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Closed Head Weight Drop model in mice - Whalen Lab

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PRECISE-TBI

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Protocol status: Working
We use this protocol and it's working, however we continuously modify it over time to optimize outcomes for different studies, for example tuning for short vs. long term cognitive dysfunction by changing the shape of the weight that is dropped.

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Disclaimer

None

Abstract

This is a protocol to describe the materials and methods utilized to perform preclinical traumatic brain injury (TBI) using a closed head injury model in mice.

The posting of this protocol is part of the mission of the PREClinical Interagency reSearch resourcE-TBI (PRECISE-TBI, precise-tbi.org) to improve clinical translation of therapeutics by providing an online catalog and standardized protocols to reduce the variability of model usage between laboratories.

Materials

Metal bolt (54g) with rounded head or machined lead cylinder (54g) and an appropriate guide tube.

Troubleshooting

1 Turn on anesthesia and fill the chamber for two minutes to achieve steady state mixture of isoflurane 2.5% and nitrous oxide 70%, Oxygen about 30%

2 Place the mouse into the anesthesia for exactly 75 seconds.

3 Ensure adequate anesthesia is achieved by use of the toe pinch test.

4 Place the mouse prone onto a Kimwipe napkin by grasping the tail with the left hand and pull the Kimwipe tight with both hands.

5 Place the head of the mouse underneath the guide tube and rotate the head in either direction so that the weight will drop onto the head just beside the ear. This avoids impact on the vertex of the head, which can lead to apnea.

6 Drop the weight through the guide tube and place the mouse supine after impact. Record the
time to righting as an estimate of loss of consciousness time.

7 Place the mouse back into its home cage to resume standard housing and husbandry.

8 Continue to monitor the mouse for pain and administer analgesic per institutional and federal guidelines for the treatment of laboratory animals and in accordance with your IACUC protocol. We do not use post-injury analgesics as they could interfere with inflammatory pathways under study.

Notes

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Note 1: For repetitive closed head injury repeat the same steps as above but expect lower loss
of consciousness time with subsequent injuries.Injuries may be spaced days, weeks, or months apart depending on the experiment.

Note 2: One can make a device to hold the Kimwipe in place to eliminate variability/bias in injury
due to the holder, however the holder should always be blinded to group.

Note 3: Sham injury is exposure to anesthesia without weight drop

Note 4: The shape and size of the weight (e.g., hardware bold, machined cylindrical lead weight,
etc.) will vary depending on the desired injury parameters.We use a 54 gram weight and
28-56″ drop height, depending on the experiment.Lower weights and drop heights do not cause post-injury cognitive or motor learning deficits (assessed by Morris water maze
and rotarod, respectively) with one injury but do with repetitive injuries.Notably, changes
in the shape of the weight (e.g., flat vs. round impact surface) can have profound effects
on behavioral outcomes, hence the weight drop models need to be calibrated in the lab
according to desired injury phenotypes (one size does not fit all).For short term cognitive
deficits we use a bolt with a rounded tip from a hardware store. For cognitive deficits that
emerge over time, we use the same injury parameters (see Wu. et al., 2022) but
use a lead cylinder and a copper plumbing guide tube for a more precisely located injury.

Note 5: Bolt weight and drop height can be manipulated to produce desired effects on behavioral outcomes but the models that we use do not produce structural brain damage.

Note 6: We use adolescent (DOL 38) mice for experiments as well as adult mice (8-16 weeks).