Effects of the phytocannabinoid (pCB) Δ^9-tetrahydrocannabivarin (Δ^9-THCV) on Diet Induced Obesity in rats.

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The global obesity epidemic has expanded through the increased availability of high calorific foods (WHO, 2015). Development of treatments is emerging from research on caloric intake and how the body regulates feeding. How the endogenous cannabinoid system (ECS), which is central to feeding regulation, can be modulated for treatment development needs further exploration (Farrimond, Mercier, Whalley, & Williams, 2011). The ECS has been shown to induce weight loss through appetite suppression (hypophagia) when stimulated by antagonist cannabinoids, which work by blocking the activation of cannabinoid 1 (CB1) receptors. The phytocannabinoid (pCB) Δ^9-tetrahydrocannabivarin (Δ^9-THCV) acts as a neutral antagonist at CB1 receptors, and is thought to hold anti-obesity metabolic properties including hypophagia (Dennis, Whalley, & Stephens, 2008). How it effects high sugar and high fat food intake is yet unknown. This study aimed to test the effects of Δ^9-THCV on feeding behaviour in diet-induced obese (DIO) rats.

24 adult, male Lister hooded rats were randomly divided into two groups with 12 rats in each. Weight gain was induced in one group through a high sugar (HS) mash plus chow diet and the other through a high fat (HF) mash plus chow diet. A Diet Induced Obesity (DIO) procedure was used, whereby the concentrations of sugar in the HS mash and oil in the HF mash were matched for caloric value. Rats were fed this controlled diet for seven weeks prior to testing.

Purified-Δ^9-THCV (GW Pharmaceuticals, England) in a sesame oil vehicle was given at doses of 0.2, 1.0 and 5.0mg/kg, plus a vehicle control (0.0mg/kg). A within-subjects design was used, measuring Δ^9-THCV on food intake (calories consumed). Drugs were administered *per ora* (p.o.) via a syringe placed into the cheek pouch of each rat. After drug treatment

subjects were deprived of food for one hour to allow for drug assimilation. Testing used standard plastic cages with a CCTV camera fitted above each. Subjects were placed individually into test cages, during which HS/HF mash and chow were available. After 240 minutes of testing the remaining food mass for each test cage was weighed. Videos were then coded for three feeding states; eating mash, eating chow and not eating.

Both groups preferred the HS and HF mash respectively. Between-groups, weight gain was significantly greater for the HF group. Post-mortem body dimension parameters showed that all animals were of a broad adiposity consistency, reflected in BMI scores which ranged from 0.70-0.83 g/cm² (*M*=0.76). This project contributes towards developing a more standardised DIO procedure and measure of weight gain in rats, showing that DIO can be induced at a relatively fast pace. However, no significant dose effects were found for any of our measures. Further studies are needed to clarify how Δ^9-THCV given for longer periods might affect feeding behaviour especially activity levels (energy expenditure). This study was completed as part of Sian Carrs MSc project.

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