$n=8$; female 14 (11.5–22) $n=8$ ($2P=0.19$) after immediate homogenization, and male 7.9 (6.6 to 11) $n=8$; female 10.6 (9.3 to 22) $n=7$ after 30 min incubation. There was less activity in acid ethanol than in Krebs solution homogenates (−71% (−55 to −86), 5 male, 4 female, $2P<0.01$, Wilcoxon test).

With female brain the PG-like activity extracted after immediate homogenization with indomethacin (1 or 10 μg/ml) was always less than controls, (−67% (−63 to −90) $n=5$, and −33 to −65% $n=4$ respectively). In male brains, however, the effect of indomethacin was concentration-dependent: 1 μg/ml increased the activity in 5/6 experiments by 83% (38 to 120) (cf. female, $2P=0.03$), but 10 μg/ml caused inhibition (−28 to −91%, $n=4$). The difference did not seem primarily due to drug penetration or substrate availability. After 30 min incubation with 1 μg/ml indomethacin, biological activity was less in all female brains (−36% (−29 to −52) $n=7$) but the effect in male brains varied (−7% (20 to −13) $n=7$) (cf. female $2P=0.02$). With 40 or 400 μg/ml arachidonic acid in the incubate, 1 μg/ml indomethacin decreased biological activity in 3 female brains (−14 to −66%) but increased activity in 3/4 male brains (0 to 250%).

Extracts of brain homogenized in Krebs solution were chromatographed for group separation of PG (Stamford & Unger, 1972). In female brains only material running as PGE was detected ($n=4$) whereas in male brains PGF-like or PGE + PGF-like material was found ($n=5$) (cf. female $2P=0.016$, Fisher's exact probability test).

Brocklehurst & Dawson (1974) obtained stimulation of PG synthesis with low concentrations of indomethacin, and biological activity sometimes increased in gastrointestinal tissues homogenized with low concentrations of non-steroidal anti-inflammatory drugs (Bennett, Fox & Stamford, 1973). Apart from sex hormones, male and female guinea-pig brains might differ in co-factors for PG synthesis; arachidonic acid or noradrenaline tended to increase thromboxane $B_2$ but prevented $PGE_2$ and $F_{2\alpha}$ formation (Wolfe, Rostworowski & Marion, 1976). Alternatively, in male brain, indomethacin might increase the estimated activity by enhancing generation of PGE (to which the bioassay is more sensitive) at the expense of PGF or thromboxanes. Wolfe, Pappius & Marion (1976) found that $PGF_{2\alpha}$ production was more inhibited by indomethacin than $PGE_2$ production in rat brain.

We thank the Migraine Trust and Wellcome Trust for support.

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# Effect of colchicine and lumicolchicine on learning in goldfish

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Cronly-Dillon, Carden and Birks (1974) have reported that intracranial (i.c.) injections of colchicine interfere with long-term memory in goldfish (*Carassius auratus*). Fish were trained in a shuttlebox using an active avoidance task (Agranoff, 1967) in which they were taught to associate a light (CS) with an electric shock (UCS). Using a comparable technique, we have studied the effects of colchicine on goldfish over a longer time period and have, in addition, compared the effects of colchicine with those of its isomer, lumicolchicine.

Fish were trained in a shuttlebox (Aim-Biosciences Ltd.) and the performance of fish receiving 10 μg colchicine or lumicolchicine compared with controls receiving vehicle (Youngs Teleost Ringer solution).

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.

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

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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