The fish (6–8 g) were injected (10 µl i.c.) under anaesthesia tricaine–methane–sulphonate (MS222, Sandoz) and left to recover for 6 h before the training session. Training was carried out in the dark for 5 days (20 trials/day) at a constant temperature of 18°C. Performance was judged by the number of responses of each fish to the CS during the training period. Results were analysed by ranking tests and values of $P < 0.05$ were taken as significant. After 5 days, the performance of the colchicine injected fish was significantly poorer than that of controls, whereas that of fish injected with lumicolchicine was not significantly different from controls. All fish significantly improved their performance during the 5 days of training.

Other fish pretreated in a similar manner were used to assess unconditioned behaviour. The incidence of spontaneous crossings between chambers of the shuttlebox did not significantly differ between any two groups.

To try to trace the distribution of colchicine, groups of 4 fish were injected with [ring C-methoxyl-^{3}H] Colchicine (Radiochemical Centre) and killed at intervals over 5 days. No attempt was made to follow the metabolic fate of the injected tritium, but radioactivity was detected throughout the brains of all fish. At 5 days, the mean d.p.m./g of whole brain was similar to that at 24 h, but in liver, radioactivity was not detected beyond 24 hours.

Colchicine is an alkaloid of well documented action. It is known to disrupt neurotubule structure, probably by combining with soluble protein subunits, whereas lumicolchicine does not bind to neurotubules (Banks & Till, 1975). It is speculated that the observed behavioural effects of colchicine may be due to the disruption of the neurotubule system. That the observed effects may be due to general toxic actions seems unlikely since unconditioned colchicine-injected fish performed as well as controls.

References

AGRANOFF, B.W. (1967). Agents that block memory. In *The Neurosciences; A Study Program*, pp. 756–764. Ed. Quarton, Melnechuk & Schmitt. New York: Rockefeller.

BANKS, P. & TILL, R. (1975). A correlation between the effects of antimitotic drugs on microtubule assembly *in vitro* and the inhibition of axonal transport in noradrenergic neurones. *J. Physiol. Lond.*, **252**, 283–294.

CRONLY-DILLON, J., CARDEN, D. & BIRKS, C. (1974). Involvement of brain microtubules in memory fixation. *J. exp. Biol.*, **61**, 443–454.

The 'wet dog shake' behaviour in the rat and 5-hydroxytryptamine

P. BEDARD & C. PYCOCK

Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, Denmark Hill, London SE5 8AF and Department of Pharmacology, University of Bristol

The 'Wet Dog' shake (WDS) in the rat is a paroxistic shudder of the head, neck and trunk, reminiscent of the purposeful movement seen in dogs. This behaviour has been reported after various physiological stimuli, following morphine withdrawal or injection of thyrotrophin-releasing hormone (Wei, Sigel, Loh & Way, 1975). The neuropharmacology of the WDS is not clear, although with all the stimuli there is the suggestion of the possible involvement of central 5-hydroxytryptaminergic mechanisms.

We have investigated the relationship between WDS response in the rat and central 5-hydroxytryptamine (5-HT) function. Administration of 5-hydroxytryptophan (5-HTP) (25–150 mg/kg, s.c.) in combination with a peripheral decarboxylase inhibitor (carbidopa, 25 mg/kg, i.p. 30 min beforehand) induced this behaviour in a dose-dependent manner. The WDS response began 15 min after 5-HTP injection, reaches a peak at 2 h and receded until the 6th hour. High doses of 5-HTP (200 mg/kg) were accompanied by stereotyped sniffing, padding of the forepaws and head weaving.

5-HTP-induced WDS was blocked by the 5-HT antagonists methysergide (5 mg/kg) and cyproheptadine (10 mg/kg). The behaviour was mimicked by the proposed 5-HT agonists lysergic acid diethylamide (0.1 and 0.2 mg/kg), 5-methoxy-N,N-dimethyltryptamine (0.5–1 mg/kg) and quipazine (1.5–10 mg/kg). Similarly treatment of rats with the 5-HT precursor L-tryptophan (25–50 mg/kg) together with the monoamine oxidase inhibitor pargyline (25 mg/kg) induced WDS.

A number of drugs thought to selectively interact with central catecholamine and cholinergic mechanisms were tested on the 5-HTP induced WDS response in rats. Only amphetamine (4 mg/kg, i.p.) and apomorphine (0.5 mg/kg, s.c.) produced significant inhibition of the response, with accompanying patterns of stereotyped behaviours.

A regional analysis of 5-HT concentrations in the

brain showed that increases in this neurotransmitter following 5-HTP pretreatment paralleled the intensity of the WDS response. However, no clear differences in 5-HT levels in different brain regions were seen.

Bilateral electrolesions of the globus pallidus or of the lateral part of the ventral nucleus of the thalamus failed to modify the 5-HTP induced WDS. Similarly, frontal section at the level of the anterior commissure did not affect the response, while mid-diencephalic sections decreased it. WDS behaviour following 5-HTP was almost completely abolished by sections at the level of the posterior commissure.

We propose that the WDS may constitute a useful animal model for quantifying 5-HT activity in the central nervous system and screening potential agonists and antagonists of certain types of 5-HT receptors. It is probable that the WDS in the rat is closely related to the head twitches in mice (Corne, Pickering & Warner, 1963) and myoclonus in guinea-pigs (Klawans, Goetz, Westheimer & Weiner, 1973), while the hyperactivity syndrome (Grahame Smith, 1971) appears different. Hopefully these various models will help us distinguish possibly distinct 5-HT receptors in the CNS.

References

CORNE, S.J., PICKERING, R.W. & WARNER, B.T. (1963). A method for assessing the effects of drugs on the central actions of 5-hydroxytryptamine. *Brit. J. Pharmac.*, **20**, 106–120.

GRAHAME-SMITH, D.G. (1971). Studies *in vivo* on the relationship between brain tryptophan, brain 5-HT synthesis and hyperactivity in rats treated with a monoamine oxidase inhibitor and L-tryptophan. *J. Neurochem.*, **18**, 1053–1066.

KLAWANS, H.L., GOETZ, C., WESTHEIMER, R. & WEINER, W.J. (1973). 5-Hydroxytryptophan-induced behaviour in intact guinea-pigs. *Res. Comm. Chem. Path. Pharmac.*, **5**, 555–559.

WEI, E., SIGEL, S., LOH, H. & WAY, E.L. (1975). Thyrotrophin-releasing hormone and shaking behaviour in rat. *Nature, Lond.*, **253**, 739–740.

Pharmacological validation of a new test for the detection of antidepressant activity of drugs

H. RIGTER, H. VAN RIEZEN & A. WREN
(introduced by H. SCHNIEDEN)

Department of Pharmacology, Organon, Oss, The Netherlands and Department of Pharmacology, Materia Medica and Therapeutics, University of Manchester, Manchester M13 9PT

We have previously reported that bilateral ablation of the olfactory bulbs of rats results in diverse behavioural changes, and that most of these are reversed by chronic pretreatment with antidepressant drugs (Van Riezen, Schnieden & Wren, 1976). Amongst effective antidepressant drugs was mianserin. This drug was a false negative in conventional animal screening tests (Van Riezen, 1972) but has been reported to be an antidepressant in the clinical situation (Murphy, 1975; Wheatley, 1975). In particular, the 'anxiosoif' test has proved bery useful in assessing behavioural changes of bulbectomized rats which are sensitive to reversal by antidepressant drugs (Wren, Van Riezen & Rigter, 1976). We have now examined the specificity of this test for antidepressants by challenging it with a variety of psychoactive drugs.

The anxiosoif test is essentially a passive avoidance paradigm in which thirsty rats learn to avoid an electrified water spout. The apparatus consists of a rectangular cage, divided into two compartments by a clear perspex lid on one half and a black lid on the other. The spout of a water bottle protrudes through the black lid. The spout and the grid floor are connected to a stimulator delivering constant pulses of 1.0 mA.

In each experiment 60 male Wistar rats, weighing 170–220 g, were used. The animals were anaesthetized with tribromoethanol; 2.5 mg/kg i.p. Three groups of 10 rats were subjected to olfactory bulbectomy by means of bilateral aspiration, and 3 groups of 10 rats received sham-operation. After surgery the rats were allowed to recover for two weeks. Intraperitoneal drug treatment began on day 14 and continued daily throughout the testing period which commenced on day 21. One group of bulbectomized rats and one group of sham-operated rats received placebo treatment and the remaining groups were treated with a single dose of a test compound. The drugs and daily dosages used were amitriptyline (10 mg/kg), mianserin (10 mg/kg), imipramine (10 mg/kg), chlorimipramine (10 mg/kg), chlordiazepoxide (7.5 mg/kg), diazepam (5 mg/kg), chlorpromazine (1 mg/kg), haloperidol (0.05 mg/kg), (*dl*-8-chloro-11-antiamino-benzo-(b)-bicyclo 3.3.1 nona-3,