

The effect of pretreatment with bicuculline on baclofen-induced hyperphagia in non-deprived rats

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We have previously demonstrated that the GABA_B receptor agonist baclofen (bac) produces a hyperphagia in non-deprived animals by an action at central GABA_B receptors (see Ebenezer et al., 2011). However, stimulation of central GABA_A receptors also produces increased feeding (see Baldwin et al., 1990) and it is possible that baclofen potentiates eating by releasing GABA which then acts on GABA_A receptors. To test this possibility, the effect of blocking GABA_A receptors with the GABA_A receptor antagonist bicuculline (bic) on baclofen-induced hyperphagia was investigated. In a preliminary study (Patel and Ebenezer, unpublished data), we showed that bic (0.5 and 1 mg kg⁻¹) did not alter food intake in 22h food-deprived rats. Furthermore, these doses did not produce convulsions in the animals. Higher doses were pro-convulsant. We therefore decided to use the 1 mg kg⁻¹ dose of bic in this study.

Male Wistar rats (n=8; b.wt. 380 – 420g) were housed in groups of 4 and had free access to food and water. During experimental sessions, the rats were injected i.p. with either saline (sal) followed by sal, sal followed by bac (2 mg kg⁻¹), bic (1 mg kg⁻¹) followed by sal, or bic followed by bac. The two injections were given 10 min apart. Immediately after the 2nd injection, the rats were placed singly in experimental cages with access to food and water, and cumulative food intake recorded, as described previously (Ebenezer et al, 2011). A repeated measures design was used, with each rat receiving all treatments; 3 – 4 days separated successive trials. The data were analysed by two way analysis of variance (ANOVA) and post-hoc Student-Newman Kuel test..

The cumulative food intake data recorded at 30 and 60 min are illustrated in Fig. 1. Bac increased cumulative food intake at both measurement intervals, while bic was without effect. Pretreatment with bic did not attenuate the hyperphagic effects of baclofen at 30 and 60 min (see Fig. 1). This was confirmed by ANOVA which revealed that there were no significant interactions between the two groups of rats and their responses to saline and bic at 30 min ($F_{(1,14)} = 2.703$, ns) and 60 min, ($F_{(1,14)} = 0.384$, ns) indicating that pretreatment with bic (1 mg kg⁻¹) does not reverse the hyperphagic effect of bac in non-deprived rats. While it is possible that higher doses of bic may have some effects on the feeding response to bac, such doses are pro-convulsant or convulsant, and would make interpretation of such data difficult. The present results thus suggest that it is unlikely that the hyperphagic effect of bac is secondary to an action at GABA_A receptors.

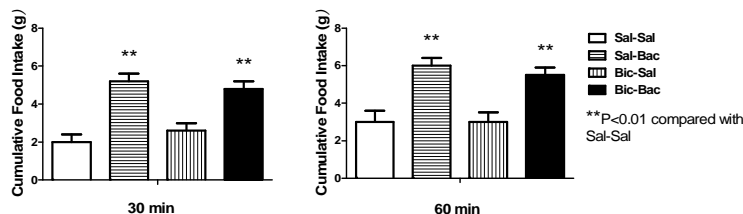


Fig.1 Effects of pretreatment with bicuculline (bic) on baclofen (bac)-induced hyperphagia in non-deprived rats.. Vertical lines rep. + s.e. mean. See text for details of statistical analysis used.

Ebenezer, I.S. *et al.* (2011) *Eur. J. Pharmacol.*, 653, 58 – 62.
Baldwin, B.A. *et al.* (1990) *Physiol. Behav.* 48, 417 – 421.