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Modulation of Feeding Behaviour by the Non-Psychoactive Phytocannabinoid Cannabigerol

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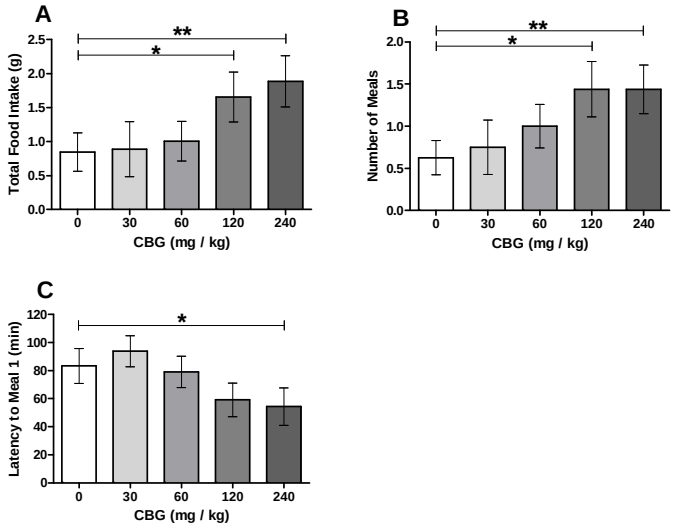
Introduction: Historically the appetite-stimulating properties of *Cannabis sativa* have been attributed to the activity of the psychoactive phytocannabinoid (pCB) Δ^9-tetrahydrocannabinol (Δ^9-THC), via partial agonism at central CB_1 receptors [1-3]. More recent evidence has demonstrated that other, non-psychoactive components of *C. sativa* can also stimulate feeding behaviour [4], and could thus have therapeutic potential in feeding-related disorders such as cancer anorexia-cachexia syndrome. Here we describe the effects of the non-psychoactive pCB, cannabigerol (CBG), on food intake, meal microstructure and locomotor activity in healthy rats.

Methods: Young adult male Lister Hooded rats (200-225g; n = 16) were tested using a well-established pre-feed paradigm for investigation of hyperphagia [2]. Briefly, following 2-hour access to a palatable wet mash pre-feed, rats were orally administered CBG (30-240 mg/kg; *p.o.*, 1ml/kg). One hour later, animals were placed into a test cage, and time, duration and size of feeding bouts were automatically recorded, with concurrent monitoring of ambulatory and rearing behaviours to investigate any clinically relevant modulation of locomotor activity. CBG was administered as a purified extract in sesame oil vehicle, with all animals receiving all doses in a within-subjects, counterbalanced design. All data are presented as mean±SEM and were analysed by one-way repeated-measures ANOVA and planned comparisons.



Results: Total food intake was dose-dependently increased ($F_{4,\ 60}$=3.967, p=0.006), with 120 and 240mg/kg CBG resulting in a two-fold increase *vs* vehicle (p=0.036 and p=0.009 respectively, figure A). Meal pattern analysis revealed that the number of

individual meals consumed was significantly increased ($F_{4, 60}$=3.306, p=0.016) by the two highest dose groups (p=0.014 and p=0.003, figure B), with the size of meals 1 and 2 combined also increased ($F_{4, 60}$=3.927, p=0.007). Additionally, there was a significant decrease in latency to first meal ($F_{4, 60}$=3.124, p=0.021), with 240mg/kg CBG advancing the onset of feeding by almost 30 minutes (p=0.016, figure C), despite the animals having pre-fed to satiety. Total ambulatory locomotion was also increased following CBG treatment ($F_{4, 60}$=7.121, p<0.0005).

Conclusion: These data provide the first evidence that CBG can stimulate both the appetitive and consummatory aspects of feeding behaviour, and may thus have therapeutic potential for the treatment of anorexia associated with cancer symptoms. Further, the stimulation of locomotor activity indicates CBG may have an additional therapeutic role in reducing the fatigue component of cachexia pathology.

[1] Williams CM et al, Physiol Behav 65:343, 1998

[2] Williams CM & Kirkham TC, Pharmacol Biochem Behav 71:333, 2002

[3] Pertwee RG, Br J Pharmacol. 153:199, 2008

[4] Farrimond et al, Psychopharmacology (Berl) 223:117, 2012