

An automated home cage observation system as a model of feeding behaviour in mice

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Introduction

Obesity is characterised by an increase in consumption of food containing high levels of sugar and saturated fats combined with a reduction in physical activity. The increased prevalence of obesity and childhood obesity in western countries has highlighted the need for anorectic agents which are effective in weight management.

The Cannabinoid (CB1) antagonist SR141716A (Rimonabant/Acomplia) has previously been shown to suppress food intake [1, 2]. However, in addition to drug induced effects on food intake and body weight, drug treatment can also affect activity levels [3, 4]. An increase in activity may lead to hyperactivity which could explain a reduction in body weight which is independent of any reduction in food consumption. Therefore, a more detailed assessment of drug-related effects on activity in conjunction with drug-induced hypophagic properties is required.

Aim

The aim of this study was to develop a novel method which would combine these two approaches and allow us to assess both the feeding behaviour and locomotor activity of free-feeding mice. The cannabinoid antagonist AM251 was used to validate this method.

Methods

Male and female C57BL6 mice (25-32g) were used in this study. The automated home cage video-based observation system 'phenotyper' was used to allow long-term continuous monitoring of behavioural activity of the mice. During testing the mice were maintained on a 12 hr light/dark cycle (lights off 7pm) with free access to food (food hopper) and water (water bottle). Animals were given 3-4 days of habituation in the phenotyper prior to drug administration in order to attain a baseline level of performance and were matched for body weight before being assigned to drug groups of AM251 (10 mg/kg) or Tween 80, with all drugs injected intraperitoneally 1-2 hours prior to the start of the dark phase of the circadian cycle. A single acute treatment or repeated dosing regime was employed with the drug administered daily for 4 consecutive days. The behaviour of the animals was monitored using the computer based tracking software Ethovision (version 3.0, Noldus, Netherlands). The parameters recorded included total locomotor activity, time spent in the area in front of the food hopper and time spent in the area close to the water bottle. These parameters were analysed in hourly intervals during

both the light and dark phases of the experimental days. In addition to these parameters the body weight of each animal, weight of food hopper (food intake) and weight of water bottle (water intake) were recorded on a daily basis immediately prior to drug injection and also post drug treatment (between the hours of 10.00 – 11.00 am of the light cycle).

Results

Acute treatment with AM251 induced a suppression of food intake and a reduction in body weight compared to vehicle treated animals. AM251 treated animals also spent less in the areas of the arena associated with food and water. In addition a reduction in locomotor activity was also observed although this was only apparent for the first few hours of the dark phase. Repeated dosing with AM251 also produced a significant suppression in body weight and food intake relative to controls, with animals spending less time in the food zone on all nights following treatment. Similar to acute treatment a decrease in overall locomotor activity was also evident.

Conclusions

These findings suggest that the home cage observation system 'phenotyper' is a sensitive and effective method to assess the hypophagic effects of possible anti-obesity drugs as it allows the long-term continuous monitoring of both food intake and behavioural activity.

References

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