

Standard Operating Procedure

MDA (Micropipette-guided Drug Administration) Method

SOP MDA (micropipette-guided drug administration)		Species: Mice
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Objective

Pharmacological administration method for per os treatments in mice. This method can potentially be used for different drugs, the preparation of the drug solution depends on the drug's properties. Below an example preparation procedure is described.

Equipment, materials

1. Sweet condensed milk (MIGROS Kondensmilch™, Migros, Zurich, Switzerland)
2. Regular Tap Water
3. 15 or 50ml Falcon Tubes
4. Ultrasonic water bath*
5. Magnetic Stirrer*
6. Channel p200 Micropipette
7. p200 Pipette Tips

*depending on characteristics of drug to be administered

Administration of Tamoxifen or other substances that do not emulsify in the sweet condensed milk solution: Add some drops of Tween20 (Polyethylene glycol sorbitan monolaurate, e.g. Sigma- Aldrich).

Procedure

Procedure Preparation Drug Solution**:

1. Dilute condensed milk with regular tap water in a 4:10 (condensed milk to water) ratio. This solution is used as vehicle.
2. Dilute the drug to be administered *per os* in water and sonicate for 20 min.
3. Mix suspended drug with vehicle solution to reach the desired concentration.
4. Keep drug and vehicle solution in constant agitation using a magnetic stirrer.
5. Drug and vehicle solution are administered at a volume of 2 ml/kg.

** this section depends on the characteristics of the drug to be administered and might need to be adapted.

MDA Procedure

1. Prepare the desired amount (2 ml/kg) of drug or vehicle solution in the tip of the p200 micropipette. For training you may use vehicle solution only.
2. Training Day 1: Restrain mouse gently and expose it to the milk solution for the first time, by offering the pipette tip to the mouth until the mouse begins to drink (see Video 1 and Figure 1A).
3. Training Day 2: Restrain mouse solely by the tail on the metal grid of the food hopper and position the pipette continually next to the mouse's mouth until it drinks (see Video 2 and Figure 1B). Animal should ingest the complete volume.
4. (Optional) Training Day 3-7: If necessary, repeat the procedure from training day 2 to familiarize the mouse with the milk solution even further. Animal should ingest the complete volume.
5. MDA (micropipette-guided drug administration): Place mouse on the metal grid of the food hopper with no or minimal restraint and offer pipette tip until the mouse voluntarily begins to drink the solution (see Video 3 and Figure 1C).

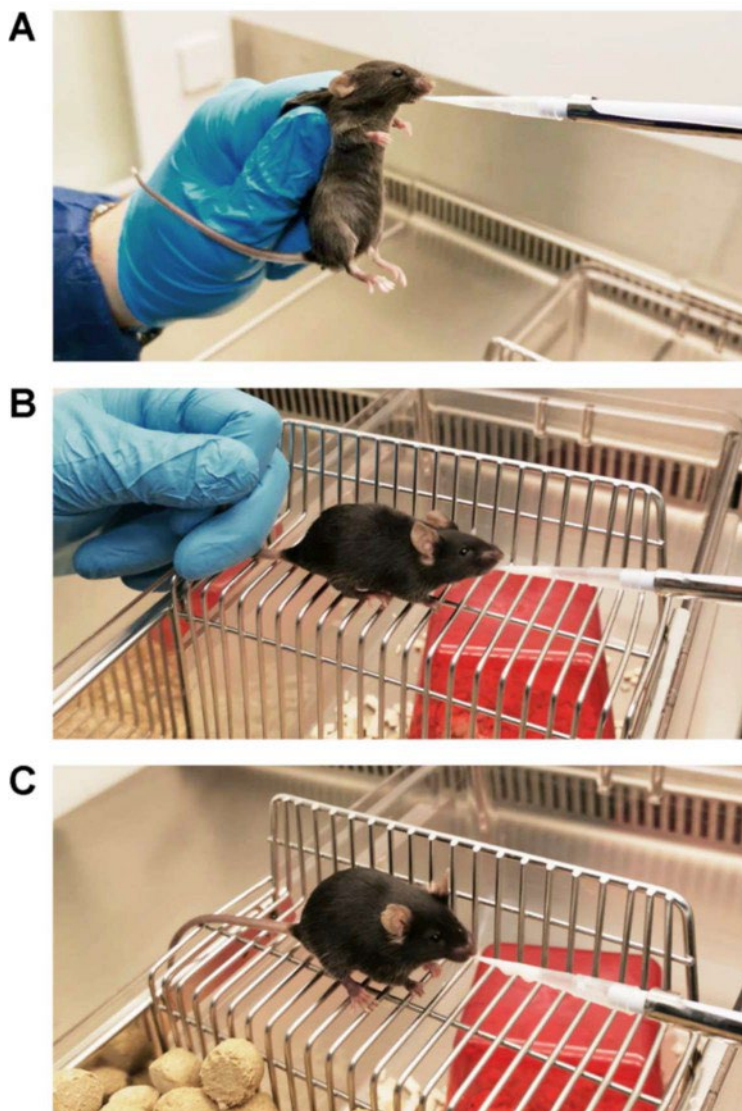


Figure 1.

Phases of the micropipette-guided drug administration (MDA) method in C57BL6/N mice.

(A) Training Day 1: Mice are fully restrained and exposed to the sweetened condensed milk solution for the first time via a conventional micropipette (see also Video 1).

(B) Training Day 2 (& 3-7): Mice are restrained solely by the tail and exposed to the sweetened condensed milk solution via a micropipette (see also Video 2).

(C) MDA treatment: Mice are no longer restrained and drink the sweetened condensed milk solution voluntarily from the micropipette (see also Video 3).

Taken from: Scarborough et al., 2020.

References

- Scarborough J, Mueller F, Arban R, Dorner-Ciossek C, Weber-Stadlbauer U, Rosenbrock H, Meyer U, Richetto J (2020). Preclinical validation of the micropipette-guided drug administration (MDA) method in the maternal immune activation model of neurodevelopmental disorders. *Brain Behav Immun* 88:461-470. doi: 10.1016/j.bbi.2020.04.015.
- Schalbetter SM, Mueller FS, Scarborough J, Richetto J, Weber-Stadlbauer U, Meyer U, Notter T (2021). Oral application of clozapine-N-oxide using the micropipette-guided drug administration (MDA) method in mouse DREADD systems. *Lab Anim (NY)* 50(3):69-75. doi: 10.1038/s41684-021-00723-0.
- Scarborough J, Mattei D, Dorner-Ciossek C, Sand M, Arban R, Rosenbrock H, Richetto J, Meyer U (2021). Symptomatic and preventive effects of the novel phosphodiesterase-9 inhibitor BI 409306 in an immune-mediated model of neurodevelopmental disorders. *Neuropsychopharmacology* 46(8):1526-1534. doi: 10.1038/s41386-021-01016-3.

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Further data/recordings available:

Video 1-3

<https://www.sciencedirect.com/science/article/pii/S0889159120302543?via%3Dihub>

Rodent MDA Website

<https://www.rodentmda.ch/>