

Effects of bile duct ligation on ketamine anaesthesia in the rat

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It has been suggested that hepatic metabolism plays an important part in the termination of the effects of ketamine anaesthesia (Livingston & Waterman, 1977) and the present studies were performed to examine the effects of hepatic damage induced by bile duct ligation on ketamine sleeping time in rats.

Adult male Wistar rats (225–300 g) were divided into control and experimental groups. The experimental rats had their bile ducts ligated under halothane anaesthesia whilst the control group were sham operated without ligation of the bile duct. At 2 h, 7 days and 9 days post operatively the rats were given an intraperitoneal injection of ketamine (75 mg/kg) and the sleeping time was measured as the time between loss and regaining of the righting reflex.

After the 9 day experiment the rats were decapitated at the point of recovery and blood samples collected. Ketamine and metabolite levels were measured as described previously (Livingston & Waterman, 1976). The levels of the anaesthetic and its metabolites at this time were as follows:

Ligated animals: ketamine 6.60 ± 0.46 $\mu\text{g/ml}$ plasma, metabolite I 2.49 ± 0.20 $\mu\text{g/ml}$ and metabolite II 1.50 ± 0.15 $\mu\text{g/ml}$. Control animals: ketamine 4.71 ± 0.37 $\mu\text{g/ml}$, metabolite I 2.46 ± 0.32 $\mu\text{g/ml}$ and metabolite II 1.85 ± 0.14 $\mu\text{g/ml}$. The levels for ketamine were significantly higher in the ligated group ($P < 0.01$) whilst the levels of metabolites I and II were not significantly altered.

The results for the effects of bile duct ligation on sleeping times are shown in Figure 1 and it can be seen that they showed a significant rise in the ligated

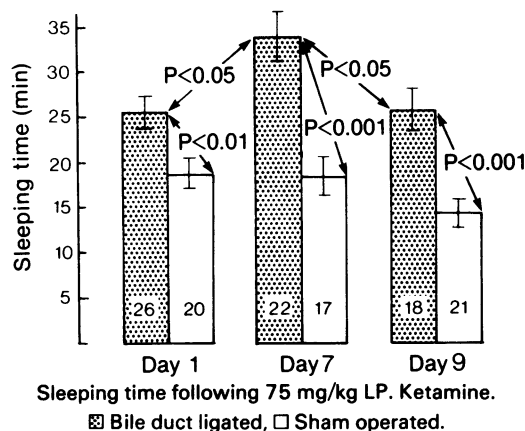


Figure 1

animals at all three time points, and whilst this is not surprising in the seven and nine day post-operation animals, since post-mortem examination showed considerable liver damage, and we have proposed that liver metabolism is a major factor in the termination of the effect of ketamine, the significant rise in sleeping time two hours after bile duct ligation may indicate the possibility of biliary excretion of this drug as a factor in the termination of its action.

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References

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Behavioural changes induced by olfactory bulb ablation and intrabulbar injection of 5,6-DHT: susceptibility to psychotropic drugs

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We have established that antidepressant drugs selectively reverse the effects of bilateral olfactory bulb ablation (van Riesen, Schnieden & Wren, 1977; Cairncross, Cox, Forster & Wren, 1977a) and have recently demonstrated that bilateral intrabulbar injection of 5,6-dihydroxytryptamine (5,6-DHT, 8 μg) produces

similar behavioural and biochemical effects to bulbectomy (Cairncross, Cox, Forster & Wren, 1977b). We have now attempted to assess the susceptibility of the 5,6-DHT-induced syndrome to alteration by psychotropic drugs.

The antidepressant drugs amitriptyline (5 mg/kg) and mianserin (5 mg/kg) caused a significant reversal of both the behavioural and biochemical effects of bulbectomy and 5,6-DHT injection (Table 1). However, these drugs had no effect on either the behaviour or the plasma 11-hydroxycorticosterone (11-OHCS) concentration of sham operated and vehicle injected rats. Amphetamine, chlorpromazine and chlordiazepoxide altered the behaviour and the 11-OHCS concentrations of 5,6-DHT treated rats in a manner very similar to their effects on bulbectomized rats. Thus the 5,6-DHT injected rat appears to selec-