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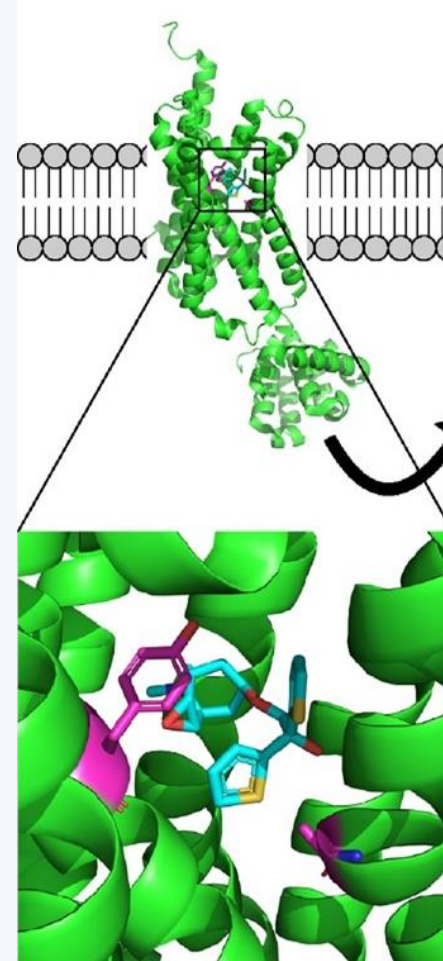
# **Short-Term vs Long-Term Effects of DREADDs in the Mouse Motor Cortex**

Christa Zianni



# DREADDs

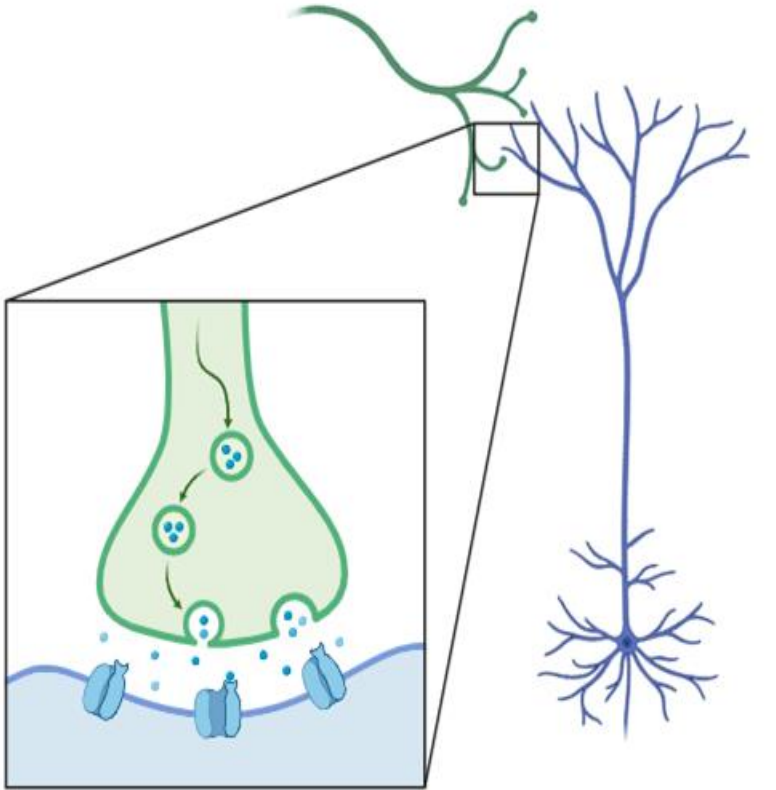
- Enables targeted activation or inhibition of brain regions or cell types
  - Useful for understanding function of cells targeted
  - Potential clinical applications
- Lack of long term studies



"GPCR-based chemogenetic silencing tools" by Lieb et al. from "Designer receptor technology for the treatment of epilepsy", used under CC BY 4.0 / Cropped from original

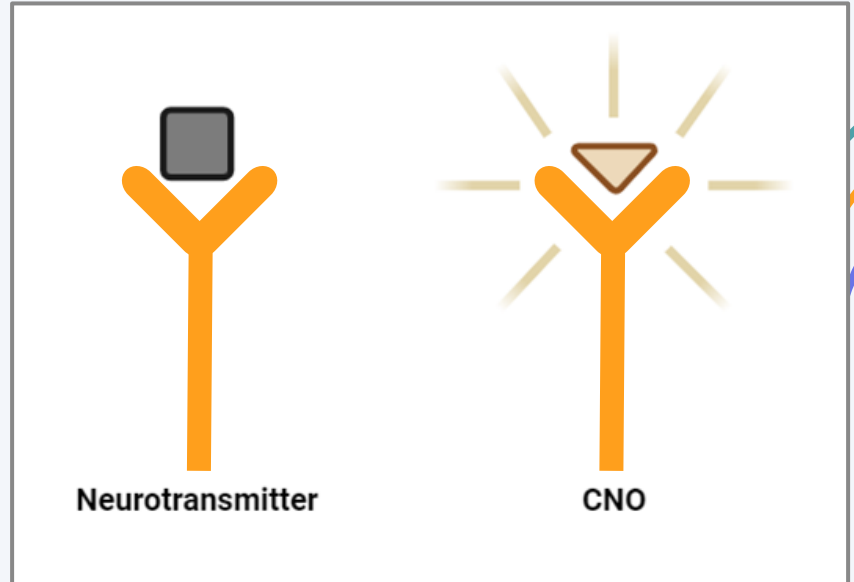
# Neuronal Communication

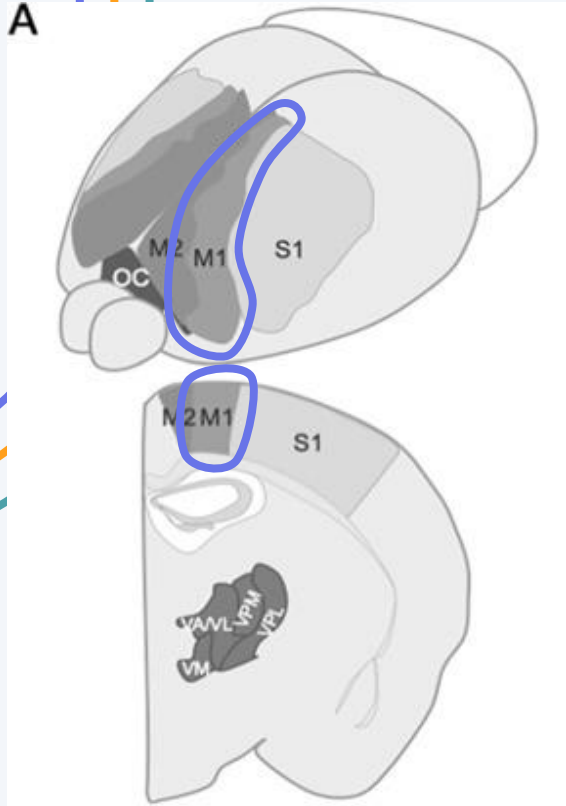
- Chemical and electrical signals
- Messenger molecules aka neurotransmitters
  - Ex: Dopamine, serotonin
- Neurotransmitters activate receptors on surrounding cells
- Receptors trigger various events



# How it Works

- DREADDs: Designer Receptors Exclusively Activated by Designer Drugs
- Cell's DNA is edited
- New DNA encodes mutated receptors
- Mutated receptors respond only to drug CNO, not neurotransmitters





By Lee et al. from "The Primary Motor Cortex: The Hub of Motor Learning in Rodents", used under CC BY 4.0 / Cropped from original



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# Methods

Surgery  
targeting  
motor  
cortex  
performed,  
excitatory  
DREADDs  
expressed

# Methods

Mice receive CNO injection, perform open field test



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Mice receive CNO through drinking water for 12 days

Mice receive CNO injection, perform open field test for 2nd time



# Methods

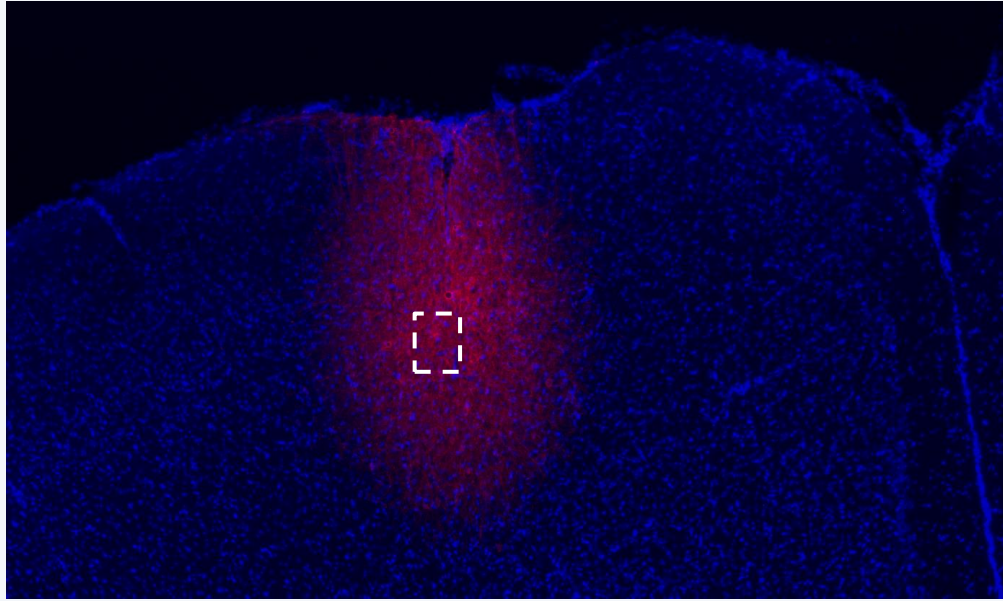
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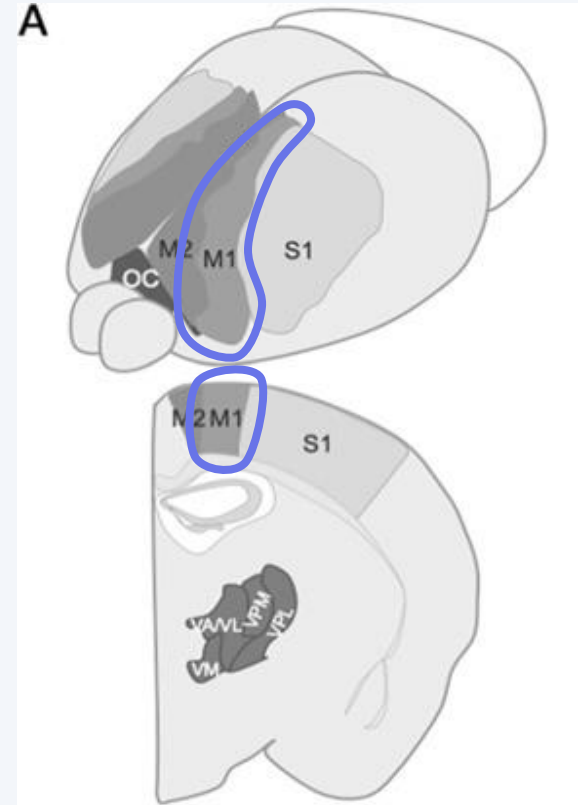
Brains are sectioned



# DREADDs Expression



mCherry (red coloration) indicates presence of DREADDs in motor cortex

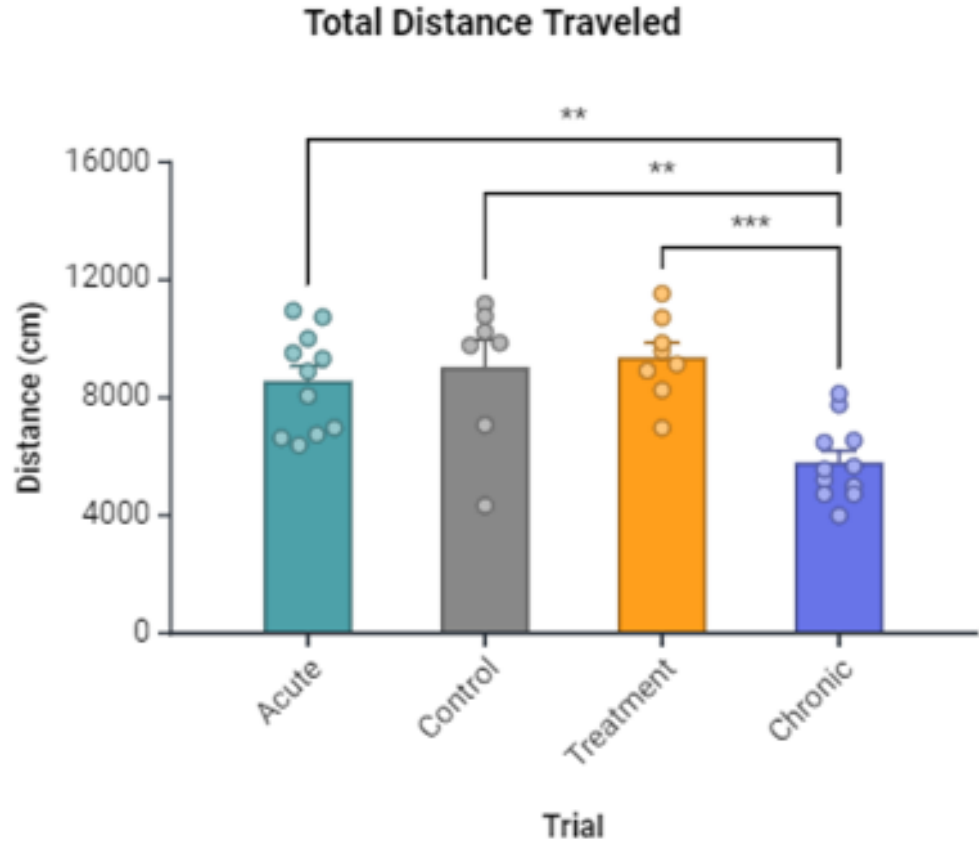


By Lee et al. from "The Primary Motor Cortex: The Hub of Motor Learning in Rodents", used under CC BY 4.0 / Cropped from original





**Chronic CNO  
administration  
leads to  
decrease in  
activity**



# What does this mean?

- Lack of control makes interpreting results hard :/
- Could be DREADDs activation or off-target CNO
- Either way:
  - Highlights brain's plasticity
    - Brain cells constantly change in response to their environment
  - Emphasizes need for long-term studies

# Why it Matters

- Clinical use
  - Neurodegenerative disease, addiction, epilepsy
  - Need to understand long-term effects
    - Do effects remain past a week? A month?
    - Do effects take time to kick in?
- Understanding brain's plasticity
  - Underlies many processes
  - Particularly relevant for pharmaceuticals, other treatments changing the brain's internal environment

# References

Lee, C., Kim, Y., & Kaang, B.-K. (2022). The Primary Motor Cortex: The Hub of Motor Learning in Rodents.

*Neuroscience*, 485, 163–170. <https://doi.org/10.1016/j.neuroscience.2022.01.009>

Lieb, A., Weston, M., & Kullmann, D. M. (2019). Designer receptor technology for the treatment of epilepsy.

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