthermic effect of amphetamine measured as described previously (Caldwell, Sever & Trelinski, 1974). Drug induced behavioural changes were measured both in rats (housed singly) and in female T.O. mice (20-25 g body weight) in groups of six (Sever, Caldwell & Williams, in preparation). The PGSIs were administered orally 1 h prior to the intraperitoneal injection of D-amphetamine (5 mg/kg). Control animals were treated with normal saline.

A dose related potentiation of amphetamine induced hyperthermia was caused by indomethacin (5-15 mg/kg) mefenamic acid (50-200 mg/kg), flufenamic acid (50-200 mg/kg) and antipyrine (50-150 mg/kg). However, paracetamol (50-300 mg/kg) had no effect on the intensity of the hyperthermia. All of the PGSIs altered the pattern of behavioural stimulation seen after amphetamine, but there was species variation in the nature of the changes. In the rat, the gross locomotor stimulation was decreased, but stereotyped behaviour was unchanged, while in the mouse, the converse occurred.

In further experiments, rats were given 6-hydroxydopamine (100 mg/kg i.v.) to destroy catecholamine-containing nerve terminals in the periphery. Forty-eight hours later, they were given PGSIs or saline, followed by amphetamine, as before. No hyperthermia was observed in either test or control group.

Indomethacin, mefenamic acid, flufenamic acid and antipyrine which are inhibitors of peripheral PG synthesis (Flower, 1974) all produced a potentiation of the amphetamine hyperthermia. However, this was not seen in animals pretreated with 6-hydroxydopamine. Paracetamol, which only inhibits brain PG synthesis (Flower, 1974), is without effect on the amphetamine hyperthermia, this hyperthermia depending on intact peripheral noradrenergic neurones (Caldwell *et al.*, 1974). It has been suggested that inhibition of PG synthesis abolishes the PG control over noradrenaline release (Smith, 1972), leading to a potentiation of the hyperthermic effect of amphetamine (Sever & Trelinski, 1974) and the results here are consistent with this view.

The pretreatment of animals with PGSIs followed by amphetamine also leads to changes in the pattern of behavioural stimulation due to amphetamine. Since the central stimulant action of amphetamine is apparently due to catecholamine release in the brain (Costa & Groppetti,