With tranylcypromine and phenelzine there was little significant difference, at a particular dose level, in the degree of inhibition of the oxidation of the 5-HT, tyramine or benzylamine by rat brain tissue. Graded doses of both compounds, which produced a progressive increase in the pharmacological response, also produced increases in the inhibition of rat brain MAO and an increase in the concentrations of noradrenaline and 5-HT.

With clorgyline, there was significant correlation between the pharmacological response and inhibition of the oxidation of tyramine but not the oxidation of either benzylamine or 5-HT by rat brain tissue. Taking the data on clorgyline, tranylcypromine, and phenelzine together there was good correlation of both pharmacological responses with inhibition of the oxidation of tyramine by rat brain MAO.

REFERENCES

GORKIN, V. Z. (1963). Partial separation of rat liver mitochondrial amine oxidases. *Nature, Lond.*, **200**, 77.

HALL, D. W. R., LOGAN, B. W. & PARSONS, G. H. (1969). Further studies on the inhibition of monoamine oxidase by M&B 9302 (Clorgyline)—I. Substrate specificity in various mammalian species. *Biochem. Pharmac.*, **18**, 1447–1454.

JOHNSTON, J. P. (1968). Some observations upon a new inhibitor of monoamine oxidase in brain tissue. *Biochem. Pharmac.*, **17**, 1285–1297.

YOUDIM, M. B. H. & SANDLER, M. (1967). Isoenzymes of soluble MAO from human placental and rat-liver mitochondria. *Biochem. J.*, **105**, 43*P*.

YOUDIM, M. B. H., COLLINS, G. G. S. & SANDLER, M. (1969). Multiple forms of rat brain monoamine oxidase. *Nature, Lond.*, **223**, 626–628.

Persistence of dose-related behaviour in mice

MARIAN DORR, DAPHNÉ JOYCE, HANNAH STEINBERG*, A. SUMMERFIELD and M. TOMKIEWICZ, *Departments of Pharmacology and Psychology, University and Birkbeck Colleges, University of London*

Female adult mice injected with several doses of a dexamphetamine-chlordiazepoxide mixture, ratio 1 : 10 by weight, were placed singly on a horizontal wooden board with sixteen evenly spaced holes (Boissier & Simon, 1964) and their activity was assessed during 3 min by determining (1) the number of times they dipped their heads into the holes and (2) the amount of walking they did across the board.

Both forms of activity were greatly increased by moderate doses of the mixture, but with the highest dose and with most doses of the separate constituents there was little difference from saline controls. This was consistent with the effects of mixtures of amphetamine and chlordiazepoxide and of their separate constituents on the behaviour of rats in Y-mazes (Rushton & Steinberg, 1966) and also of amphetamine–amylobarbitone mixtures and their constituents on mice tested on a hole board (Joyce, Porsolt, Steinberg & Summerfield, 1968).

One week later the mice were retested on the same hole boards, but this time without any drugs or injections (Bradley, Joyce, Murphy, Nash, Porsolt, Summerfield & Twyman, 1968). The absolute amounts of both kinds of activity were now considerably lower, but the shapes of the " dose-response " curves strikingly resembled those obtained with the drugs on the first occasion.

Analogous long-term effects have previously been found with amphetamine–barbiturate mixtures in rats where a single drug experience had detectable effects on behaviour for periods of up to three months (Rushton, Steinberg & Tomkiewicz,

1968), and in mice retested without drugs one week later (Bradley *et al.*, 1968).

Although the dose-dependence of these effects has not yet been explored in great detail, it was clear from the present experiments that the amount of activity on the second trial was reduced by a constant proportion regardless of the actual doses administered at trial 1. Such a re-emergence of the dose-response curves on the second trial could not have been predicted from the results of previous experiments.

These findings suggest that dose-related behaviour patterns can be elicited long after the original administration of drugs; this may be relevant to clinical practice.

We thank U.C.L. B.Sc. students, graduates in our departments and Dr. R. Peto for their help. The work was supported by grant MH-03313 from the National Institute of Mental Health, U.S. Public Health Service.

REFERENCES

BOISSIER, J. R. & SIMON, P. (1964). Dissociation de deux composantes dans le comportement d'investigation de la souris. *Archs int. Pharmacodyn. Thér.*, **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.

JOYCE, D., PORSOLT, R. D., STEINBERG, H. & SUMMERFIELD, A. (1968). Behaviour of mice after administration of an amphetamine-barbiturate mixture (with 16 mm. film). *Br. J. Pharmac. Chemother*, **32**, 433.

RUSHTON, R. & STEINBERG, H. (1966). Drug combinations and their analysis by means of exploratory activity in rats. In *Neuropsychopharmacology*, ed. Brill, H. *et al.*, vol. 5, pp. 464–470. Amsterdam: Excerpta Medica.

RUSHTON, R., STEINBERG, H. & TOMKIEWICZ, M. (1968). Equivalence and persistence of the effects of psychoactive drugs and past experience. *Nature, Lond.*, **220**, 885–889.

Disappearance in rats with septal lesions of the stimulatory effect of hyoscine on exploratory behaviour

A. MULAS and G. PEPEU*, *Department of Pharmacology, School of Pharmacy, Cagliari University, Italy*

Electrocoagulative lesions were stereotactically placed in the septal region of male Wistar rats weighing 80–100 g, according to the coordinates of the rat atlas of Konig & Klippel (1963). Three days later the rats were rated for aggressiveness and hypermotility using the scale and procedure described by King (1958). Only those animals which showed a score close to the maximum were used.

Exploratory behaviour was investigated in a symmetrical Y shaped runway (Marriot & Spencer, 1965) counting the number of complete entries into the arms of the runway. Unoperated rats were used as controls. Neither operated nor unoperated rats had any previous experience of the experimental apparatus.

All the drugs were injected subcutaneously 30 min before testing. At the end of the experiments the operated rats were killed and the extent of the lesion was checked by histological examination.

The results are listed in Table 1. They show a marked difference between the effects of hyoscine on the exploratory behaviour of controls and that of septal rats. Hyoscine increases such behaviour in unoperated rats and decreases it in the septal rats. Amphetamine stimulates exploratory activity in both groups of animals.