ELSEVIER

Journal of Neuroscience Methods 162 (2007) 180–186

JOURNAL OF NEUROSCIENCE METHODS

www.elsevier.com/locate/jneumeth

Pharmacological validation of a novel home cage activity counter in mice

K. Ganea, C. Liebl, V. Sterlemann, M.B. Müller, M.V. Schmidt *

Max Planck Institute of Psychiatry, Munich, Germany

Received 26 September 2006; received in revised form 11 January 2007; accepted 15 January 2007

Abstract

Many behavioural tests in rodents are based on the premise that basal locomotor activity of the animals is similar between the tested groups. The measurement of basal home cage activity is therefore an essential parameter, that should be included in all studies which employ tests of anxiety or cognition. Currently available systems for the assessment of home cage locomotion are often complex and expensive. Here we describe and validate a novel, simple and cost-efficient apparatus for the assessment of basic home cage locomotor activity in rodents. Circadian dark–light activity patterns can be reliably obtained with the home cage activity counter. Furthermore, changes in locomotion induced by novelty or pharmacological treatment were reliably and sensitively detected by the apparatus. Thus, the here presented home cage activity counter can be used for the measurement of basal home cage locomotor activity.

Keywords: Locomotion; Home cage; Mice; Anxiety; MK-801; Diazepam; D-Amphetamine

1. Introduction

In behavioural neuroscience the observation of home cage activity is a widely used parameter to assess the influence of genetic mutations, experimental treatment or drug effects on basal locomotion. Home cage activity in contrast to the activity displayed in a novel test environment is of specific importance, as differences in general activity can also influence test results in many behavioural tests (Kazlauckas et al., 2005). Locomotor behaviour is highly context-specific and large differences can be observed between novelty-induced locomotion and home cage activity (Galani et al., 2001). Confounding factors like differences in anxiety-related behaviour may result in alterations of activity patterns in rodents under stressful situations, emphasizing the need for locomotor activity measurement under stress-free conditions. On the other hand pre-existing differences of basal locomotion will affect many anxiety-related tests, such as the open field, the dark–light box or the elevated plus maze. Thus, there are several advantages in observing the activity of animals in their familiar home cage environment. First, the influence of unfamiliar situations, such as a novel environment or human intervention is kept to a minimum. In addition, the animal's activity is not affected by a disturbing monitoring apparatus. Furthermore home cage observation allows for a continuous locomotor observation over consecutive days.

Various methods measuring rodent activity in their home cages are already described, which all have certain advantages and disadvantages. A very common locomotion monitoring device is the running wheel, which comprises the premise that activity of the animal is depending on the motivation to run (Mollenauer et al., 1991). Some other recording systems like implantable telemetry transmitters or implantable magnets (Gegout-Pottie et al., 1999; Storch et al., 2004; Tang and Sanford, 2002), which register locomotion via an external sensor plate, require an invasive operation before the test, which is often not ideal for further experimental procedures. Video-tracking systems are commonly and effectively used but they are generally limited to the light cycle and can be very costly (Noldus et al., 2000). In addition, as the camera needs to be able to track the animal at all times, special observation cages are needed. The same holds true for methods like ultrasonic systems, infrared sensors or microwave radar systems (Clarke and Smith, 1985; Pasquali et al., 2006; Young et al., 2000). These systems are in general very sensitive and well validated, but the experimental set-up is complex and often expensive. Additionally, such systems require a specialized hardware interface to translate the data into an usable output format. Therefore, the effort is only profitable in case of a frequent use of the locomotion recording system.

* Corresponding author at: Max Planck Institute of Psychiatry, RG Molecular Stress Physiology, Kraepelinstr. 2-10, 80804 Munich, Germany.
Tel.: +49 89 30622 519; fax: +49 89 30622 610.
E-mail addresses: mschmidt@mpipsykl.mpg.de, schmidt_mathias@gmx.com (M.V. Schmidt).

0165-0270/$ – see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.jneumeth.2007.01.008

The aim of the current study was to establish and to validate a novel home cage activity counter for the recording of basal activity in rodents. The activity counter is based on a mechanical recording system, which has been designed by our research group. There are a number of main requirements, which this locomotion monitoring device should fulfil. First, the monitoring should be continuous and automatic and the output must be easy to analyse. Second, in order to have the possibility to record a large number of animals at the same time, the construction of the test apparatus should be easy to realize and cost-efficient. Third, to minimize concomitant disturbances of animals, the method should not be invasive or aversive and testing should be carried out in standard housing cages. Finally, recording should be able to take place in the same housing room and should not be limited to the light cycle.

2. Methods

2.1. Animals and housing conditions

Experiments were carried out with male CD1 mice from Charles River Laboratories (Sulzfeld, Germany). The animals were 12 weeks old on the day of arrival. All animals were single housed in standard cages (45 cm × 25 cm × 20 cm) under a 12L:12D cycle (lights on at 7:00 h) and constant temperature (23 ± 2 °C) conditions. Food and water were provided *ad libitum*. The experiments were carried out at the animal facility of the Max Planck Institute of Psychiatry in Munich, Germany, and started after a habituation period of 2 weeks following arrival.

The experiments were carried out in accordance with European Communities Council Directive 211-2531-79/05. All efforts were made to minimize animal suffering during the experiments. The protocols were approved by the committee for the Care and Use of Laboratory Animals of the Government of Upper Bavaria, Germany.

2.2. Home cage activity counter (Hac)

The basic principle of the home cage activity counter is based on a tiltable platform on which the empty home cage can be adjusted in balance (Fig. 1). When the animal is placed into the cage the platform will either tip to the left or right side, depending on the position of the animal. Thus, each time the animal crosses the centreline of the cage, the animal's weight shift will cause the cage to tip to the other side. Underneath the platform an electronic switch measures the number of cage tips, which are then displayed on an electronic counter. The margin of platform tilting is reduced to a minimum, so that the animals are not disturbed by movements of their home cage. The cage can be adjusted on the counter lengthwise or across, with the limitation that the water and food supply should also be in balance. This can be achieved by fixing a small water bottle in the middle of the cage grid, with an equal amount of food on either side. The home cage activity counter can be constructed to fit different cage sizes. For this experiment the platform was fitted to the size of our mouse cages.

2.3. Detailed apparatus description

A parts list, including dimensions and approximate prizes can be found in Table 1. The custom build apparatus consists of a basal polyvinyl platform (8 mm × 250 mm × 350 mm), which stands on four base aluminium feet. On the two short sides of this platform, two polyvinyl square ends (20 mm × 20 mm × 40 mm) are mounted. These square ends are fitted with two bearings and connected by a steel rod (Ø6 mm × 350 mm). On two places of the steel rod a polyvinyl holder is fixed, on which a second (upper) platform (4 mm × 170 mm × 250 mm) is mounted. In order to enable the adjustment of the margin of upper platform tilting, the two long sides of the lower platform are fitted with an additional polyvinyl square end carrying a brass screw. For the measurement of the number of upper platform tilts a small electronic switch is adjusted underneath one long side of the upper platform and connected to a digital display, which is tight fitted on the basal platform (Fig. 1C).

2.4. Experimental design

2.4.1. Experiment 1: basal locomotor activity throughout the circadian rhythm

In order to assess the basal home cage activity of CD1 mice, a total of six animals was used. Each animal was placed individually in a new standard cage which had been adjusted on the activity counter platform. Following 20 h of habituation, locomotor activity monitoring started at the beginning of the dark phase. The locomotor activity of the animals was scored consecutively for three dark phases and three light phases. The total number of cage crossings was registered during each observed phase.

2.4.2. Experiment 2: locomotor activity induced by novel environment

In this experiment we assessed the sensitivity of the home cage activity counter to measure small changes in activity induced by novelty. A total of six animals were placed individually in their home cage on the activity counter platform on the day before testing. Following 20 h of habituation, locomotor activity was recorded every 10 for 60 min. The animals were then transferred to a novel, but otherwise identical cage, and locomotor measurement continued for another 60 min. After this period the animals were returned to their home cages and locomotor activity was recorded for one more hour.

2.4.3. Experiment 3: pharmacological validation by MK-801 and D-amphetamine

Here we tested the ability of the home cage activity counter to detect a pharmacologically induced increase in locomotor activity, induced by either MK-801 or D-amphetamine. The experiment was performed separately for both drugs. A total of 12 animals per pharmacological validation (six per treatment group) was used. After 20 h of habituation in a new cage on the platform, the test started at 11:00 h during the light phase. During the first 2 h basal activity of the animals was recorded.