induced hypothermia in mice (Morpurgo and Theobold, 1965 ; Whittle, 1967) even though this compound finds clinical use in a completely opposite context to the antidepressants, as a major tranquillizer. In view of the apparently anomalous activity of chlorpromazine in the reserpine reversal test, we have carried out experiments to establish whether the thermogenic response to chlorpromazine is mediated by the same mechanisms as the thermogenic response to desipramine, a clinically proven antidepressant structurally related to chlorpromazine.

Groups of 6 male, albino mice (18–20 g) were injected subcutaneously with reserpine 2 mg/kg, and maintained at an environmental temperature of $20 \pm 1°$ C ; 17 h later, the test compound or control vehicle was administered. Oesophageal temperatures were recorded every hour using an orally-inserted probe.

A dose-related reversal of reserpine-induced hypothermia in mice was demonstrated with orally-administered chlorpromazine and desipramine.

The reserpine-induced hypothermia was also reversed by the injection of chlorpromazine or desipramine directly into the cerebral ventricles by the method of Haley & McCormick (1957). Desipramine was approximately 30 times as potent as a thermogenic agent when administered by the intracerebral, rather than the oral, route. Similarly, the thermogenic potency of chlorpromazine was increased some 8 to 15 times.

Pretreatment of the mice with chlorisondamine (1 mg/kg S.C.) 1 h before oral administration of chlorpromazine or desipramine completely abolished the thermogenic responses.

The reversal of reserpine hypothermia by desipramine was not demonstrated in mice bilaterally adrenalectomized 24 h before reserpinization. The reversal of reserpine hypothermia by chlorpromazine was considerably reduced, but not completely abolished, by adrenalectomy.

These results indicate that there needs to be functional ganglionic transmission for the manifestation of the thermogenic activities of chlorpromazine and desipramine, and that the activities are central, rather than peripheral, in origin. The presence of intact adrenal glands is required for the demonstration of the thermogenic response to desipramine and of the full response to chlorpromazine in reserpinized mice. The retention of some thermogenic activity, although much reduced, by chlorpromazine in adrenalectomized mice suggests that part of the temperature elevation elicited by this drug in reserpinized mice is mediated by effector systems apart from those involving the adrenal glands.

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The role of monoamines in the hyperthermia produced in cats and rabbits by irradiation of the hypothalamic area

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Irradiation of the hypothalamic area with X-rays in a dose of 600 or 200R produced, both in cats and rabbits, a rise in rectal temperature of about 1°C. The

rise began after a latent period of 60 to 90 min. In cats it was prevented when p-chloro-methyl amphetamine, a specific depletor of 5-hydroxytryptamine (5-HT) was injected intraperitoneally in a dose of 5 mg/kg 24 h before the irradiation. This finding is in accord with the hypothesis put forward by Feldberg & Myers in 1963, that 5-HT plays a role as a mediator of hyperthermic responses in the hypothalamus of cats. In rabbits in which the catecholamines, noradrenaline and adrenaline, produce a rise in body temperature when acting on the anterior hypothalamus (Cooper, Cranston & Honour, 1965) the irradiation hyperthermia appears to be mediated by catecholamines because the hyperthermia was prevented by an intraperitoneal injection of either ergotamine (0·6 mg/kg) or propranolol (1 mg/kg). Since propranolol is a specific beta-adrenoceptor blocking agent, beta receptors appear to be involved, and they appear to be central not peripheral receptors because the irradiation hyperthermia was not affected by an intraperitoneal injection of another beta-adrenoceptor blocking agent, sotalol (MJ1999), up to 10 mg/kg, which lacks central effects. Moreover, 3–5-days-old rabbits, in which cranial adrenergic pathways have not yet developed, did not respond to irradiation with a rise in temperature. Finally, the finding that an intravenous injection of theophylline (2 mg/kg) enhanced the irradiation hyperthermia, may point to the participation of cyclic AMP in the response.

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Chronic ingestion of nicotine modifies the behaviour of mice after ethanol

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Bhagat, Bayer & Lind (1971) reported that chronic injection of nicotine (1 mg/kg, five times a day) increased ethanol-induced hypnosis. As nicotine and alcohol are drugs commonly used by man when awake the present study examined the possibility that chronic use of nicotine may modify behaviour after non-hypnotice doses of alcohol. Because repeated injections over weeks might be expected to act as a stress, and thereby modify behaviour, the effect of giving nicotine in the daily drinking water was investigated.

For fourteen days preceding the behavioural test groups of 48 mice had access only to drinking water containing amounts of nicotine calculated to give each mouse (body weight about 40 g) approximately 0 (controls), 50, 100 or 200 μg per day of nicotine hydrogen tartrate. All groups drank similar amounts. During the behavioural test (Boissier & Simon, 1964), 24 h after the last opportunity to ingest nicotine, a form of exploration (head-dips into holes) was recorded for a 3 min exposure to a novel environment (Bradley, Joyce, Murphy, Nash, Porsolt, Summerfield & Twyman, 1968). Twenty min before the test, sub-groups of mice received either 0·3 ml saline or 0·1, 0·2 or 0·3 ml, I.P., of a 25% v/v ethanol solution. Half the mice received only ethanol and half received also, I.P., one-quarter the dose of nicotine they had ingested daily.