General information to accompany Lafayette Instrument Automated Mouse Reaching Chamber - Model 80870

Abstract

Recent rapid development of transgenic, knock-in and knock-out mouse models of genetic disorders has necessitated advancements in sensitive operant behavioral testing to properly identify phenotypic expression. Since rats have historically been the preferred rodent for behavioral assessment, techniques and equipment are now being adapted to accommodate the mouse models typically used by geneticists. The automated forepaw reaching chamber provides sensitive measures of motivation, cognition and fine motor coordination in the mouse. This chamber was adapted from an apparatus previously used to provide manually recorded data on the effects of caudate lesions in rats. The chamber offers several advantages over "staircase" chambers in allowing researchers to assess mishandled (dropped) food pellets, as well as providing detailed information on latency measures.

Introduction

In developing a reliable and valid model for assessment of motor deficits, several protocol features should be considered.

- **Methods should be relatively simple, yet sensitive enough to measure subtle effects of neural damage.**
- **Methods should be able to differentiate motor abnormalities from task errors produced by learning and memory deficits.**
- **Methods should be easily incorporated into a range of laboratories, especially those where behavioral testing is not the primary research focus.**

One sensitive measure of motor behavior deficits is assessment of forelimb reaching tasks. Such tasks have been widely used to establish and quantify substantia nigra, basal ganglia and cortical damage. Several variations of this task have been reported including a forepaw lever pressing task and a raised reaching task requiring use of one forepaw for stabilizing the body and the other for food pellet retrieval. The commonly used "staircase" apparatus and protocol for assessing forelimb reaching is advantageous in that the testing apparatus is relatively simple and inexpensive to construct, and does not require experimenter monitoring for data collection on some measures of paw reaching effectiveness. However, this apparatus has the disadvantage of lacking the capacity to record latency measures for initiating and completing behaviors, and does not provide data on ratio of successful reach attempts to total reach attempts.

Methods

1. Pellets used in the operant chamber and home-cage training hopper should be 20 mg in size. One vendor for such pellets is Research Diets, Inc. New Brunswick, NJ (www.researchdiets.com).

2. Once weaned to rodent chow animals may be tested in the chamber at any time. If research is not designed to measure initial acquisition of motor behaviors, it is highly advantageous to use a home-cage training hopper (e.g. Lafayette Instruments Model 80875) for all home-cage feeding at least one week prior to initial testing. Such a devise allows animals to associate a reaching hole with food, and to learn the basic motor functions required for pellet retrieval. Training animals in the operant cage itself is possible, but such training is time consuming and anxiety associated with introducing animals to a new environment significantly impedes learning the basic reaching procedure.

3. Animals that have been pre-trained for reaching with home-cage training hoppers will generally become proficient at paw reaching in the operant chamber within two or three trials.

4. Once animals become proficient in the chamber, a 3 to 5 minute test period per animal will yield significant data. For example within the first ten test sessions, animals may be inducing 100 to 200 photo-beam breaks and successfully retrieving 2 to 10 pellets in a 5 minute test period.

Results

1. Measures that may be recorded within a test session using a single side of the chamber include the following:

- **Latency to onset of reaching behavior**
- **Number of photo-beam breaks**
- **Number of pellets extracted from the pellet hopper**
- **Number of pellets dropped outside of the cage**
- **Number of pellets dropped inside of the cage**
- **Number of pellets consumed**

2. Additional measures that may be recorded within a test session using both sides of the chamber include the following:

- **Latency to onset of incorrect choice reaching behavior**
- **Latency to onset of correct choice reaching behavior**
- **Number of incorrect choice photo-beam breaks**
- **Number of correct choice photo-beam breaks**

Interpreting Results

1. Profound motor deficits may be indicated by a significant decrease in the number of photo-beam breaks caused by an inability of the animal to successfully extend a forepaw through the reaching hole. Such profound deficits may also increase latency to initiate reaching behavior.

2. Moderate motor deficits may be indicated by a significant increase in the number of photo-beam breaks relative to the number of pellets consumed by the mouse. The number of pellets consumed is calculated as the number of pellets removed from the hopper, minus pellets dropped inside and outside of the operant chamber. Moderate motor deficits may also be indicated by an increase in the number of pellets dropped outside of the chamber, as animals lose required grasping and retrieving ability.

3. Mild motor deficits may be indicated by an increase in the number of pellets dropped inside the chamber. Such dropped pellets may indicate an inability to coordinate motor function of both forepaws simultaneously to manipulate food for eating.

4. Motivation deficits may be indicated by a significant increase in latency to initiate reaching behavior.

5. Cognitive deficits may be apparent with using alternating reward locations. In this case increased latency to correct hole choice and significant photo-beam breaks on the incorrect hole indicate cognitive dysfunction.

Trouble Shooting

1. Photo-beam not functioning:

- **Check power source**
- **Adjust hopper to insure photo-beam passes unobstructed through hopper wall holes**

2. Animals unable to successfully retrieve pellets into chamber

- **Hopper may be adjusted too far from chamber**
- **Animals may not be adequately trained to retrieve pellets**
- **Animals may be behaviorally deficient (test unaffected animals as a control)**

3. Pellets do not freely move from tubes into hopper

- **Pellets often lack symmetry required for free rolling movement. Tubes may need to be gently "tapped" by research assistant during testing to ensure continuous availability in hopper.**

Advantages

1. **Staircase reaching chamber can not assess cognitive functions. The automated reaching chamber can be used to assess simple cognitive functions by alternating baited hopper within or between trials. Latency measures, in combination with quantifying reach attempts into the nonbaited hopper indicate deficits in this reversal task.**

2. **Trough-type reaching chambers do not discourage scooping behavior. One problem recognized by researchers assessing fine coordinated forepaw reaching behaviors is that animals may adapt to motor deficits by "scooping" pellets from a trough type feeder, rather than using a coordinated grasp. The automated chamber allows the distance between hopper and cage to be adjusted so scooped pellets drop out of reach. These dropped pellets may then be quantified as a measure of ineffective reaching behaviors.**

3. **Staircase and trough-type reaching chambers do not quantify unsuccessful reach attempts. By quantifying pellets prior to, and following conclusion of, an experimental period the number of pellets successfully retrieved and consumed by the rat is established. Photocell recording of total reach attempts allows researchers to then establish effectiveness of motor behaviors using a ratio of total reach attempts to successful reach attempts.**

4. **Staircase and trough-type reaching chambers do not quantify latency measures. Latency to initiate reaching may be used to help establish cognitive, motivation and motor deficits. Automated system accurately records first reach attempt, and times for all subsequent attempts.**

Disadvantages

1. **Automated chamber does not differentiate between left and right forepaw use. In research where unilateral lesions are used, it may be useful to assess differences between left and right forepaw use. Previous research with trough type chambers have used a "cuff" to foil reaching with one forepaw through a narrow passage. Such a cuff could be used with the automated chamber.**