Studies on the role of catecholamines in the frontal cortex

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The frontal cortex is believed to play a role as an inhibitor of behavioural stimulation (Iversen, Wilkinson & Simpson, 1971). Although it is thought that the frontal cortex modulates the activity of dopaminergic neuronal systems (Glick & Cox, 1976) the mechanisms governing this effect are obscure. The existence of dopamine (DA) (Thierry, Stinus, Blanc & Glowinski, 1972) and noradrenaline (NA) (Fuxe, 1965) terminals in this region might suggest that the catecholamines play an important role at this site. DA and NA have a behaviourally stimulant role in limbic and extrapyramidal areas, but their roles in cortical regions are unknown. In this study we have compared the effects of electrolytic and 6-hydroxydopamine (6-OHDA) lesions on the behavioural responses produced by DA agonists and antagonists.

Bilateral electrolytic (2 mA for 10 s) or 6-OHDA (8 μg/2 μl plus 20 mg/kg desipramine, i.p.) lesions were placed stereotaxically in the frontal cortex of male Porton rats (A 10.3, L ± 0.8, V + 1.5; König & Klippel, 1963).

Both types of lesion significantly enhanced the stereotypic effects of (+) – amphetamine (1.25–5.0 mg/kg, i.p., $P<0.05$). Apomorphine (0.25–1.0 mg/kg, s.c.) – induced stereotypy was unaffected by electrolytic cortical lesions, but the effects of apomorphine (0.25 and 0.5 mg/kg) were significantly reduced by prior 6-OHDA lesioning ($P<0.005$). The cataleptic state induced by fluphenazine (0.5–2.0 mg/kg, i.p.) was reduced by electrolytic lesions of the frontal cortex ($P<0.05$) but not by 6-OHDA lesions.

The intracortical injection of DA (3.12–50 μg bilateral) into this region, induced a dose-dependent state of catalepsy, with an onset of 10–20 min and a duration of at least 3 hours. At no time were any signs of hyperactive or stereotyped behaviour observed. Intracortical injections of low doses of fluphenazine (1 and 5 μg) were without significant effect on either the stereotypic or locomotor responses induced by amphetamine (5 mg/kg i.p.), while a higher dose (10 μg) significantly reduced the stereotypic component ($P<0.05$. Mann-Whitney U test).

The results suggest that catecholamines may play a large part in the inhibitory role of the frontal cortex, and imply that this area may be an important site for the control of mesolimbic and extrapyramidal systems, where stereotyped, hyperactive and cataleptic responses are thought to be initiated. The reduction of apomorphine-induced stereotypy by 6-OHDA lesions, which might be expected to promote postsynaptic receptor sensitivity and the behavioural inhibition or catalepsy produced by intracortical dopamine, suggest that this transmitter may play a major part in frontal cortical behavioural inhibition – in direct opposition to its stimulant role in other brain areas.

CJC is an MRC student.

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The effect of desipramine on neuronal responses to tyramine and noradrenaline in the cerebral cortex

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It has been reported that the tricyclic antidepressant drug, desipramine, can both potentiate and antagonise neuronal responses to noradrenaline (Bradshaw, Roberts & Szabadi, 1974). We have now examined how neuronal responses to tyramine are affected by desipramine.

Spontaneously active single neurones were studied in the somatosensory cortex of the halothane anaesthetised rat. Drugs were applied by microelectrophoresis. The following drug solutions were used: (–)-noradrenaline bitartrate (0.05M, pH 3.0–3.5); tyramine hydrochloride (0.05M, pH 5.0); (±)-homocysteic acid (0.05M, pH adjusted to 8.0 with NaOH); desipramine hydrochloride (0.005M, pH 4.5). Our techniques have been described elsewhere (Bradshaw *et al*, 1974).

The effects of tyramine and noradrenaline were compared on 103 cells: 75 cells were excited and 26 cells were depressed by both drugs; 2 cells were excited by noradrenaline, but depressed by tyramine. The relative potencies of the two drugs were compared