Measuring basal and complex behaviors of rats in automated social home cage systems using IntelliCage for rat technology

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Introduction

Classical phenotyping of rodent models is traditionally assessed with a number of time-consuming test batteries in which animals are tested individually and experimental procedures are often difficult to standardize. For behavioral testings of mice, the IntelliCage for mice has been successfully applied for mouse phenotyping with fast and efficient test procedures for evaluation of exploratory behavior and diurnal patterns [1,2], appetive and aversive learning [3,4] and fear conditioning [5]. Based on the fact, that most of the behavioral testings have been assessed in rats, the IntelliCage for mice has been modified with the aim to test rats for their behavior within this automated home-cage system.

Aim

In order to validate the IntelliCage for rats, we introduce the transgenic huntington rat (tgHD rats) as an animal model for Huntington`s disease (HD) into an adjusted prototype of IntelliCage for rats. The tgHD rats have been shown to represent neuropathological hallmarks of HD with behavioral abnormalities including motor dysfunction, anxiety and depressive-like behavior and impaired learning abilities [6,7]. Using the IntelliCage for rats, the tgHD rats were tested for a number of behavioural parameters that have been suggested as possible read-outs for the IntelliCage, including parameters of basal activity, operant learning, spatial learning and anxiety-like behavior.

Material and Methods

At the age of six-weeks, two groups of male rats, each composed of five tgHD rats and their wildtype littermates (wt) were matched and subjected to the IntelliCage for rats. The IntelliCage for rats was designed with a technical setup composed of four conventional Typ 4 cages that are interconnected with each other, and each cage given animals access to one recording chambers (corner).

IntelliCage experiments included a contineous experimental designs including a period of habituation of animal groups to the system (seven days), nose poke adaptation (three days duration), and the learning paradigms side discrimination, reversal of side discrimination (each two days). Data were achieved by the IntelliCage software packages IntelliCage Controller, Designer and Analyzer (New Behavior AG).

Results

Within the habituation period, general behavior of the animals was monitored in the cage system with free access to water and included corner visits, nosepoke and lick performances. Comparison of the over the first 90 minutes revealed no differences between tgHD and wt rats in exploratory behavior, indicated as latency to visit the first corner and cumulative number of corner entries. In addition, we found that during habituation, the IntelliCage for rats reliably monitors total number of corner entries, nosepokes and licks in both groups, reflecting a circadian pattern with no differences in group activity. All animals visit the four corners during the first circadian interval with increased corner visits during the dark phase.

The second experimental module involved adaptation to nosepoke for fluid access and furthermore, to nosepoke on the correct side, which is indicated by a green light. Rats learned fast to nosepoke for water, reaching a stable response after 1 day of adaptation, in addition, both animals groups learned within one day to discriminate between the correct side and the incorrect side independent of the genotype (side error 22% tgHD, 19% wt). These results were re-confirmed by changing the side.

To conclude, animals accept the setup of the IntelliCage for rat, indicating that the system can be used as a suitable tool to measure rat ethological and triggered behaviors.

Discussion

Using this technical and experimental setting, additional more complex learning paradigms including place learning are currently validated in the IntelliCage for rats. Experimental modules in the IntelliCage for rats will be run successively in a longitudinal study to elaborate age-related deficits in learning and memory in the tgHD rats. Results will be compared to classical comprehensive phenotyping including tests to monitor locomotor activity, spontaneous alternation and learning paradigms in terms of reliability and sensitivity.

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