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# Optogenetic modulation of dopaminergic neurons

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Cristian González-Cabrera<sup>1</sup>, Matthias Prigge<sup>1</sup>

<sup>1</sup>Neuromodulatory Network Group, Leibniz Institute for Neurobiology, Magdeburg.

TeamPrigge



Team Prigge

Leibniz Institute for Neurobiology

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Optical deep brain stimulation can reactivate NM-laden neurons and rescue behavioral phenotypes.



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**We use this protocol and it's working**

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## Abstract

This protocol describes an optogenetic activation of neuromelanine-laden dopaminergic neurons in the SNc-VTA. We induce neuromelanin (NM) in the SNc-VTA through viral expression of a humane tyrosinase virus. Furthermore we express a red-absorbing opsin in one hemispherend and blue absorbing in the other hemisphere. We detail how we optognetic stimulateanimals in over four weeks.

THis optogenetic deep brain stimulation induces a reduction in neuromelanine levels in dopaminergic neurons, and rescues behavioral phenotypes as evaluate in the grip strength test.

## Troubleshooting

## Viral Injection

- 1 Stereotactic injection of viruses into DAT-Cre (JAX# 006660) animals

### **Viral Constructs:**

1.- pAAV-hSyn1-dlox-ChrimsonR\_tdTomato(rev)-dlox-WPRE

2.- pAAV-hSyn1-dlox-hCHR2(H134R)\_mcherry(rev)-dlox-WPRE

3.- pAAV\_Ef1a\_DIO\_hTyrHA\_minBack

### **Injections:**

- Bilateral injections were performed.
- Right hemisphere: viruses 1 and 3.
- Left hemisphere: viruses 2 and 3.
- Viruses were combined 50:50 and injected a total Volume of 600ul per hemisphere

### **Stereotactic coordinates:**

- Substantia nigra

ML: 1.4mm AP: 3.25mm DV: 4.0 (blunt needle / NF34BL-2)

### **Injection set-up:**

- Hamilton syringe coupled to a WPI injector (UMP3T-1) ([link](#))
- Injection speed 100nl/min

## Experimental Timeline

- 2
  - Animals were left to accumulate neuromelanin for 6 or 10 weeks.
  - Animals were stimulated for 30 minutes for 4 weeks. Stimulation during 5 days and two days rest.
  - The stimulation was 635nm, 5ms pulse, 10 Hz at 10mW. 3 seconds ON 10 seconds OFF.

## Optical stimulation

- 3
  - fibers are attached bilaterally to the animals
  - the animal is placed in open field arena
  - stimulation is controlled via PulsePal (OpenEphys [link](#)) on a MRL\_III-635L laser