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.

Performance was tested 1 and 4 h after injection, though with 30 mg/kg oxprenolol the monkeys failed to respond to or to complete the task at 1 hour. The data were analysed by analysis of variance.

Total response time was increased at 1 h with 20 and 25 mg/kg oxprenolol ($P<0.05$ and 0.001 respectively) and with 20, 25 and 30 mg/kg metoprolol ($P<0.01$, 0.001 and 0.001 respectively). Quadratic equations were fitted to the data for each drug, but, as the equations did not differ, the data were combined. The curve was forced through the origin to give the relation for increase in total response time with dose as 0.176 $(mg/kg)^2 - 1.63$ (mg/kg). Total response times at 4 h were also increased, and this effect was observed with all doses above 15 mg/kg metoprolol and 20 mg/kg oxprenolol ($P<0.01$).

Analysis of accuracy of response was carried out by combining the data for 5 and 10 mg/kg, 15 and 20 mg/kg and 25 and 30 mg/kg. At 1 h accuracy of response was impaired with 5 and 10 mg/kg ($P<0.01$) and 15 and 20 mg/kg ($P<0.01$) oxprenolol, and with 15 and 20 mg/kg ($P<0.05$) and 25 and 30 mg/kg ($P<0.001$) metoprolol. At 4 h accuracy of response was impaired with 25 and 30 mg/kg oxprenolol ($P<0.001$), but with metoprolol the effect was observed throughout the dose range ($P<0.01$), even though with 5–10 mg/kg no effect was observed 1 h after injection.

These results suggest that the β-adrenoceptor antagonists modify delayed differentiation in a way different from that observed with barbiturates and benzodiazepines. With barbiturates and benzodiazepines impaired differentiation is observed only when total response time is increased, but with metoprolol and oxprenolol accuracy of response may be impaired without prolongation of the total response time.

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Cocaine and amphetamine as discriminative stimuli in rats

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Amphetamine can serve as a discriminative stimulus since rats can be trained to make different behavioural responses depending on whether they have received the drug or saline. Little is known about the discriminative stimulus properties of cocaine, which has therefore been compared directly with amphetamine using the procedure described by Kuhn, Appel and Greenberg, 1974. Initially, rats were trained to press bars for water reinforcement; a tandem schedule of reinforcement was used in which, after a variable interval of time (mean = 1 min) in which bar-pressing had no consequences, the 10th bar-press was reinforced. Half of the rats were then reinforced for pressing the left bar when drugged and the right bar after saline. To balance out position preferences, these contingencies were reversed in the remaining rats. Four rats were trained with (+)-amphetamine sulphate (1.0 mg/kg, i.p.) injected 30 min before 30 min training sessions. Another 4 rats were trained with cocaine hydrochloride (10.0 mg/kg, i.p.) injected 15 min before sessions.

Amphetamine, but not cocaine, increased the overall rate of responding by about 32% ($P<0.05$); however, choice of the correct bar developed at about the same rate for both drugs. After 30–35 training sessions, discriminative control by the drugs was confirmed in brief (5 min) test sessions in which no responses were reinforced. Responding on the bar previously appropriate for amphetamine was $91.4 \pm 5.3\%$ after amphetamine, as compared with $6.4 \pm 4.9\%$ after saline (means $\pm$ s.e. mean $P<0.01$). The corresponding results with cocaine were $85.6 \pm 6.9\%$ and $5.4 \pm 1.5\%$ ($P<0.01$).