

to the right or the left. The asymmetry in both groups of rats could not be correlated with changes in the 5-hydroxytryptamine concentrations but occurred with lesions that were not quite central and extended into the reticular formation on one or other side. The results suggested that 5-hydroxytryptamine was not involved in the amphetamine-induced rotation seen in rats with unilateral lesions in the substantia nigra but that a similar rotational motor activity could be produced by the destruction of a system other than the nigrostriatal dopamine system.

When a single unilateral lesion was placed in the mesencephalic reticular formation in the area of the cerebellar-rubral tract ipsilateral turning occurred that was potentiated by amphetamine. There was a reduction in the noradrenaline content of the cerebral cortex on the lesioned side (by 80%) while the dopamine in the striatum was unaffected. The effect of amphetamine in this case may be due to stimulation of motor activity on the non-lesioned side with the possible involvement of noradrenergic neurones. It has been suggested that the stereotyped behaviour produced by amphetamine may be due to dopamine release and the locomotor stimulation to the release of noradrenaline (Taylor & Snyder, 1971).

#### REFERENCES

- ANDÉN, N.-E., DAHLSTRÖM, A., FUXE, K. & LARSSON, K. (1966). Functional role of the nigro-neostriatal dopamine neurons. *Acta pharmac. toxic.*, **24**, 263-274.
- TAYLOR, K. M. & SNYDER, S. H. (1971). Differential effects of D- and L-amphetamine on behaviour and on catecholamine disposition in dopamine and norepinephrine containing neurons of rat brain. *Brain Res.*, **28**, 295-309.
- UNGERSTEDT, U. (1969). Behavioural registration of dopamine synaptic activity in the brain after 6-hydroxy-dopamine lesions. *Acta physiol. scand.*, **77**, Suppl. 330, p. 117.

#### Effect of oxypertine on anxiety-induced behaviour in baboons

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Oxypertine (Integrin, Winthrop) has been used for some time as an effective antipsychotic agent in schizophrenia, and Hollister (1963, 1971) has shown that it influences preferentially the affective components rather than paranoid tendencies, greatest improvement being recorded in symptoms of anxiety and depressed mood. Recent clinical studies (Jaffe, 1971; Tyson, 1970) have indicated that this drug has anti-anxiety activity after total daily doses of 30-60 mg. The technique of human intrusion into an established colony of baboons (*Papio cynocephalus*) as a means of inducing anxiety and aggression in the leader of the colony has been used to confirm this observation (Beattie, Berry & Lister, 1970; Berry, Beattie & Lister, 1970). Oxypertine, 0.25-4 mg/kg orally, produced a marked suppression of anxiety-induced aggression in the leader of the colony. The effects of the drug were detectable 20 min after dosing and lasted for up to 5 hours. The maximal effects occurred 60-120 min after dosing. No sedation or other undesirable effects were recorded at these dose levels. Slight ataxia was seen after an oral dose of 8 mg/kg oxypertine, though this effect was transient. No signs of sedation were detected at any dose level studied.

These experiments again illustrate the value of the baboon as a test for evaluating anti-anxiety drugs and demonstrate the close correlation between the minimal effective dose in the baboon with the recommended therapeutic dose in man (Table 1).

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**, 460P.
- 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.