TABLE 1. *Comparison of minimal effective anxiolytic doses in the baboon and the recommended human therapeutic dose*

Drug	Min. effective dose—baboon (mg/kg)	Human dose (mg/kg)
Chlordiazepoxide	0·5	0·5
Diazepam	0·7	0·5
Medazepam	0·5	0·5
Oxypertine	0·25	0·5

(For the purposes of comparison the weight of the human subject has been taken as 60 kg and the standard human doses from MIMS, vol. **13**, No. 10, 1971.)

REFERENCES

BEATTIE, I. A., BERRY, P. A. & LISTER, R. E. (1970). Methods for detecting anti-anxiety drugs using baboons (*Papio cynocephalus*). *Br. J. Pharmac.*, **38**, 460*P*.

BERRY, P. A., BEATTIE, I. A. & LISTER, R. E. (1970). Methods for detecting anti-anxiety drugs using baboons (*Papio cynocephalus*). Proc. 7th Congr. Collegium Internationale Neuropsychopharmacologicum, Prague.

HOLLISTER, L. E., OVERALL, J. E., KIMBELL, J. E., BENNET, J. L., MEYER, F. & CAFFEY, E. (1963). Oxypertine in newly admitted schizophrenics. *J. New Drug*. Jan–Feb, 26–31.

HOLLISTER, L. E. & OVERALL, J. E. (1971). Oxypertine and thiothixine in newly admitted schizophrenics. *Clin. Pharmac. Ther.*, **12**, 531–538.

JAFFE, G. (1971). Clinical evaluation of oxypertine (Integrin) as an anxiolytic in general practice. *Clin. Trials J.*, **8**, 3–7.

TYSON, V. (1970). Two trials with a new psychotherapeutic drug in the treatment of anxiety. *Practitioner*, **204**, 306–309.

Selective effects of lithium on two forms of spontaneous activity

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Cox, Harrison-Read, Steinberg & Tomkiewicz (1971) have recently shown that pretreatment with lithium attenuates the hyperactivity induced in rats by a dexamphetamine-chlordiazepoxide mixture. We have found an even more striking effect of lithium on drug-induced hyperactive behaviour in mice.

Female adult mice (Porton strain), injected intraperitoneally in the morning with 3 meq/kg of isotonic lithium chloride or an equal volume of saline, were divided into four groups and injected 3 h later with dexamphetamine, 0·5 mg/kg,1·18 mg/kg or 2·36 mg/kg; chlordiazepoxide, 7·5 mg/kg, 12·5 mg/kg or 25·0 mg/kg; a mixture of dexamphetamine and chlordiazepoxide (0·5+7·5) mg/kg, (1·18+12·5) mg/kg, (2·36+25·0) mg/kg (all dissolved in saline); or with saline (10 ml/kg) alone. Twenty minutes after this injection the mice were placed singly on a horizontal wooden board with sixteen evenly-spaced holes (Boissier & Simon, 1964) and the number of times they dipped their heads into the holes in 3 min was counted.

Immediately after this test the mice were placed singly in photocell activity cages and the number of beam breaks during 20 min was recorded automatically.

Mixtures of 0·5 and 1·18 mg/kg dexamphetamine combined with 7·5 and 12·5 mg/kg respectively of chlordiazepoxide markedly increased the activity of saline pretreated mice tested on the hole board. Activity after any dose of the separate drugs or a mixture containing 2·36 mg/kg dexamphetamine and 25·0 mg/kg chlordiazepoxide was not significantly different from controls injected with saline (c.f. Dorr, Steinberg, Tomkiewicz, Joyce, Porsolt & Summerfield, 1971). Lithium pretreatment completely prevented the increase in activity produced by the (0·5+7·5) mg/kg and (1·18+12·5) mg/kg mixtures but did not reduce the activity of animals in any of the other drug groups and slightly increased the activity of the saline control animals.

In the photocell activity cages only one dose of dexamphetamine (2·36 mg/kg) and the mixture containing this ingredient dose significantly increased activity. Lithium pretreatment, however, failed to prevent these increases. This may have been because the activity cages provided a qualitatively different environment with little scope for the characteristically 'manic' hyperactivity observable on the holeboards, because the mice had already previously been tested, and because in any case photocells do not readily discriminate between various kinds of movement.

REFERENCES

BOISSIER, J. R. & SIMON, P. (1964). Dissociation de deux composantes dans le comportement d'investigation de la souris. *Archs int. Pharmacodyn. Thér.*, **147**, 342–387.

COX, C., HARRISON-READ, P. E., STEINBERG, H. & TOMKIEWICZ, M. (1971). Lithium attenuates drug-induced "manic" activity in rats. *Nature, Lond.*, **232**, 336–338.

DORR, M., STEINBERG, H., TOMKIEWICZ, M., JOYCE, D., PORSOLT, R. & SUMMERFIELD, A. (1971). Persistence of dose related behaviour in mice. *Nature, Lond.*, **231**, 121–123.

Previous environment and responses to morphine

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Long-term isolation induces several biochemical, pharmacological and behavioural changes in mice and rats (Garattini, Giacolone & Valzelli, 1969; DeFeo, Baumel & Lal, 1970). We have found that 12 or 12·5 mg/kg intraperitoneally of morphine reduced the activity of male rats tested in Y-mazes (Rushton & Steinberg, 1963). Isolating rats for 40 days between weaning and testing counteracted these effects of morphine. Putting previously isolated rats into groups of 12 for 24 h before the test abolished the effect of isolation. However, 24 h of isolation of previously grouped rats did not alter the activity-reducing effects of morphine.

In contrast with these results, isolation for 40 days actually enhanced the analgesic effects of 8 mg/kg morphine which were measured in a 'tail-press' apparatus, using a struggle response as the measure of pain.

In chronic experiments, previously grouped or isolated rats did not differ in the rates at which they learned to self-administer solutions of morphine. The method used was similar to that described by Kumar, Steinberg & Stolerman (1968). The proportion of total fluid drunk in the form of morphine solutions when water was also available was taken as an index of dependence. Isolated and grouped rats made dependent on morphine by regular injections showed no differences in the amounts of weight lost after substitution of morphine by saline injections.

The apparent absence of effects of previous isolation in the chronic experiments may be due to disturbances associated with the experimental procedures, especially as the first experiment had shown that the effects of isolation were labile since they could be abolished by short periods of grouping. It is unlikely that the modification of acute responses to morphine was simply due to general changes in the rate of metabolism of the drug, since the two responses that were measured showed opposite results.

REFERENCES

DEFEO, J. J., BAUMEL, I. & LAL, H. (1970). Drug environment interactions: acute hypoxia and chronic isolation. *Fedn Proc.*, **29**, 1985–1990.

GARATTINI, S., GIACOLONE, E. & VALZELLI, L. (1969). Biochemical changes during isolation-induced aggressiveness in mice. In: *Aggressive Behaviour*, ed. Garattini, S. & Sigg, E. B., pp. 179–187. Amsterdam: Excerpta Medica.

KUMAR, R., STEINBERG, H. & STOLERMAN, I. P. (1968). Inducing a preference for morphine in rats without premedication. *Nature, Lond.*, **218**, 564–565.

RUSHTON, R. & STEINBERG, H. (1963). Mutual potentiation of amphetamine and amylobarbitone measured by activity in rats. *Br. J. Pharmac. Chemother.*, **21**, 295–305.