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.

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

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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,

6a (10a) diene hydrochloride) (Org 6582) (10 mg/kg), and apomorphine (0.5 mg/kg).

The rats were maintained on a 23.5 h water deprivation schedule during the 4 testing days. They were allowed to drink in the apparatus for 10 min on day 1 and 2 of the test to obtain a measure of stable base-line levels of water intake. The procedure was repeated on day 3 and 4 except that the spout was electrified at every twentieth lick. The number of licks and shocks were recorded.

Removal of the olfactory bulbs tended to produce an increase in base-line levels of drinking in most experiments. With the exception of mianserin, antidepressant drugs (amitriptyline, imipramine, chlorimipramine) did not reverse this increase. The delivery of shock at every twentieth lick on day 3 and 4 led to a decrease in drinking behaviour in sham-operated animals. Water intake was even further decreased after treatment with Org 6582. The anxiolytic drugs chlordiazepoxide and diazepam attenuated passive avoidance behaviour in sham-operated rats, i.e. the shock-produced reduction in water intake was less pronounced in these animals.

Bulbectomized rats showed deficient avoidance behaviour: placebo-treated operated rats took more shocks than the corresponding sham-operated rats on day 3 as well as day four. This effect of the operation was selectively reversed by treatment with the antidepressants amitriptyline, imipramine, mianserin and chlorimipramine. A similar effect was obtained with Org 6582. Org 6582 was used in this investigation since it is a more potent and more selective inhibitor of 5-hydroxytryptamine re-uptake than chlorimipramine (Goodlet, Mireylees & Sugrue, 1976). Chlordiazepoxide, diazepam and chlorpromazine aggravated the deficiency in avoidance behaviour of bulbectomized rats. Apomorphine was virtually ineffective.

These results indicate that the alterations in passive avoidance behaviour induced in rats by the ablation of the olfactory bulbs can be reversed by antidepressants in distinction to anxiolytic and neuroleptic drugs. These data further strengthen the view that some of the behavioural changes which are seen in bulbectomized rats may serve as an animal model for the detection of antidepressant activity of drugs.

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Effect of metoprolol and oxprenolol on delayed differentiation behaviour in the monkey (*Macaca mulatta*)

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In previous studies we have used a delayed differentiation task to study the behavioural effects of drugs (Nicholson, Wright & Ferres, 1973; Nicholson & Wright, 1974, 1976). The task involves the recognition of like or unlike visual stimuli separated by a few seconds, and the monkey is required to press a lever if the stimuli are like and to refrain from pressing a lever if the stimuli are unlike. Delayed differentiation has proved useful in the analysis of the activity of barbiturates and benzodiazepines, and so we have used the task to study β-adrenoceptor antagonists which may also have central effects (Leszkovszky & Tardos, 1965; Bainbridge & Greenwood, 1971).

Five male monkeys (*Macaca mulatta*) of mean body weight 11.6 kg were used. On separate occasions each monkey was injected intraperitoneally with 5, 10, 15, 20, 25 or 30 mg/kg metoprolol or oxprenolol. The drug vehicle alone (saline) was injected on four occasions. A random order of injection was used, and each injection was separated by at least four days.