The olfactory bulbectomized rat: a simple model for detecting drugs with antidepressant potential

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The effects of bilateral olfactory bulb ablation in male Sprague-Dawley rats will be demonstrated. Two simple behavioural tests, step-down passive avoidance (van Riezen, Schnieden & Wren, 1977) and irritability (King, 1958) and one biochemical test, measurement of plasma 11 hydroxycorticosterone concentrations (Mattingly, 1962), adequately characterize the syndrome and can be used to demonstrate its susceptibility to antidepressants. Rats weighing 200 to 250 g were subjected to either olfactory bulb ablation or sham-operation under equithesin (3 ml/kg). Two weeks after the operation rats received either i.p. saline or drug injections once daily for seven days and were subjected to the behavioural tests on the eighth day. Immediately following these tests the rats were sacrificed and blood collected in heparinized tubes for assay of 11 hydroxycorticosterone. The drugs to be demonstrated include the standard antidepressant amitriptyline (5 mg/kg) and two relatively new antidepressants mianserin (5 mg/kg) and viloxazine (2 mg/kg). The results are shown in Table 1. All three drugs caused significant reversal of both the behavioural and the biochemical effects of olfactory bulbectomy. Other drugs under test, which are ineffective in this model include chlordiazepoxide (5 and 15 mg/kg) and chlorpromazine (1 and 3 mg/kg).

Table 1 Effects of antidepressant drugs on changes in behaviour and 11-hydroxycorticosterone (11-OHCS) concentrations induced by olfactory bulbectomy in the rat

	Passive avoidance[1] *(no. of trials)*	*Irritability*[1] *(score)*	*Plasma 11-OHCS*[1] *(μg/100 ml)*
Sham-operation	3.4 ± 0.3	1.8 ± 0.6	18.5 ± 1.3
Bulbectomy	7.8 ± 1.2*	4.8 ± 0.4*	42.7 ± 4.4*
Amitriptyline (5 mg/kg)	3.6 ± 0.7	1.4 ± 0.5	19.6 ± 2.4
Mianserin (5 mg/kg)	2.4 ± 1.1	2.6 ± 0.6	22.7 ± 2.3
Viloxazine (2 mg/kg)	3.8 ± 0.9	3.0 ± 0.6	18.8 ± 1.7

[1] Results expressed as the mean ± s.e. mean of between 6 and 12 rats.
* Represents results which are significantly different ($P < 0.001$) to those of sham-operated rats.
All drug pretreatment results are significantly different ($P < 0.05$–0.001) to saline treated bulbectomized rats.

References

KING, F.A. (1958). Effects of septal and amygdaloid lesions on emotional behaviour and conditioned avoidance responses in the rat. *J. Nerv. Dis.*, **126**, 557–563.

MATTINGLY, D. (1962). A simple fluorimetric method for the estimation of free 11-hydroxycorticoids in human plasma. *J. Clin. Path.*, **15**, 374–379.

VAN RIEZEN, H., SCHNIEDEN, H. & WREN, A.F. (1977). Olfactory bulb ablation in the rat: behavioural changes and their reversal by antidepressant drugs. *Br. J. Pharmac.*, (in press).