# Comparison of Home-Cage Activity Systems Using Transgenic Mouse Lines and Pharmacological Interventions

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## Introduction

A number of different Home-Cage activity systems have been developed in order to assess the behaviour of mice. Automated home-cage activity systems enable the establishment of continuous and long-term monitoring of locomotor activity, feeding behaviour and circadian rhythmicity in rodents [1-4]. They allow a handling free assessment of drug and behavioural effects in a longitudinal design.

## Aim

The main aim of this present study was to evaluate the performance of transgenic and pharmacologically treated mice in two variants of home-cage activity systems, allowing us to perform a comparison of the behavioural setups.

## Methods

Two variants of home-cage activity observation systems were used in this study: 1) the PhenoMaster (TSE Systems, Bad Homburg, Germany) and 2) the PhenoTyper (Noldus IT, Wageningen, The Netherlands). In both tests, animals were singly housed and subjected to a 12 hour light/dark cycle (lights on @ 7am, temperature 23 ± 2°C, relative humidity of 40 – 60 %) with free access to food and water. All experiments being performed in accordance with Home Office regulations. Mice were placed into the cages and given 2 days of habituation before assessment of circadian/ultradian activity over continuous day-night cycles.

1. The PhenoTyper is a video-based observation system for long-term continuous assessment of behavioural activity in mice via a built-in digital infrared sensitive video camera and infrared light sources in a top unit of each cage. The body-centered recording of the animal (EthoVision 3.1) was sampled at 12.2 Hz. Data was stored online and calculated for parameters including: i) total locomotion during day and night cycles; ii) time spent in the food zone (area in front of the feeder) and iii) time spent in the water zone (area in front of the water bottle).
2. The PhenoMaster system consists of a test cage (42 x 26.5 x15 cm) positioned in a metal frame containing regular infrared beams in both X and Z coordinates at a distance of 3 cm and at a rate of 100Hz. These enable the continuous recording of exploratory activity over long time periods. Cage lids were fitted with two weight transducers supporting a feeder and a water bottle allowing an automated measurement of food and water intake. All data was stored online and parameters calculated included: i) daily food consumption; ii) daily water consumption and iii) total distance moved in day and night cycles.

Two different studies were employed: i) Evaluation of the cannabinoid antagonist AM251 as a possible treatment for obesity and ii) Behavioural phenotyping of a mouse model of Rett Syndrome.

i) C57BL6 mice (25-30g) were used in this study to assess the effect of the CB1 antagonist AM251 on body weight and feeding behaviour. Mice were matched for body weight prior to an intraperitoneal injection of either AM251 (10 mg/kg) or vehicle (Tween 80) 1-2 hours before the start of the dark phase of testing. In addition to the parameters measured by the activity cages the body weight of each mouse and weight of food hopper (food intake) and water bottle (water intake) were recorded.

ii) Female mice in which the endogenous Mecp2 gene was silenced by insertion of a targeted *lox stop* cassette ($Mecp2^{Stop}$) were crossed with males hemizygous for the CreESR transgene [5]. For the purpose of this study only heterozygous Mecp2 $^{Stop/+}$ females without the cre-ER transgene and wild-type (WT) littermates were used and were aged 10 – 12 months at the start of testing. Mice were assessed in the PhenoMaster and PhenoTyper for a period of 5 days in order to evaluate locomotor activity, circadian activity and food/water intake.

## Results

i) Acute treatment with AM251 in both the PhenoMaster and PhenoTyper induced a suppression of food intake and a reduction in body weight compared to vehicle treated mice. AM251 treated animals spent less time in the food zone of the PhenoTyper and displayed a significant reduction in food consumption in the PhenoMaster. In addition to AM251 induced effects on feeding behaviour a reduction in locomotor activity was also evident in the activity cages although this was only apparent for the initial few hours of the dark phase.

ii) Mecp2 $^{Stop/+}$ mice displayed a significant reduction in overall locomotor activity compared to WT's in both the PhenoMaster and PhenoTyper. The differences in activity were particularly evident for the nocturnal dark phases of testing with little to no difference apparent during the light phases. In both home cage activity systems the $Mecp2^{Stop/+}$ mice displayed normal circadian rhythm with both genotypes displaying elevated locomotor activity during the dark hours and were less active during the light phase. In addition to differences in locomotion a significant alteration in feeding behaviour was also observed with Mecp2 $^{Stop/+}$ mice presenting with an increased body weight compared to WT's, along with enhanced food consumption in the PhenoMaster and time spent in food zone in the PhenoTyper.

## Conclusions

These findings suggest that the home cage activity observation systems ' PhenoTyper' and 'PhenoMaster' are sensitive and effective at determining drug induced changes in feeding behaviour and in the validation of the locomotor phenotype evident with a mouse model of Rett syndrome. Replication of behavioural observations in two different recording environments supports the quality of the equipment and the reliability of the phenotype.

## References


1. De Visser, L., van den Bos, R., Kuurman, W.W., Kas, M.J.H., Spruijt, B.M. (2005). Novel approach to the behavioural characterization of inbred mice: automated home cage observations. *Genes, Brain and Behav* 1-9.

2. Riedel, G., Fadda, P., McKillop-Smith, S., Pertwee, R.G., Platt, B., Robinson, L. (2009). Synthetic and plant-derived cannabinoid receptor antagonists show hypophagic properties in fasted and non-fasted mice. *Br. J. Pharmacol.* **156**, 1154-1166.

3. Theander-Carrillo, C., Wiedmer, P., Cettour-Rose, P., Nogueiras, R., Perez-Tilve, D., Pfluger, P., Castaneda, T.R., Muzzin, P., Schürmann, A., Szanto, I., Tschöp, M.H. (2006). Rohner-Jeanrenaud F. Ghrelin action in the brain controls adipocyte metabolism. *J Clin Invest.* **116**(7), 1983-1993.

4. Edelsbrunner, M.E., Painsipp, E., Herzog, H., Holzer, P. (2009). Evidence from knockout mice for distinct implications of neuropeptide-Y Y2 and Y4 receptors in the circadian control of locomotion, exploration, water and food intake. *Neuropeptides* **43**(6), 491-497.

5. Guy, J., Gan, J., Selfridge, J., Cobb, S., Bird, A. (2007). Reversal of neurological defects in a mouse model of Rett syndrome. *Science* **315**, 1143–1147.