A novel task to assess reversal learning in mice in a home-cage environment

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Background

In several neurological and psychiatric disorders, executive functions, a collection of higher cognitive functions including attentional control, planning and flexibility, are affected. Measuring executive functions in mice is important in understanding the mechanisms underlying cognitive deficits in these disorders. The majority of currently available behavioral tests targeting these cognitive domains are operant tasks, which require extended training periods. Here, we describe a novel test for the cognitive measure 'reversal learning' in an automated home-cage environment called the PhenoTyper that circumvents extended training periods and the requirement of labor intensive animal-handling.

Methods

The task was implemented in an automated home-cage (PhenoTyper model 3000, Noldus Information Technology, Wageningen, The Netherlands), in which behavior was video tracked by a camera mounted in the top. Hardware actions were triggered by the position of the mouse (EthoVision HTP 2.1.2.0, based on EthoVision XT 4.1, Noldus Information Technology, Wageningen, The Netherlands). The cage was equipped with a shelter with two entrances, a feeding station, and spouts of a water bottle and a pellet dispenser.

After an initial habituation period to the home-cage, a wall with three holes was placed in front of the pellet dispenser spout. For two days, mice had to learn to earn food (Dustless Precision Pellets, 14 mg, Bio-Serve, Frenchtown, NJ, USA) by going through the left hole in the wall (Initial learning). During this period the dispenser distributed 1 reward for every 5 times the mouse went through this correct left hole (FR5 schedule). The middle and right hole were the incorrect holes and passing these holes did not have any consequences. During the subsequent 2 days, the correct hole was switched to the right hole (Reversal learning).

The number of passages needed to reach a criterion of 24 out of 30 passages through the correct hole, computed as a moving window, was used as a measure of performance during both stages. The number of passages through the left hole during the reversal stage provided a measure of perseverative errors. The number of passages through the middle hole represents a measure of random errors, because this hole was never rewarded [1]. The total number of passages, as well as total distance moved, were assessed as measures of general activity.

Experiments were carried out in accordance with the European Communities Council Directive of 24 November 1986 (86/609/EEC), and with approval of the Animal Experiments Committee of the VU University.

Results

C57BL/6J mice were able to attain the performance criterion of 80% correct within 1 day. Reversal learning requires suppression of the initially acquired response, while learning a new, competing, rule [2]. As expected, mice took significantly longer to attain the performance criterion during the reversal phase, compared to the initial learning phase. Nonetheless, all individuals were able to attain the criterion within the two available reversal learning days.

Task activity was predominantly limited to the dark phase, suggesting that task performance had no impact on circadian rhythm.

Conclusions

We have developed a 4-day protocol for reversal learning, which runs without human intervention. This task provides an easy and efficient way of screening mice for reversal learning in a home-cage environment, with improved animal welfare in comparison to conventional operant paradigms.

References

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