The effect of drugs on various parameters of mouse behaviour in a modified head-dipping test

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(introduced by M. GINSBURG)

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The head-dipping test developed by Boissier & Simon (1962, 1964) has been used to examine the behavioural effects produced by a variety of drugs, but its application as a screening method is limited by its failure to discriminate between drugs as divergent in their effects in man as amphetamine and chlordiazepoxide, both of which stimulate head-dipping in mice (Bradley, Joyce, Murphy, Nash, Porsolt, Summerfield & Twyman, 1968; Nolan & Parkes, 1973).

The apparatus described by Boissier & Simon is a horizontal board perforated with evenly-spaced holes. A 'dip' is scored when mice lower their head far enough into a hole for the eyes to disappear beneath the plane of the board. The test situation has been altered by dividing the board with low, narrow walls into square compartments (10 × 10 cm), each with a hole (3, 5 cm diameter) at the centre, so that additional behavioural parameters can be observed. Thus 'rearing' is scored when mice raise themselves onto the hind legs and the fore-paws rest on a partition wall, and 'crossing' is scored when the animal climbs over the wall dividing one compartment from another.

In contrast to the findings with the unmodified test by Bradley *et al.* (1968) and by Nolan & Parkes (1973), amphetamine, chlordiazepoxide, diazepam and amylobarbitone were found not to increase dipping significantly. However, rearing and crossing were stimulated in a dose-dependent manner by chlordiazepoxide and by diazepam, and to a lesser extent by amylobarbitone, while both parameters were inhibited by amphetamine and chlorpromazine, the latter drug in doses producing overt signs of sedation.

These results suggest that by choice of suitable parameters of mouse behaviour it might be possible to detect and distinguish the activities of several classes of CNS-acting drugs in this simple test.

References

BOISSIER, J.R. & SIMON, P. (1962). La reaction d'exploration chez la souris. *Therapie.*, **17**, 1225–1232.

BOISSIER, J.R. & SIMON, P. (1964). Dissociation de deux composantes dans le compartement d'investigation de la souris. *Arch. Inter. Pharmacodyn.*, **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*, **220**, 187–188.

NOLAN, N.A. & PARKES, M.W. (1973). The effects of benzodiazepines on the behaviour of mice on a hole-board. *Psychopharmacologia*, **29**, 277–288.

Prostaglandins and the release of histamine from rat peritoneal mast cells

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Prostaglandin E_1 (PGE_1) increases cyclic AMP levels in rat mast cells and inhibits the release of histamine by antigen (Kaliner & Austen, 1974). In the present study, we have further investigated the actions of prostaglandins and drugs affecting prostaglandin metabolism on histamine release following chemical or immunological challenge.

Mast cells were obtained by lavage of the rat peritoneal cavity with a modified buffer solution (12 ml, pH 7) containing bovine serum albumen (0.1% w/v). The solution was withdrawn, centrifuged, and the cell pellet re-suspended in the buffer. The incubation techniques, which allow at least 24 samples to be obtained from the mast cells of one rat, will be demonstrated. The histamine released from the mast cells was assayed fluorometrically (Shore, Burkhalter & Cohn, 1959) or on the superfused guinea-pig ileum.

Non-steroid anti-inflammatory drugs, which inhibit prostaglandin biosynthesis (Vane, 1971), caused a parallel displacement of the dose-response curve for the release of histamine by compound 48/80 (0.1–1 μg/ml). The dose causing 50% inhibition of submaximal histamine release (ID_{50}) was 3.5, 9.0 and 21.5 μg/ml for sodium meclofenamate, flufenamic acid and indomethacin, respectively. These drugs also inhibited histamine liberation induced by antigen (either horse serum or egg albumen) from sensitized mast cells, or that induced by adenosine triphosphate or crude phospholipase-A. Although these aspirin-like drugs had no consistent effect on non-specific histamine liberation with the surface-active agents Triton X-100 (0.01%) or *n*-decylamine (25 μg/ml), the release of histamine following incubation of mast cells with a calcium ionophore (A23187, 0.25 μg/ml; Foreman, Mongar & Gomperts, 1973) was markedly reduced (ID_{50} for meclofenamate