5-HT-like action and, assuming hydrolysis of the ester was not immediate, are compatible with a basic charge distribution on the molecule. Although *p*-chlorophenethylamine contracted the RSS, the 5-HT-like results were not attributable to its presence in the PCPA methyl ester, the only contaminant found with thin-layer chromatography (three different solvent systems) being free PCPA (1-2%). Effects on the guinea-pig ileum could be due to PCPA methyl ester affecting calcium influx. In experiments using the superfused RSS and rat colon (Piper & Vane, 1971), bronchoconstriction which developed in guinea-pigs was apparently due to liberation of prostaglandin $F_{2\alpha}$ by PCPA methyl ester.

J.E.W. is an M.R.C. scholar.

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The effect of intraventricular 6-hydroxydopamine on the response of the conscious cat to pyrogen

CAROL A. HARVEY & A.S. MILTON*

Department of Pharmacology, The School of Pharmacy, London University and Department of Pharmacology, University Medical Buildings, Foresterhill, Aberdeen

Previously it has been shown that in the cat depletion of brain 5-hydroxytryptamine (5-HT) reduces the hyperthermic response to both bacterial pyrogen and prostaglandin E_1 (PGE_1) (Harvey & Milton, 1974). As both noradrenaline (NA) and 5-HT are thought to be concerned with temperature regulation in this species it was of interest, therefore, to determine whether depletion of brain catecholamines would also affect the response to hyperthermic agents.

Hypothalamic NA depletion was produced by injecting 6-hydroxydopamine (6-OH-DA) into the third ventricle via a previously implanted cannula. Three separate doses of 6-OH-DA (500 μg) were administered at 3 day intervals (Milton & Paterson, 1973). Fever was produced by injecting the O-somatic-antigen of *Shigella dysenteriae* (2 μg/kg) into a saphenous vein. All experiments were at an ambient temperature of 20-22° C.

Following the first dose of 6-OH-DA there was a rapid and massive fall in deep body temperature which was accompanied by panting and ear skin vasodilatation and with the animal lying prostrate on the floor of the cage. Approximately 8 h after the 6-OH-DA injection the body temperature had returned to pre-injection level. The second dose of 6-OH-DA also produced a fall in deep body temperature, but the effects were considerably less than after the first injection. The third dose of 6-OH-DA was without significant effect, and at this time body temperature was within the normal range.

In each animal fever was produced both before and after the 6-OH-DA treatment, and it was found that in all experiments there was a significant potentiation of the fever following the 6-OH-DA, both in the total thermal response and in the maximum temperature rise.

The fall in deep body temperature seen after the first dose of 6-OH-DA is consistent with a large outpouring of NA stimulating heat loss pathways. Following the second dose of 6-OH-DA when NA levels would be expected to be markedly reduced the response was small, and after the third dose at a time when not only should depletion be complete but also neuronal degeneration have taken place there was no change in deep body temperature. That the deep body temperature was normal following 6-OH-DA treatment indicates that at an ambient temperature of 20-22° C, in the cat, noradrenergic heat loss is not involved in maintaining body temperature. There is evidence that during fever, which is considered to be due to PGE release (Feldberg, Gupta, Milton & Wendlandt, 1973), heat loss pathways may exert some control (Bligh & Milton, 1973). Therefore, if in the cat, heat loss pathways are noradrenergic, their inactivation by depletion and degeneration

would explain the exaggerated response to bacterial pyrogen observed after 6-OH-DA treatment.

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Effects of some dopamine receptor stimulants on cobalt-induced epilepsy in the rat

R.C. DOW, A.G. HILL & JUDITH K. McQUEEN*

MRC Brain Metabolism Unit, University Department of Pharmacology, 1 George Square, Edinburgh EH8 9JZ

In adult male PVG rats epileptogenic lesions were produced in frontal motor cortex by the implantation of cobalt. The method has been described in detail previously (Dow, McQueen & Townsend, 1972). Electrocorticograms (ECoG) were recorded from the conscious animal and taped records were analysed for epileptiform spikes by the computer techniques of Hill & Townsend (1973). The drugs were administered intraperitoneally to rats between one and three weeks after cobalt-implantation when both primary and secondary foci are established. DL-amphetamine (0.25-10 mg/kg), apomorphine (1-10 mg/kg) and ergocornine (2.5-10 mg/kg) suppressed firing from the foci in a dose-related manner. This effect could be reduced by prior administration of spiroperidol (0.5 mg/kg) which itself exacerbated cobalt-induced spikes. However, ET495 (7-2″pyrimidyl)-4-piperonyl-piperazine) reported to be a specific dopamine receptor stimulant (Corrodi, Fuxe & Ungerstedt, 1971) did not suppress the epileptiform spikes in the dose range 1-20 mg/kg i.p. The possible sites of action of these drugs and the implications of the results will be discussed.

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