Levodopa-induced dyskinesia mouse model

In 1 collection

Beatriz E Nielsen[1]

[1]University of Colorado Anschutz Medical Campus

Beatriz E Nielsen
University of Colorado Anschutz Medical Campus

OCT 30, 2023

OPEN ACCESS

DOI:
dx.doi.org/10.17504/protocols.io.8epv5xxb5g1b/v1

Protocol Citation: Beatriz E Nielsen 2023. Levodopa-induced dyskinesia mouse model. **protocols.io** https://dx.doi.org/10.17504/protocols.io.8epv5xxb5g1b/v1

Protocol status: Working

Created: Aug 19, 2023

Last Modified: Oct 30, 2023

ABSTRACT

This protocol describes a mouse model of levodopa-induced dyskinesia (LID) and the behavioral assessment of its motor deficits. It includes open field locomotor activity and scoring of abnormal involuntary movements (AIMs).

PROTOCOL integer ID:
86705

Keywords: ASAPCRN

Levodopa-induced dyskinesia mouse model development

1 Generate unilaterally high dose 6-OHDA-lesioned mice (protocol linked below):

Protocol

NAME
6-OHDA mouse model of Parkinson's disease

CREATED BY
Beatriz E Nielsen

PREVIEW

2 3 weeks after 6-OHDA injections, verify unilateral dopamine depletion by assessing forelimb use assymetry in the cylinder test (protocol linked below).

Protocol

NAME
Motor behavioral assessment

CREATED BY
Beatriz E Nielsen

PREVIEW

3 Start daily intraperitoneal (i.p.) injections of 2.0 mg/kg of L-DOPA (3,4-dihydroxy-L-phenylalanine) plus 12 mg/kg of benserazide hydrochloride dissolved in sterile saline for 7-8 days.

- Behavioral motor tests (open field and dyskinesia) are formally conducted in different days at the end of the treatment (days 7 and 8).
- Acute brain slices for electrophysiology recordings must be prepared 30min – 1 h after the last L-DOPA administration, while mice are still in the dyskinetic period.

Expected result

Contralesional rotations and levodopa-induced dyskinesia (LID) abnormal involuntary movements (AIMs) typically begin within 00:10:00 of injection, last approximately 02:00:00, and terminate spontaneously.

Open field: locomotion

1h

4 Set up behavior room:

- Place up to four clear plastic cylinders (25.4 cm diameter; 30.5 cm height) with a mat below and an overhead mounted camera (organized in two rows 2x2).
- Set up lighting minimizing total room light, reducing shadows within the chamber, and ensuring camera is able to detect the mice.
- Clean each cylinder with 70% ethanol.
- Turn on camera, adjust zoom and focus.
- Capture a background video or image before placing the mice in the cylinders.

Habituation:

- Bring mice to the behavior room in their home cages and leave undisturbed for at least 30-40 minutes.
- No previous habituation to the open field arena is required.

5 Inject i.p. the last dose of L-DOPA and benserazide (day 7 or 8) and place mice into cylinders (one mouse per cylinder).

6 00:30:00 after last L-DOPA injection, start video recording for another 00:30:00 period. 1h

7 Remove mice from cylinders and return them to home cage.

8 Clean the cylinders between mice with 70% ethanol and allow to fully dry before starting another group of mice.

9 Post-hoc analysis:
Run tracking EthoVision software to calculate the following parameters:
- Total distance traveled.
- Mean velocity.
- Rotations (threshold: 90-180°, minimum distance traveled: 2 cm).

Equipment	
EthoVision	NAME
Software	TYPE
Noldus	BRAND
RRID:SCR_000441	SKU
https://www.noldus.com/ethovision-xt	LINK
RRID:SCR_000441	SPECIFICATIONS

Dyskinesia: Abnormal Involuntary Movements (AIMs) score

2h 43m

10 Dyskinesia is assessed using the Abnormal Involuntary Movement score (AIMs) (Cenci and Lundblad, 2007).

CITATION

Cenci MA, Lundblad M (2007). Ratings of L-DOPA-induced dyskinesia in the unilateral 6-OHDA lesion model of Parkinson's disease in rats and mice..
LINK
https://doi.org/10.1002/0471142301.ns0925s41

Set up behavior room:
- Place clear plastic cylinders (25.4 cm diameter; 30.5 cm height) with a mat below.
- Clean each cylinder with 70% ethanol.
- Handheld camera (cell phone camera is sufficient).

Habituation:
- Bring mice to the behavior room in their home cages and leave undisturbed for at least 30-40 minutes.

11 Place mice into the cylinders (one per cylinder).

12 Record 00:01:00 video for each mouse (time= 0 min). 1m

13 Inject i.p. the last dose of L-DOPA and benserazide (day 7 or 8) in the first mouse. After 00:01:00 inject the second mouse and so on until all mice are injected (maximum of 20 mice in 20 minutes). 1m

14 00:20:00 after the first injection, start 00:01:00 video recording mice following the same order as injections in step 13. 21m

15 Repeat step 14 every 00:20:00 for a total period of 02:00:00 (There must be videos recorded for 0 min, 20 min, 40 min, 60 min, 80 min, 100 min and 120 min time points for each mouse). 2h 20m

16 Return each mouse to its home cage. Clean cylinders and mats with 70% ethanol.

17 Post-hoc analysis:
Score for each of the three body segments: axial, limb, and orolingual (ALO) AIMs. The AIM scale ranges from 0 to 4 for each body segment during a 1-minute period.
For each segment:

- 0 = normal movement.
- 1 = abnormal movement for <50% of the time.
- 2 = abnormal movement for >50% of the time.
- 3 = abnormal movement for the entire period that can be interrupted by sensory stimuli (e.g. hitting the cylinder).
- 4 = continuous abnormal movement, uninterruptible.

Note

Take into account that rotations with all four limbs on the floor is not scored as axial dyskinesia. The mouse must be on 2 feet and with its trunk twisted.

Total AIM score is calculated as the sum of scores for AOL, being 12 the maximum score in 1 minute.
An integrated AIM score can be calculated as the area under the curve (AUC) in a plot of total AIM score vs time for the total duration of the dyskinetic episode (2h).