

EFFECTS OF PROPRANOLOL ON BODY WEIGHT REDUCTION IN RATS INDUCED BY CHRONIC ADMINISTRATION OF BACLOFEN

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We have reported that chronic administration of the GABA_B receptor agonist baclofen (bac; 4 mg kg⁻¹) reduces body weight by increasing metabolic rate (Patel et al., 2010). Rothwell *et al.* (1986) have previously demonstrated in an acute experiment that bac microinjected into the ventromedial nucleus of the hypothalamus of urethane-anaesthetised rats activates brown fat metabolism (BFM) which is attenuated by pretreatment with the β-adrenoceptor antagonist propranolol (prop), suggesting that BFM is secondary to the activation of sympathetic nervous system activity. The present study was conducted to examine the effects of chronic administration of prop on the effects of bac on body weight in non-deprived rats.

Male Wistar rats (n = 8; body weight – 375 – 455 g) were injected i.p. once daily for 25 days with either saline (sal) followed 30 min later by sal, sal followed by bac (4 mg kg⁻¹), prop (10 mg kg⁻¹) followed by sal, or prop (10 mg kg⁻¹) followed by bac (4 mg kg⁻¹). Body weight was recorded daily, as described previously (Patel *et al.*, 2010). The body weight data for each rat were expressed as a percentage of the animal's body weight recorded on the first day of the experiment. The results were analysed by 3 way analysis of variance (ANOVA) and by *post-hoc* Dunnett's test

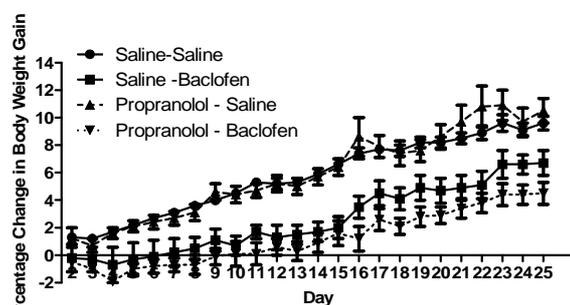


Fig. 1. Effects of propranolol pretreatment on body weight changes induced by chronic administration of baclofen. Vertical line represent \pm s.e. mean.

The results are shown in Fig. 1. Bac (4mg kg⁻¹) significantly reduced body weight gain from Day 4 to Day 25 (at least $P < 0.05$ on each of these days) compared with saline. Prop (10 mg kg⁻¹) on its own had no significant effects on body weight. Pretreatment with prop did not attenuate the effects of bac on body weight.

The results indicate that pretreatment with prop (10 mg kg⁻¹) has no effect on the reduction in body weight produced by bac. It has also been found that pretreatment with a higher dose of prop (i.e. 20 mg kg⁻¹) is also without effect (unpublished results) These data tentatively suggest that the effects of bac on metabolic rate may not be due to sympathetic activation of brown fat.

Patel et al. (2010) Eur. J. Pharmacol. 635, 129 – 134.

Rothwell et al. (1986) Neuropharmacol. 25, 627 – 631.

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