SELF-ADMINISTRATION IN MICE
SURGICAL PROCEDURES AND TECHNIQUES

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Overview

The technique of self-administration is an extremely useful model of human drug-seeking behavior. It is also the gold standard test for assessing the potential abuse liability of new pharmaceutical compounds in a preclinical setting.

The self-administration model consists of an operant behavior setup in which a drug is available, usually via intravenous route, as a reinforcer of some behavioral response. It is used primarily to predict abuse liability, but also in evaluating treatments for drug addiction. The model is used effectively in laboratories utilizing rats and non-human primates. However, the maintenance of chronic intravenous self-administration has been historically more difficult in mice, despite the abundant interest in and availability of transgenic mice.

Some laboratories have come up with their own “homemade” methods of getting good self-administration behavior in mice. Recently, we have checked in with Drs. Andrew Lawrence and Robyn Brown at the Florey Neuroscience Institutes located on the campus of the University of Melbourne, Parkville, Australia, who were generous enough to give us some extra details on the surgical approach utilized in the Lawrence laboratory.
Materials

- Inhalation Anesthetic (i.e. 1.5-2% Isoflurane)
- Surgical Instruments
- 3.5 cm length of Silastic® Tubing
- Limonene
- 22 Gauge Needle
- Sutures
- Silicone
- Instant Adhesive
- Dental Acrylic

Note: When performed by trained and experienced surgeons, this procedure should take no longer than 10 to 20 minutes.
Catheter Construction

STEP 1: Prepare the Needle
- Prepare a 22 gauge needle by bending it in a “U” shape that is at a right angle to the Luer hub as shown in Figure 1.
- Blunt the end of the needle by filing off the point so as to prevent puncturing the catheter tubing applied in later steps.

STEP 2: Attach Catheter Tubing to the Prepared 22 Gauge Needle
- Treat the distal end of the Silastic® tubing with limonene, this will soften the tubing, facilitating attachment to the needle.
- Push the softened end of the catheter tubing over the “U” shaped needle as shown in Figure 2.
- Apply silicone to the joint of the silastic tubing and the needle.
- Also apply a small ‘ball’ of silicone 1cm from the distal end of the tubing.

STEP 3: Create a cap for the final catheter assembly.
- Saw off the tip of a 1mL syringe and plug with epoxy.

Figure 1: Prepped 22 gauge needle with blunted end.

Figure 2: 22 gauge needle with catheter tubing attached.
Surgical Procedure and Cannula Maintenance

Surgical Procedure

STEP 1: Insert the Jugular Catheter

- Place the mouse under inhalation anesthesia, such as isoflurane (1.5-2%).
- Once the mouse is completely anesthetized, make an incision along the midline of the skull.
- Turn the animal over and make an incision below the neck halfway between the midline and the forelimb.
- Using blunt dissection, isolate the jugular vein.
- Feed the catheter through from the incision on the head such that the catheter tubing runs subcutaneously over the shoulder from the head to the jugular vein. The needle end of the catheter should be attached to a 1mL syringe containing lightly heparinised saline with antibiotic.
- Feed two pieces of suture under the vein, one above and one below the insertion point, and very loosely tie such that cannulation can still take place.
- Using a stereoscope, insert the catheter tubing 1 cm into the jugular vein and anchor with suture.
- Test that the catheter is appropriately inserted and anchored by gently pulling the syringe in and out to test that blood moves back and forth.

Figure 3: Assembled catheter being fed through the head incision to the jugular.
STEP 2: Position the Catheter and Seal the Incision

- Turn the animal over and affix the bottom of the curved needle to the skull with instant adhesive, followed by dental acrylic (Figure 4). Build up a solid base of dental acrylic to keep the catheter firmly in place (Figure 5).
- Plug the needle luer with the specialized cap prepared prior to surgery.
Post-Surgical Recovery and Maintenance

RECOVERY:
- Allow 3-4 days for recovery, flushing the catheter twice daily with heparinised saline in order to maintain catheter patency.
- After recovery, mice can be maintained in self-administration experiments for 3-4 weeks.

MAINTENANCE:
- To maintain the cannula after surgery and between uses, flush twice daily (typically before and after self-administration sessions) with heparinised saline.
- Seal the port with the removable plug when not in session.
- Note: Catheter patency is tested using a mix of ketamine/midazolam.
Further Reading


