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.

An analysis of variance indicated significant differences attributable to level of nicotine pre-treatment ($P<0.01$) and to ethanol dose ($P<0.001$). Comparisons of individual means showed that groups pre-treated with the highest nicotine dose (200 μg daily) did not differ from controls in the absence of ethanol injection but made significantly fewer head-dips ($P<0.05$ and $P<0.01$) for the lowest and intermediate doses of ethanol (0·1 ml and 0·2 ml) which did not have a behavioural depressant effect in the controls. The results demonstrate that chronic ingestion of high doses of nicotine in drinking water can induce behavioural depression after doses of ethanol which do not have this effect when given alone.

Mice which had received 0 and 0·3 ml of 25% ethanol before the behavioural test were given only water to drink and were replaced, one week later, in the test environment, without ethanol injection (Green, Joyce & Summerfield, 1971). Head-dips into holes were counted. An analysis of variance revealed a significant effect of pre-treatment nicotine dose ($P<0.05$)—an increased number of dips with increasing dose—but no effect of ethanol injection. This observation indicates that chronic nicotine may influence learning or memory processes.

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Some effects of the hallucinogenic drug 2,5-dimethoxy-4-methylamphetamine on the metabolism of biogenic amines in the rat brain

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Studies have been made of the effects of a number of phenylethylamines on the metabolism of brain monoamines with the aim of differentiating neurochemically between the stimulant and the psychotomimetic drugs of this series (Leonard & Shallice, 1971 ; 1972). From their effects on amine metabolism it was possible to distinguish amphetamines which have a pronounced stimulant effect on the behaviour of rats ((+)-amphetamine, (+)-methamphetamine and p-nitromethamphetamine) from the non-stimulant drug, p-bromomethamphetamine.

In an attempt to determine more precisely the relationship between the chemical structure and the pharmacological activity of some of the phenylethylamines a study has now been made of the hallucinogenic amphetamine, 2,5-dimethoxy-4-methyl-amphetamine (DOM). This is the active principle of 'STP', a drug which was widely used by some of the 'hippie' communities in the United States (Snyder, Faillace & Hollister, 1967).

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