

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 ($200 \mu\text{g}$ 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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REFERENCES

- BHAGAT, B., BAYER, T. & LIND, C. (1971). Effects of chronic administration of nicotine on drug-induced hypnosis in mice. *Psychopharmacologia*, **21**, 287–293.
BOISSIER, J. R. & SIMON, P. (1964). Dissociation de deux composés dans le comportement d'investigation de la souris. *Arch. Int. Pharmacodyn. Théor.*, **147**, 372–387.
BRADLEY, D. W. M., JOYCE, D., MURPHY, E. H., NASH, B. M., PORSOLT, R. D., SUMMERFIELD, A. & TWYMAN, W. A. (1968). Amphetamine-barbiturate mixture: effects on the behaviour of mice. *Nature, Lond.*, **220**, 187–188.
GREEN, S. E., JOYCE, D. & SUMMERFIELD, A. (1971). Strain differences in immediate effects and after-effects of scopolamine on behaviour. *J. Pharmac., Paris*, **2**, 225–226.

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-methylamphetamine (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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DOM caused piloerection, behavioural stimulation and pronounced 'head twitching' in high doses (60 mg/kg). Lower doses had a less marked effect. DOM reduced the brain concentration of noradrenaline and elevated that of 5-hydroxytryptamine. Brain dopamine was initially elevated and then reduced by the drug.

Tritiated tyrosine and tryptophan were used to study the effect of DOM on the rate of incorporation of these amino acids into the biogenic amines. It was found that DOM increased the rate of incorporation of tyrosine into noradrenaline but reduced the incorporation of tryptophan into 5-hydroxytryptamine. No effect on the incorporation into dopamine could be detected. DOM also reduced the depletion of brain 5-hydroxytryptamine which followed the administration of p-chlorophenylamine. These results suggest that DOM may increase the 'turnover' of noradrenaline and reduce that of 5-hydroxytryptamine. The changes in the brain concentration of tyrosine and tryptophan could not account for the effect of DOM on brain amines.

These results are qualitatively similar to those found in previous investigations for other hallucinogenic drugs (Leonard & Tonge, 1969; Tonge & Leonard, 1969; Tonge & Leonard, 1970).

REFERENCES

- LEONARD, B. E. & SHALLICE, S. A. (1971). Some neurochemical effects of amphetamine, methylamphetamine and p-bromomethylamphetamine in the rat. *Br. J. Pharmac.*, **41**, 198-212.
- LEONARD, B. E. & SHALLICE, S. A. (1972). The effect of p-nitromethylamphetamine on biogenic amines and amino acid precursors in the rat brain. *Br. J. Pharmac.* In the Press.
- LEONARD, B. E. & TONGE, S. R. (1969). The effects of some hallucinogenic drugs upon the metabolism of noradrenalin. *Life Sci.*, **8**, pt. 1, 815-825.
- SNYDER, S. H., FAILLACE, L. A. & HOLLISTER, L. (1967). 2,5-dimethoxy-4-methyl-amphetamine (STP): A new hallucinogenic drug. *Science*, **158**, 669-670.
- TONGE, S. R. & LEONARD, B. E. (1969). The effects of some hallucinogenic drugs upon the metabolism of 5-hydroxytryptamine in the rat brain. *Life Sci.*, **8**, pt. 1, 805-814.
- TONGE, S. R. & LEONARD, B. E. (1970). The effect of some hallucinogenic drugs on the amino acid precursors of brain monoamines. *Life Sci.*, **9**, pt. 1, 1327-1335.

Monoamine metabolites in *Octopus vulgaris*

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Monoamine oxidase (MAO) is present in various tissues of cephalopods (Blaschko & Hawkins, 1952). The fact that dopamine (DM) and 5-hydroxytryptamine (5-HT) are present in neural tissues of cephalopods (Juorio, 1971) suggested that it may be metabolized by MAO to form 3,4-dihydroxyphenylacetic acid (DOPAC) and 5-hydroxyindolylacetic acid (5-HIAA) respectively. Table 1 shows that DOPAC and 5-HIAA are present in the optic lobes of *Octopus vulgaris*. The administration of an inhibitor of MAO (pargyline 100 mg/kg, 3 h) produced a marked fall in the concentration of both DOPAC and 5-HIAA (Table 1). The administration of L-DOPA (200 mg/kg, 3 h), the amino acid precursor of DM, led to a fifty-fold increase in the level of DOPAC.

These results suggest that in *Octopus*, the neural effects of DM and 5-HT are at least partly terminated by MAO.