

Effects of the GABA_B receptor antagonist SCH90511 ((+)-2S)-5,5-dimethyl-3-morpholineacetic acid) on food intake in fasted mice.

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We have previously demonstrated that the GABA_B receptor agonist baclofen (bac) increases food intake in satiated or non-deprived animals by a central mechanism of action (1). In order to test the hypothesis that endogenous GABA, acting at central GABA_B receptors, plays a physiological role in the control of feeding behaviour, we argued that blocking these receptors with a centrally active GABA_B receptor antagonist should reduce food intake in hungry animals (2). In the present study we tested this possibility with the GABA_B receptor antagonist SCH90511, which is water soluble and can penetrate the blood brain barrier and enter the brain when administered systemically.

Sixteen hour fasted male C57BL/6 mice (n=11; body weight: 23 – 28g) were injected i.p. with either physiological saline, or SCH90511 (50 and 100 mg kg⁻¹) and 10 min later placed singly in separate experimental cages with free access to food and water. Cumulative food intake was measured at 60 min and 120 min, as described previously (3). A repeated measures design was used with each mouse receiving all treatments. The data was analysed by ANOVA and *post-hoc* Tukey test.

The results are illustrated in Figure 1. The 50 mg kg⁻¹ dose of SCH90511 significantly reduced food intake at 60 min (P<0.05), but not at 120 min. The 100 mg kg⁻¹ dose significantly decreased food consumption at both 60 and 120 min (P<0.01 in both cases). The doses of drug used in this study did not produce any overt behavioural changes in the mice.

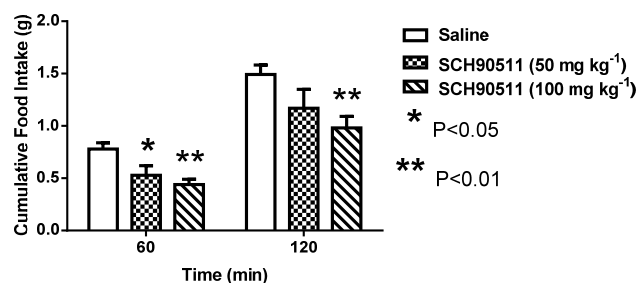


Figure 1. Effects of SCH90511 on food intake in 16h fasted mice.

The results show that ip administration of the GABA_B receptor antagonist SCH90511 produces a dose-dependent reduction in food intake in fasted mice. We have previously found that lower doses of SCH90511 (i.e. 5 – 20 mg kg⁻¹) has no effect on food intake in food-deprived mice (unpublished results). These results are in agreement with previous findings where we demonstrated that both intracerebroventricular and ip administration of the GABA_B receptor antagonist CGP 35358 decreased food intake in hungry rats in a behaviourally specific manner (2). Thus, the present findings give further credence to the hypothesis that endogenous GABA, acting at central GABA_B receptors, plays a physiological role in the regulation of food intake (2).

1. Patel S M and Ebenezer I S (2010) *Eur J Pharmacol* **593**: 68 - 72
2. Patel S M and Ebenezer I S (2004) *Eur J Pharmacol* **503**: 89 - 93
3. Ebenezer I S and Prabhaker M (2007) *Eur J Pharmacol* **569**: 90 - 93