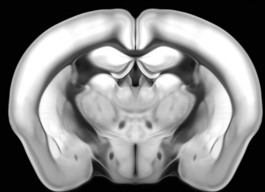


Chemogenetics: A Neurobiological Review

Elizabeth A. Sneddon-Yepez, Ph.D.



GEORGE I. AB

Quick Facts

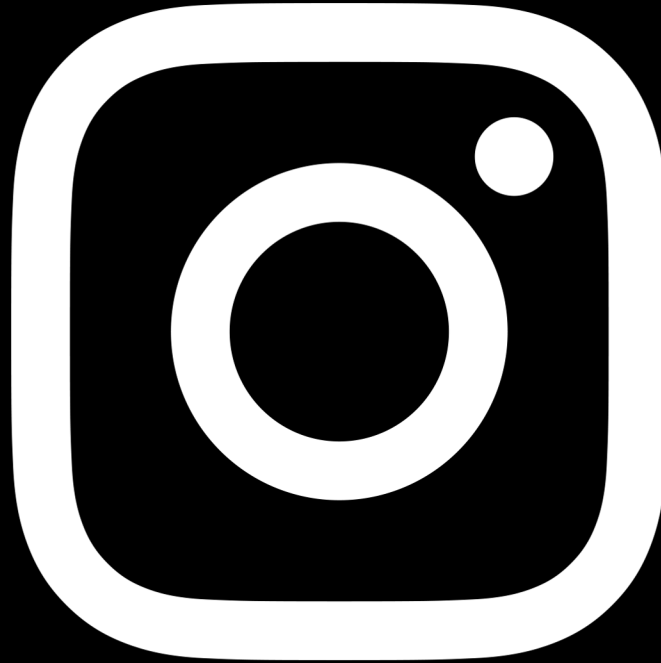
Made of cells called neurons

Around 100 billion neurons

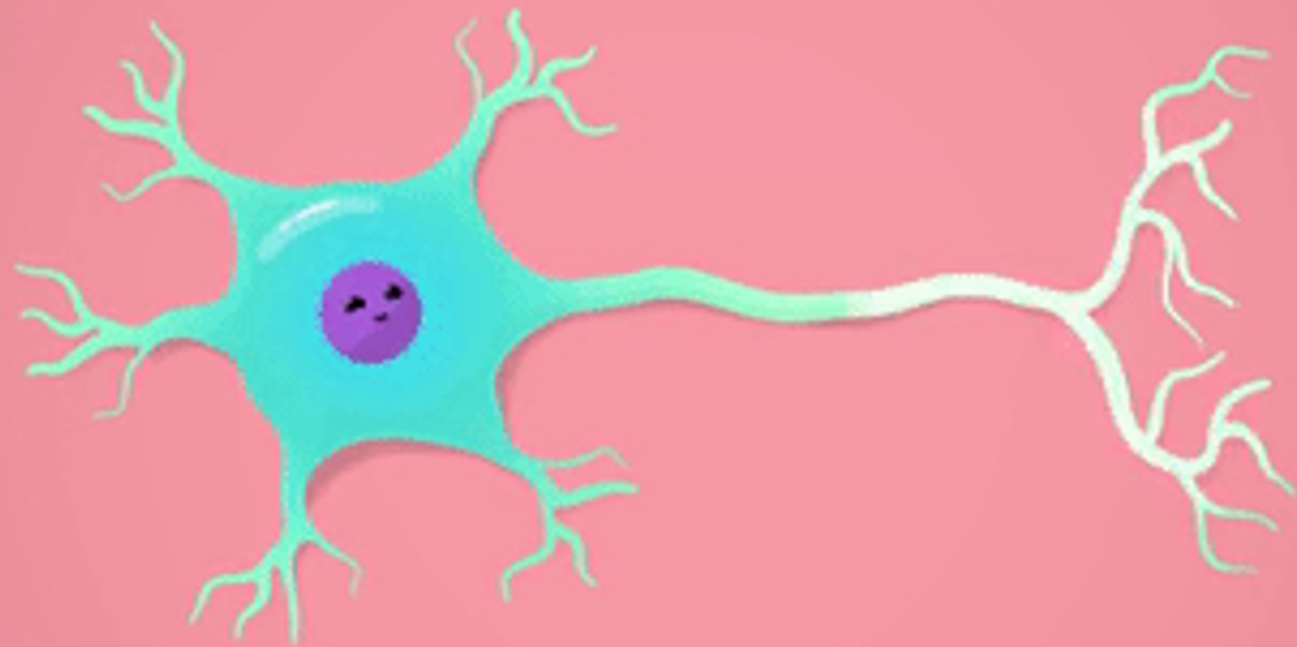
Each neuron can have around 40,000 connections



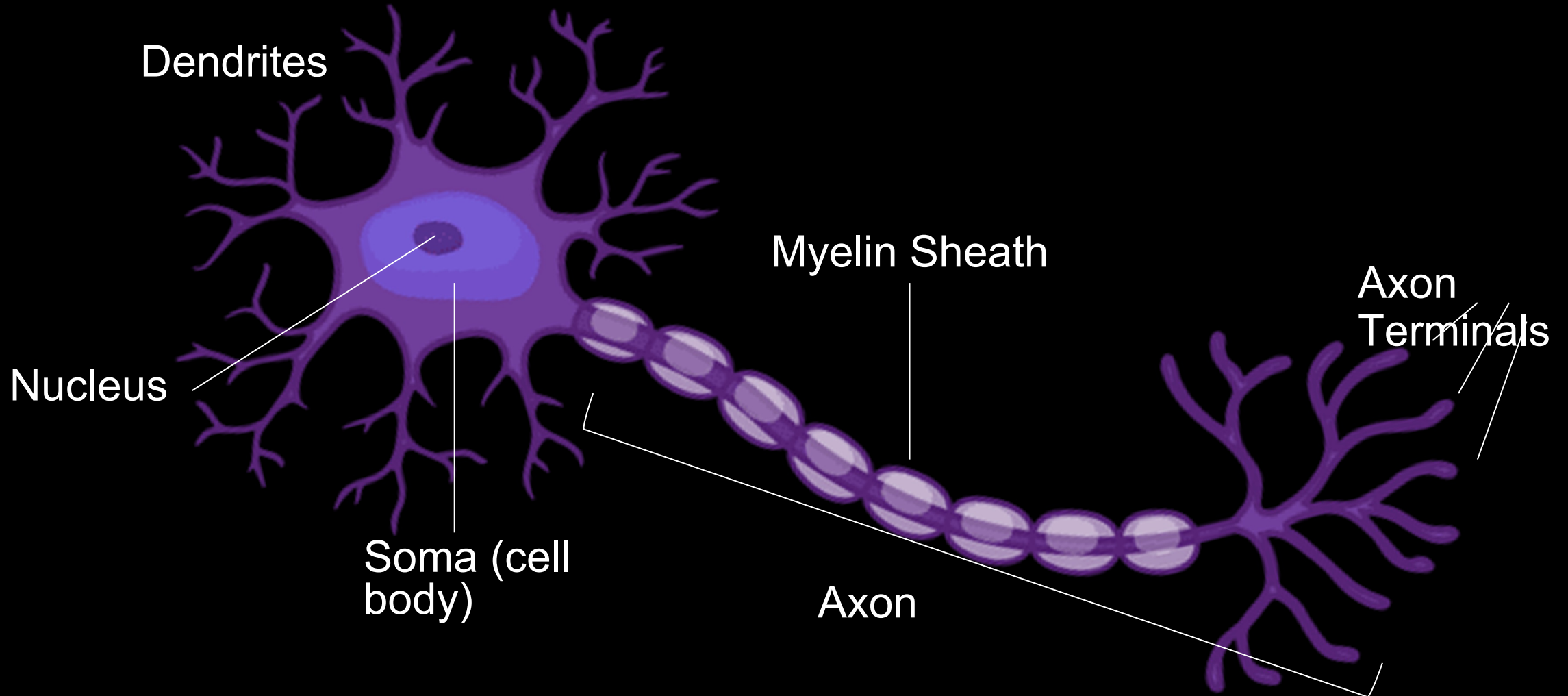
Way more connections than your average Instagram user!



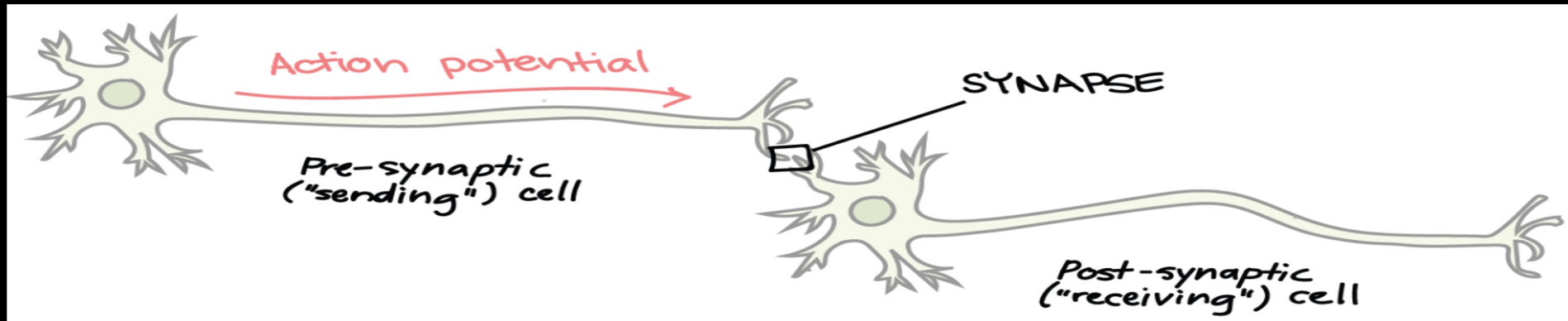
Average number of Instagram followers per person = ~150

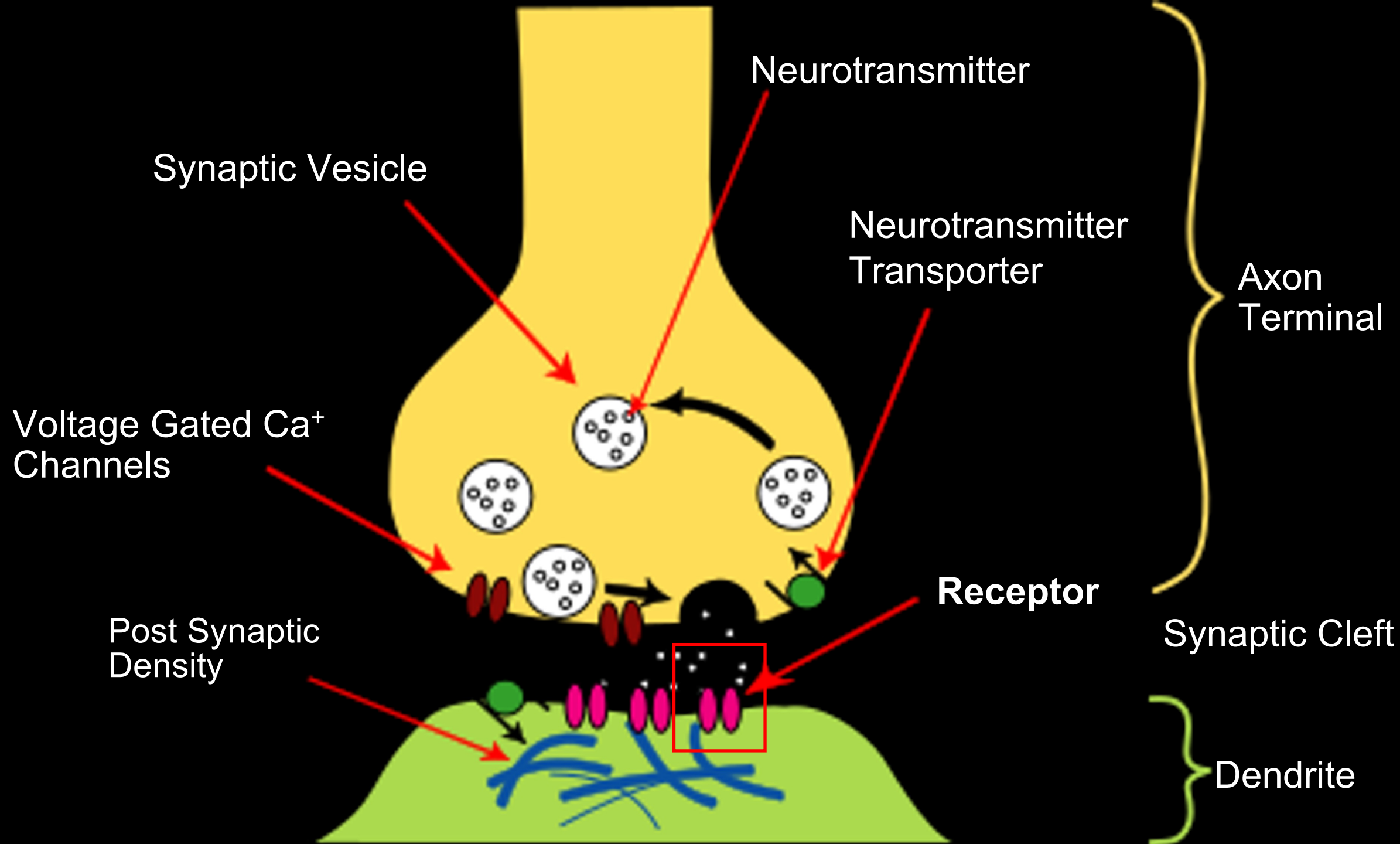


Neuroanatomy of a Neuron



More Neuroanatomy!





Chemo-genetics

- **Chemo** →
a combining form with the meanings “chemical,” “chemically induced,” “chemistry,” used in the formation of compound words:
e.g., chemotherapy
- **Genetics** →
of, relating to, or produced by genes

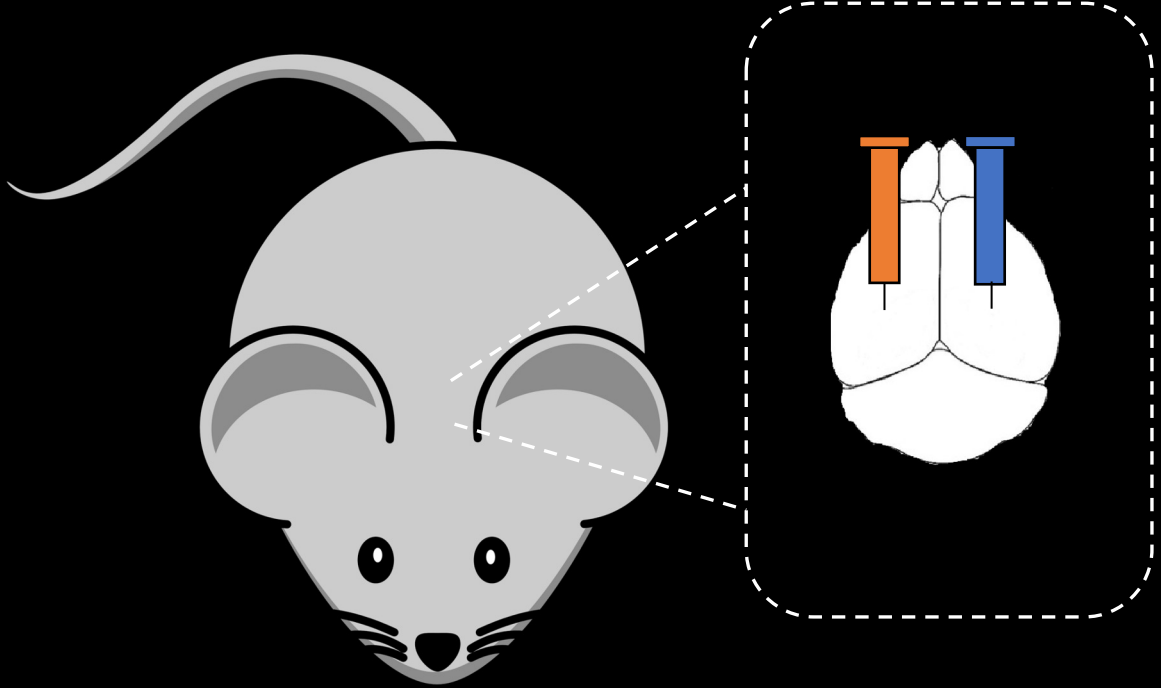
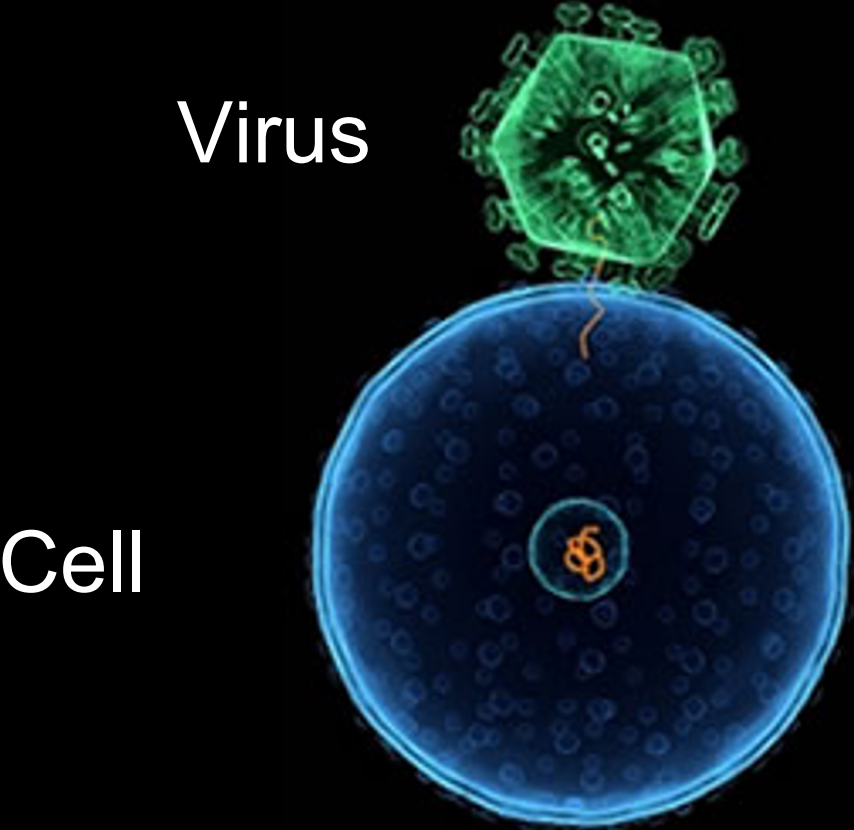
Chemogenetics: What is it?

- How we can **engineer proteins** to interact with unrecognized **small molecules** (Forkmann and Dangelmayr, 1980; Sternson and Roth, 2014; Strobel, 1998)
- Used to interrogate brain function and **examine the relationship** between neuronal signaling and behavior (Addgene, 2018)



Designer **R**eceptors **E**xclusively **A**ctivated by **D**esigner **D**rugs

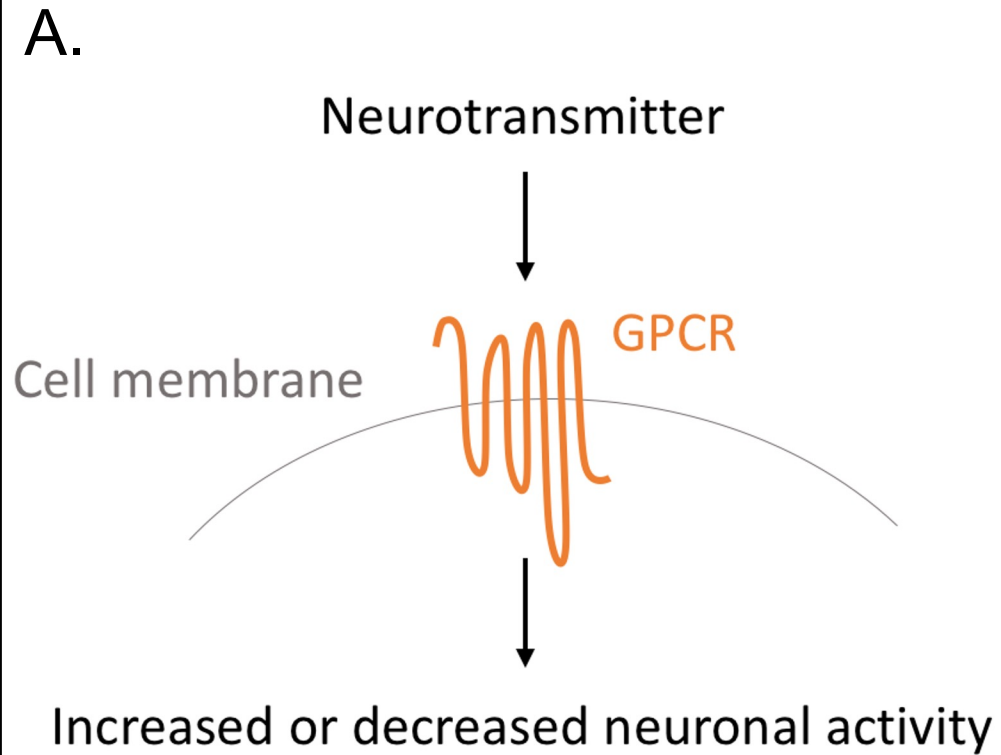
How does a virus work?



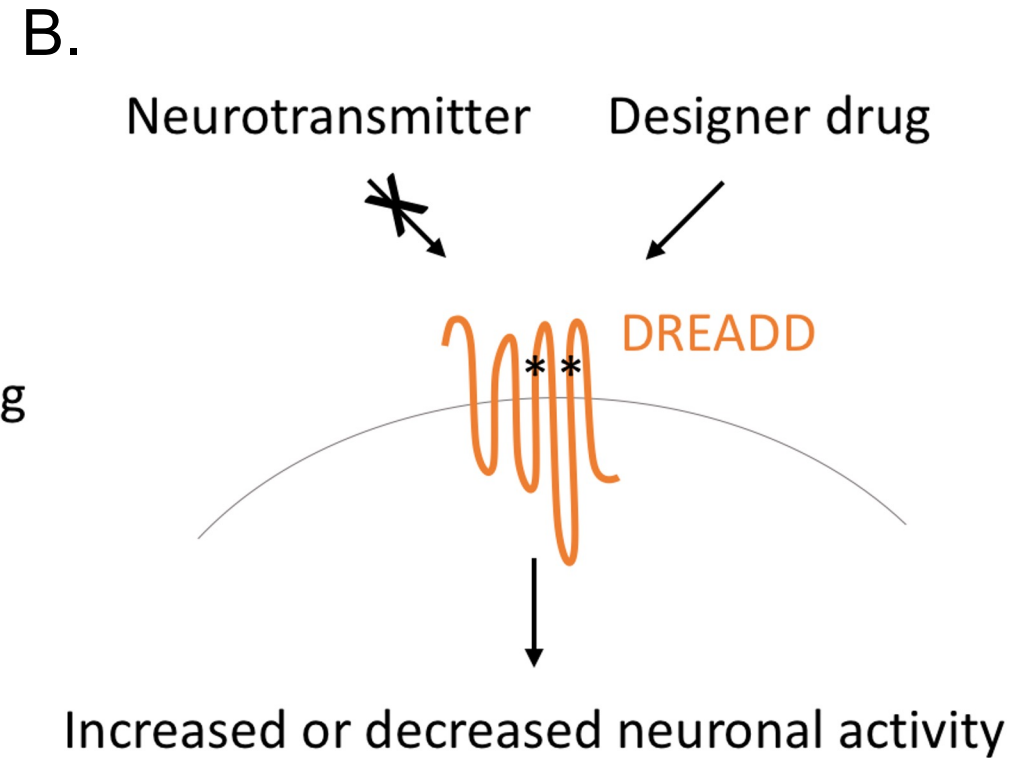
Inhibitory = Turn Off

Excitatory = Turn On

How DREADDs Work:



Protein engineering

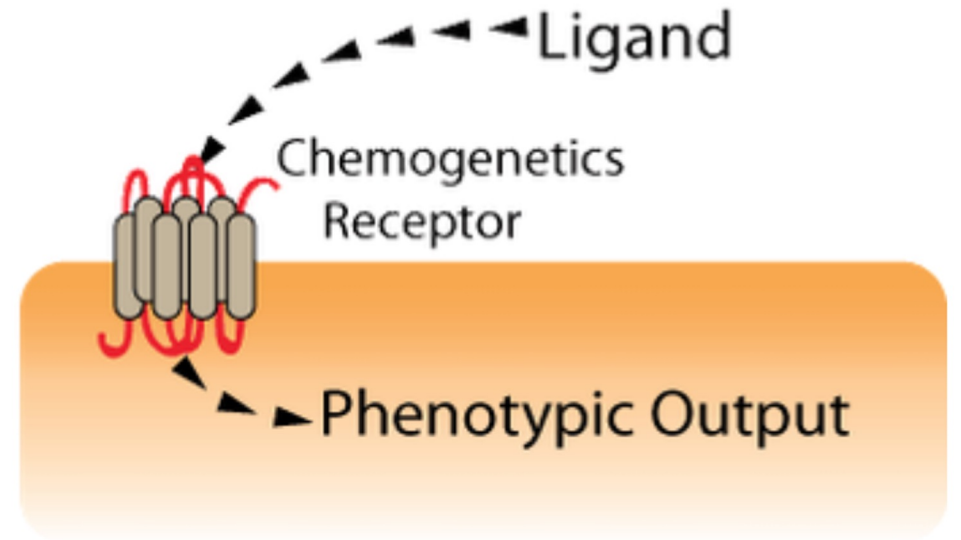
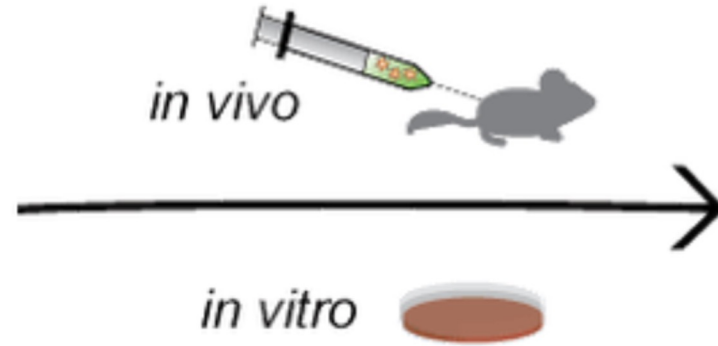


How DREADDs Work:

Chemogenetics
Plasmid



Delivery

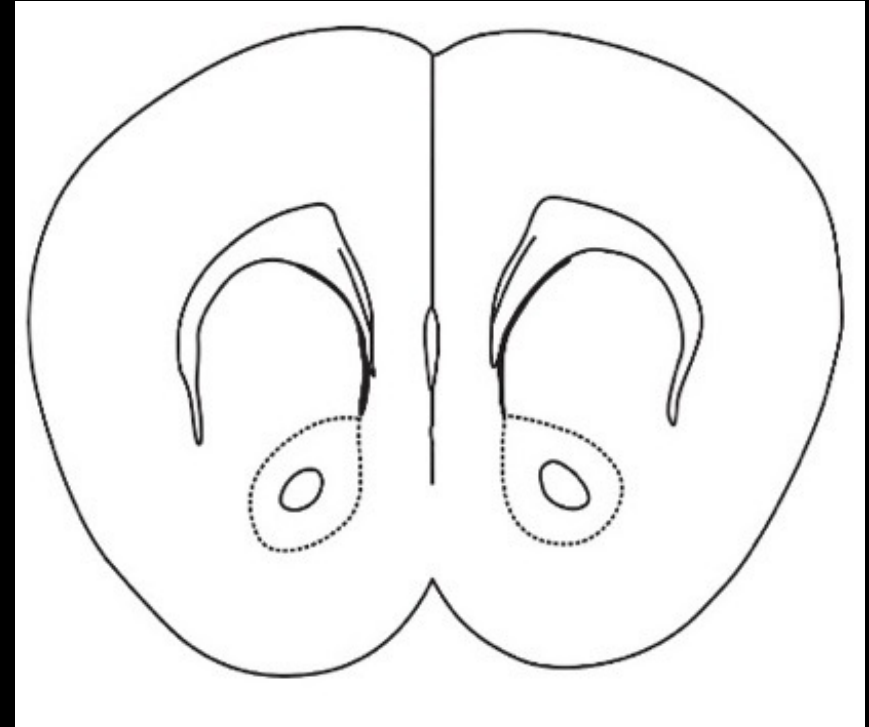


Clozapine-n-oxide (CNO)

How are DREADDs used in practice?

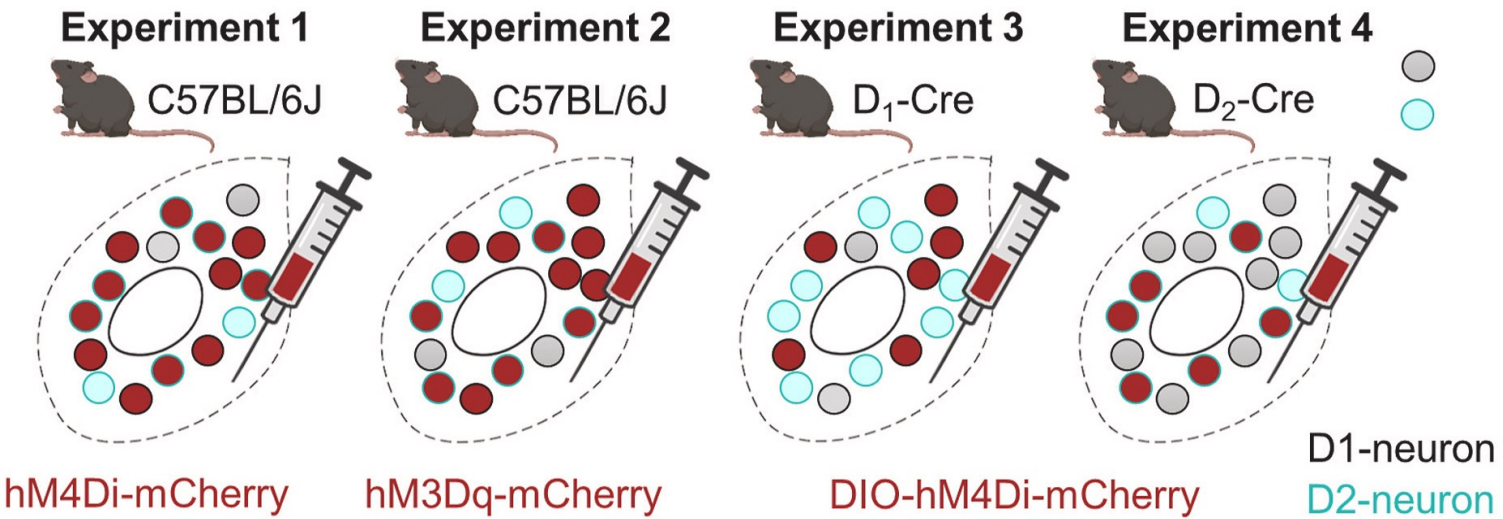
Compulsive-like alcohol consumption

- Drinking despite negative consequences
 - DUI, broken relationships, loss of job, health problems, etc.
- Nucleus accumbens core
 - Evaluation of reward & initiating motor movement
 - Necessary for compulsive intake
 - Validated in rodent and human models

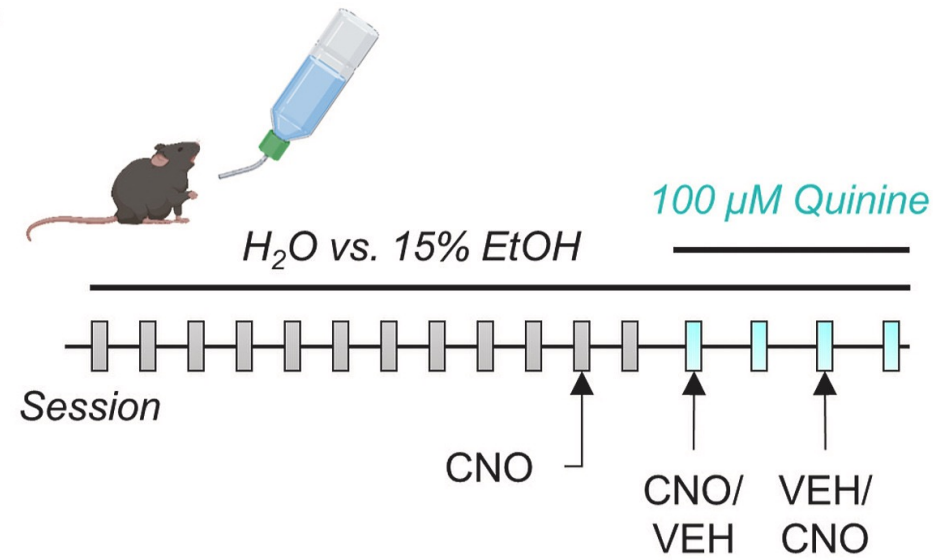




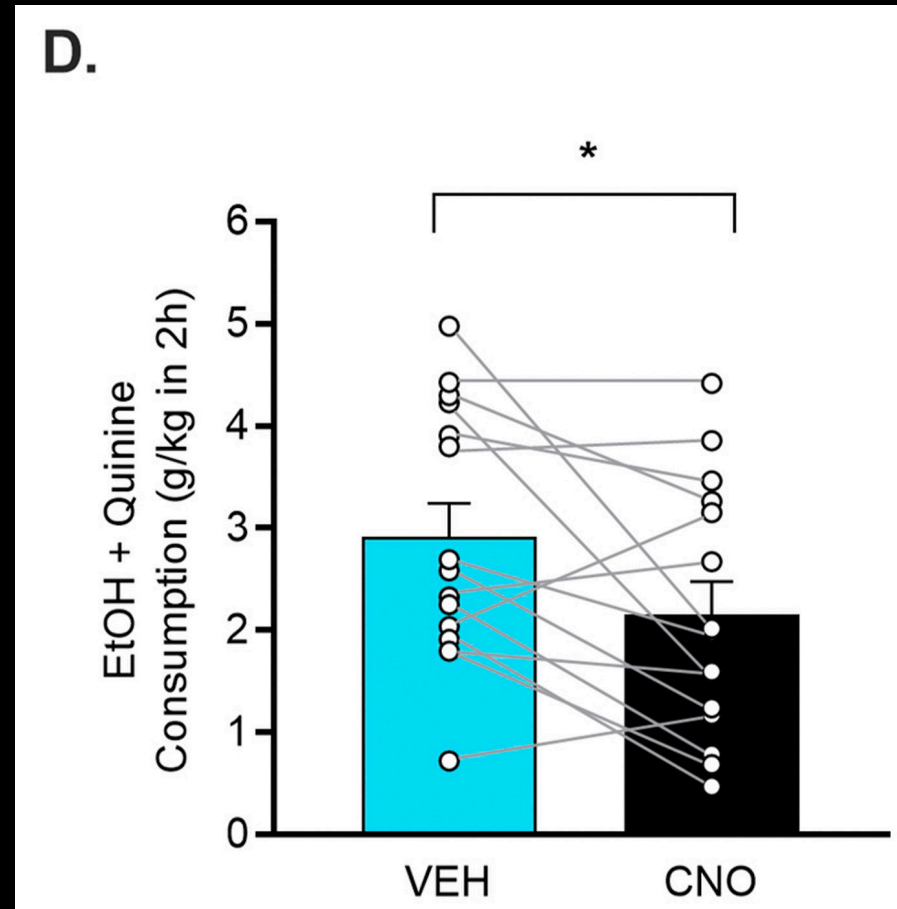
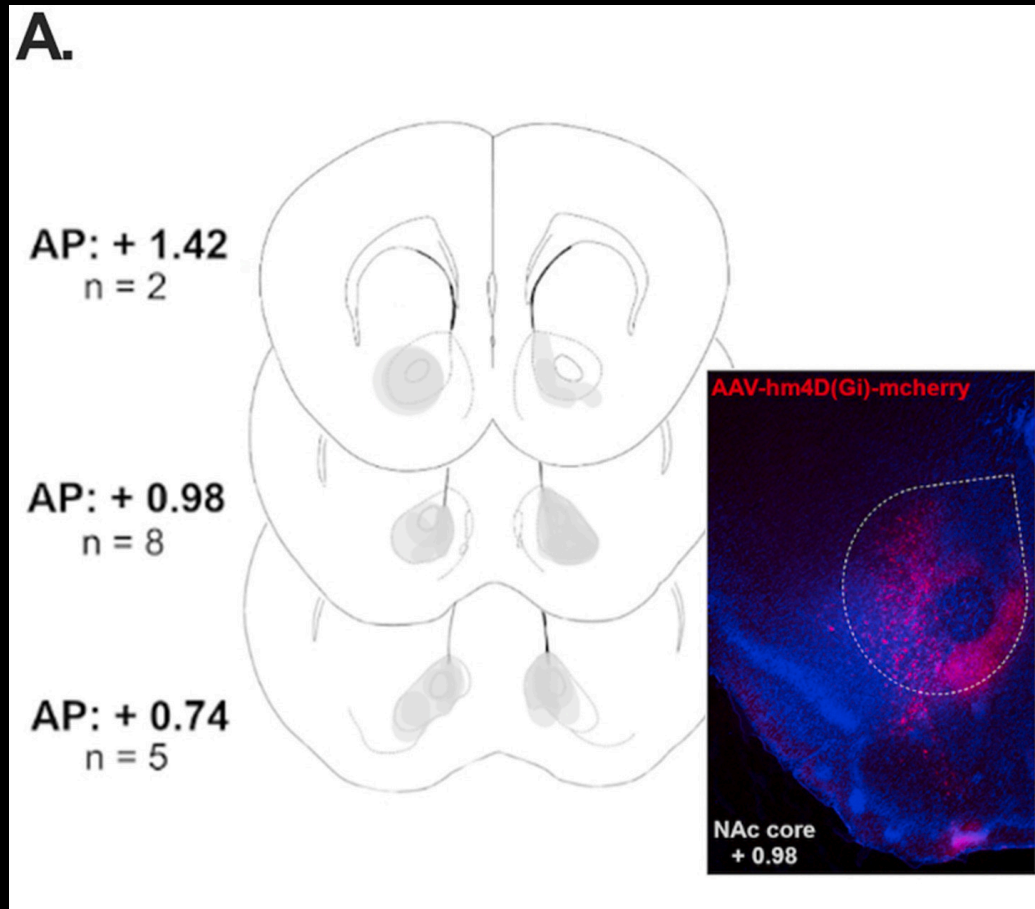
A.



B.

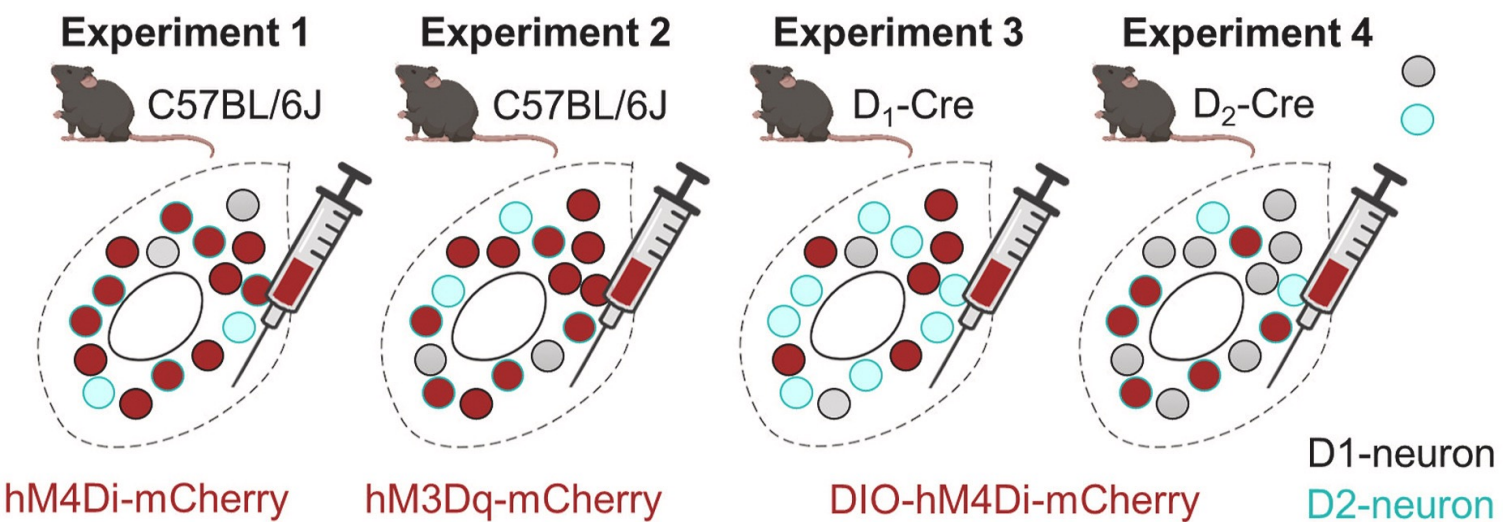


Inhibition of the NAc core with hM4Di decreased aversion-resistant intake of quinine-adulterated EtOH

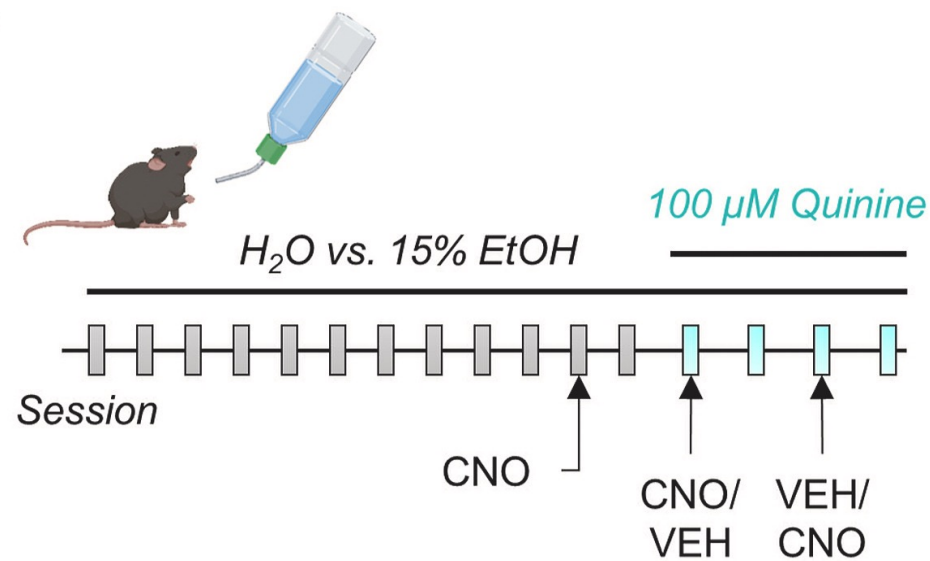




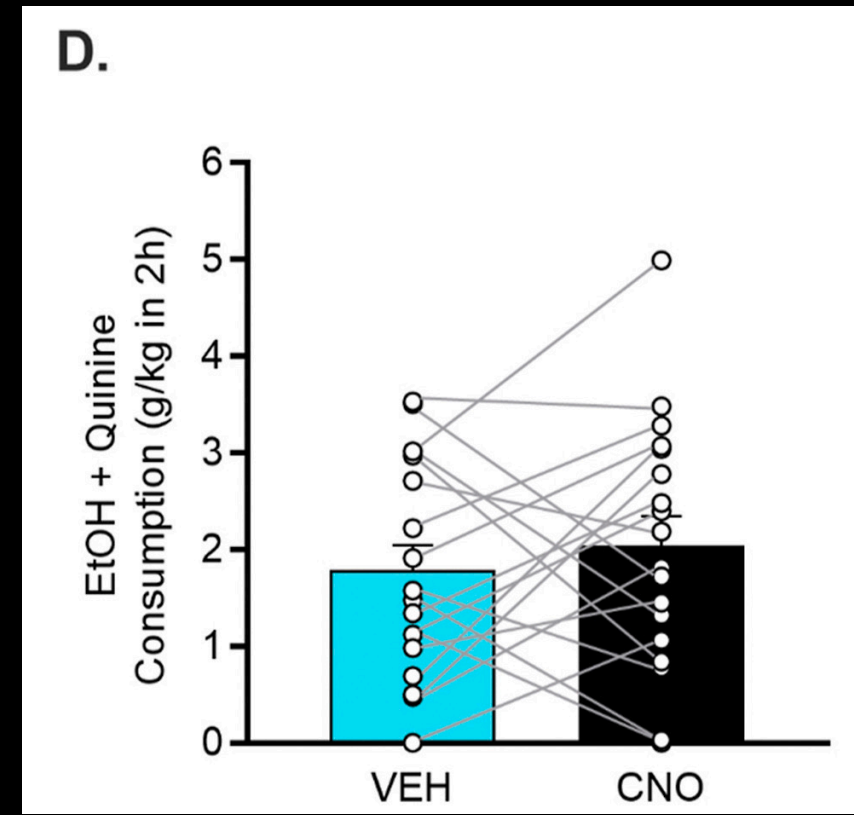
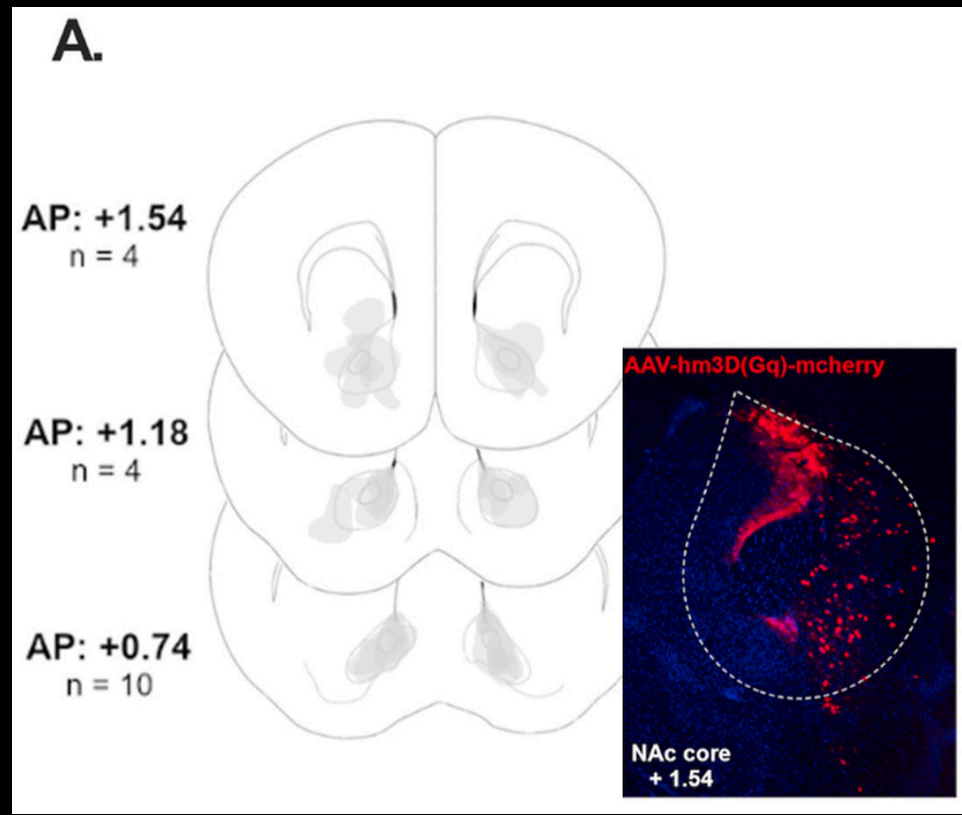
A.



B.

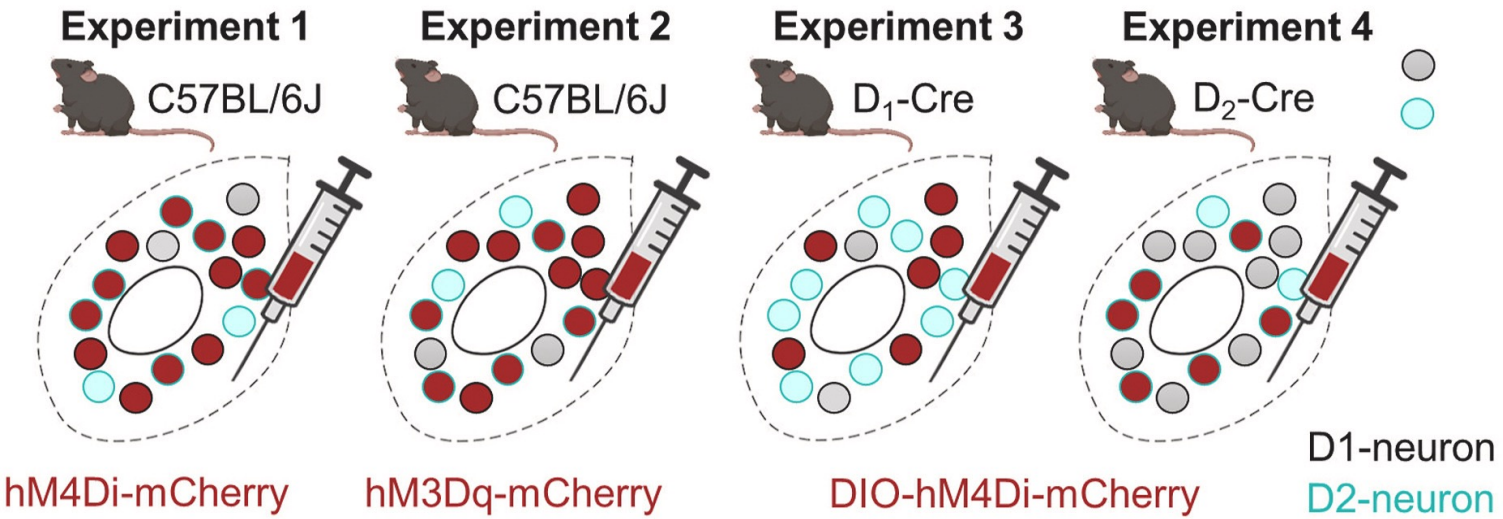


Excitation of the NAc core with hM3Dq did not influence aversion-resistant intake of quinine-adulterated EtOH

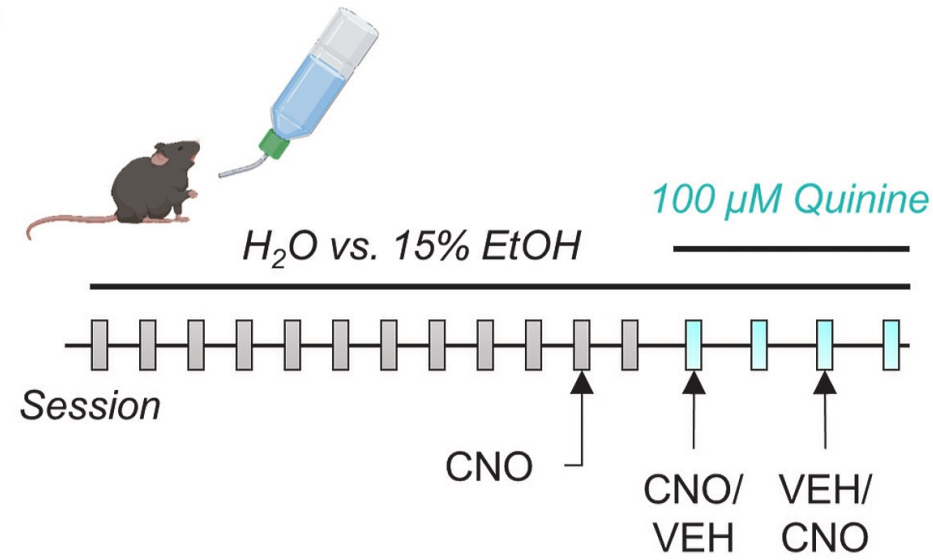




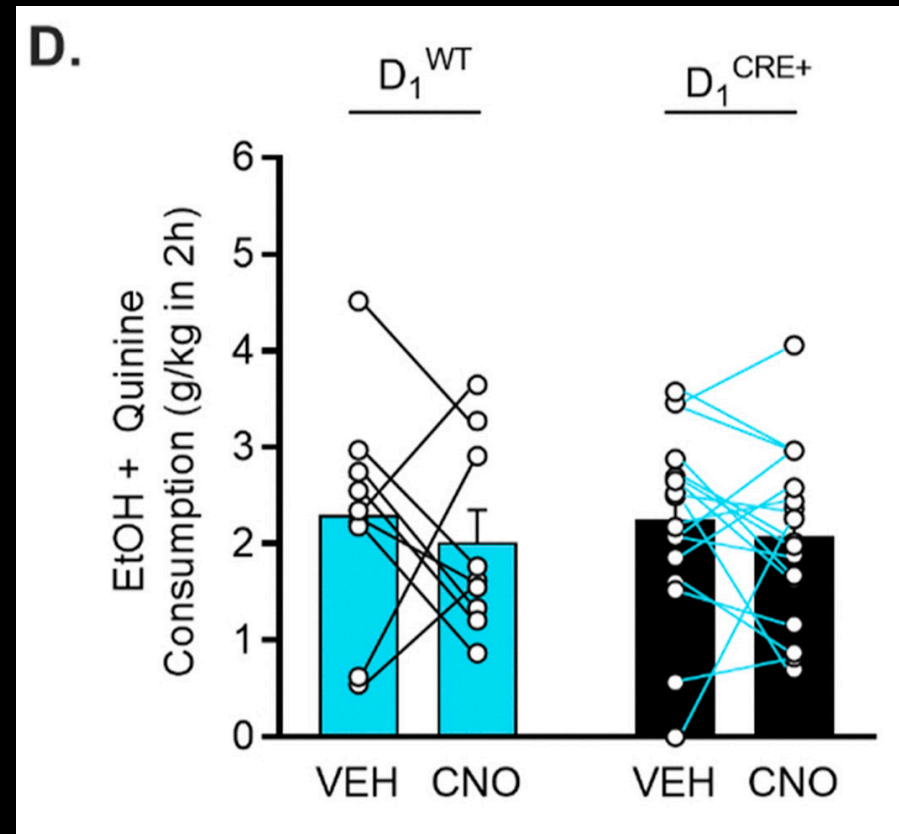
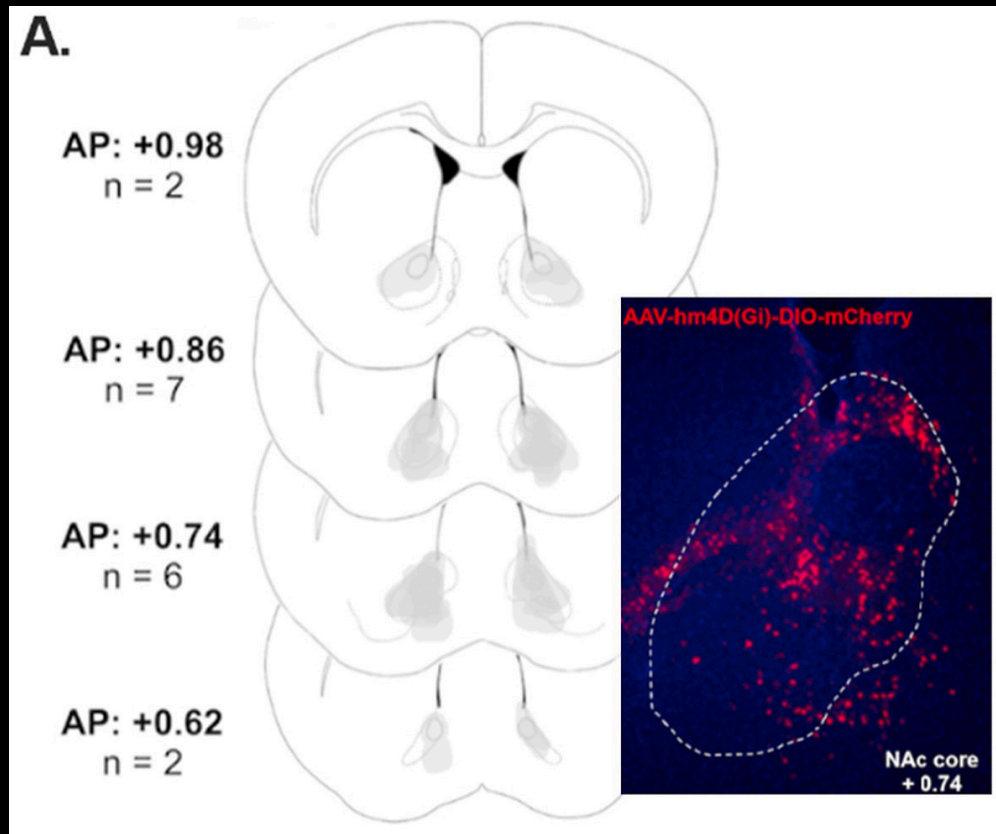
A.

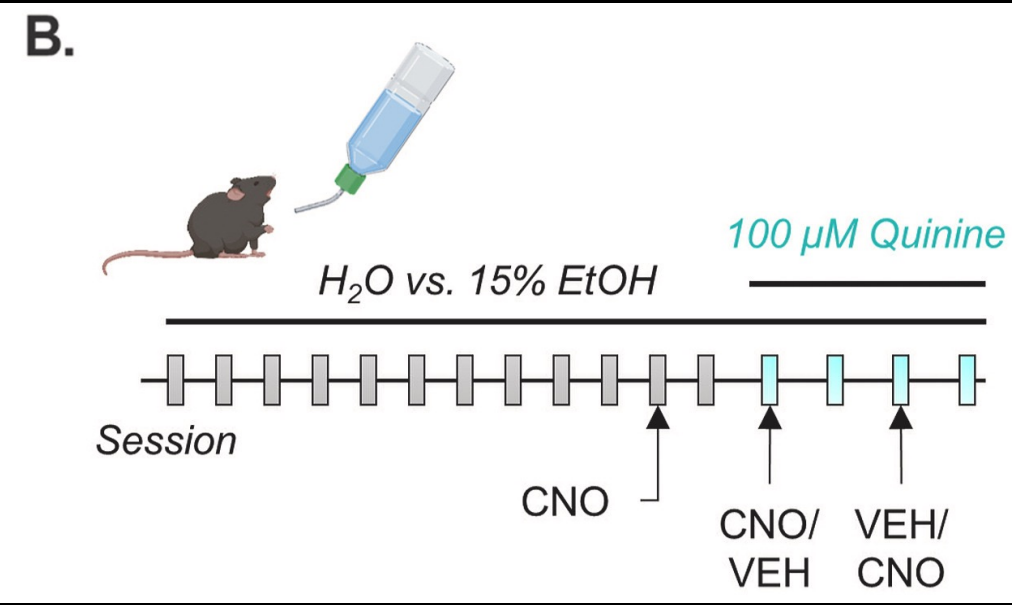
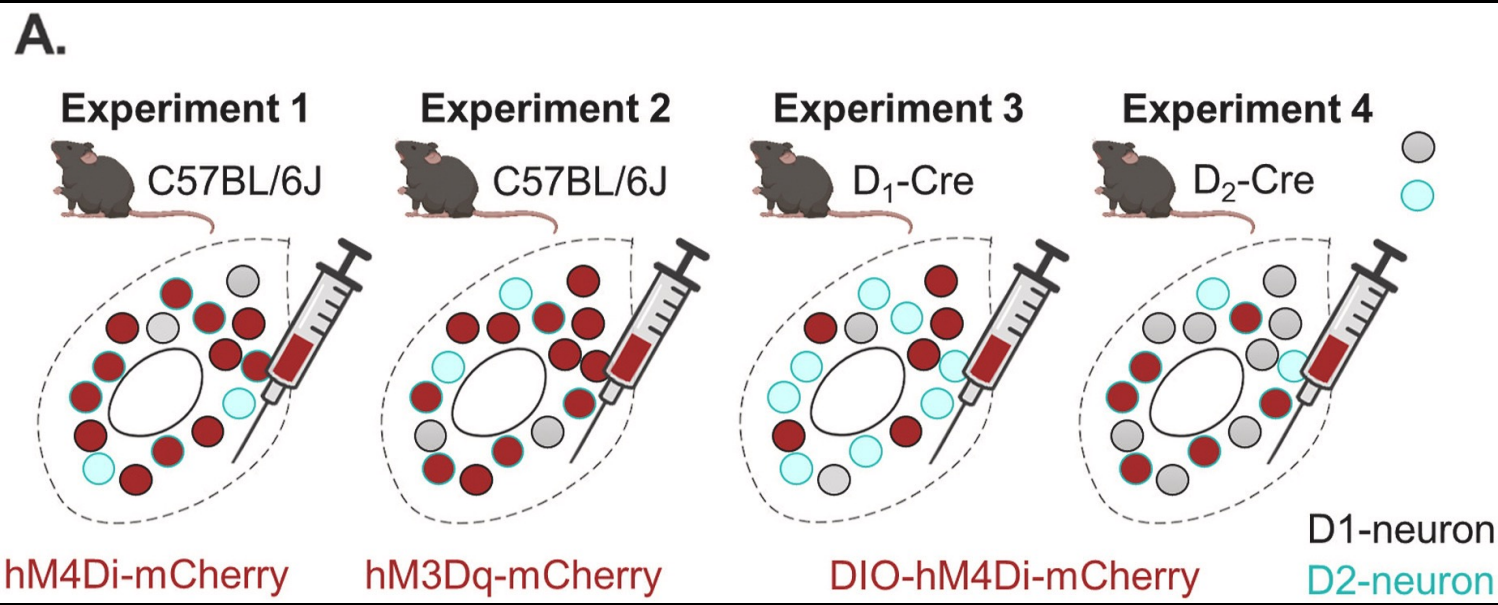


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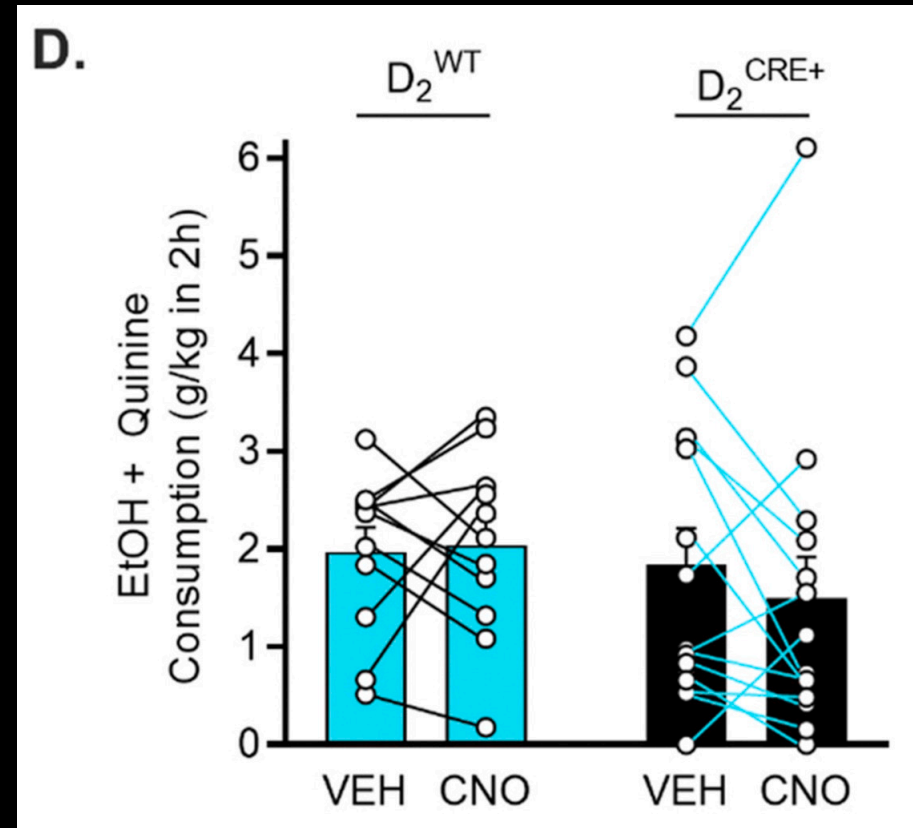
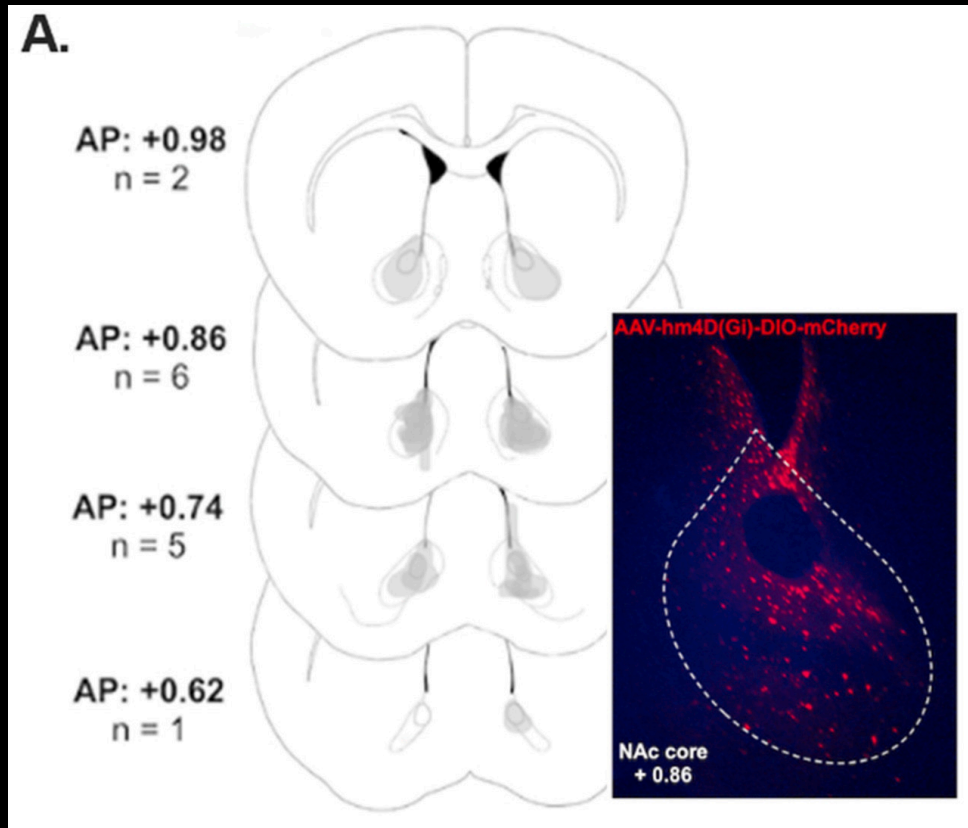


Inhibition of D₁ receptor-expressing neurons did not influence aversion-resistant intake of quinine-adulterated EtOH

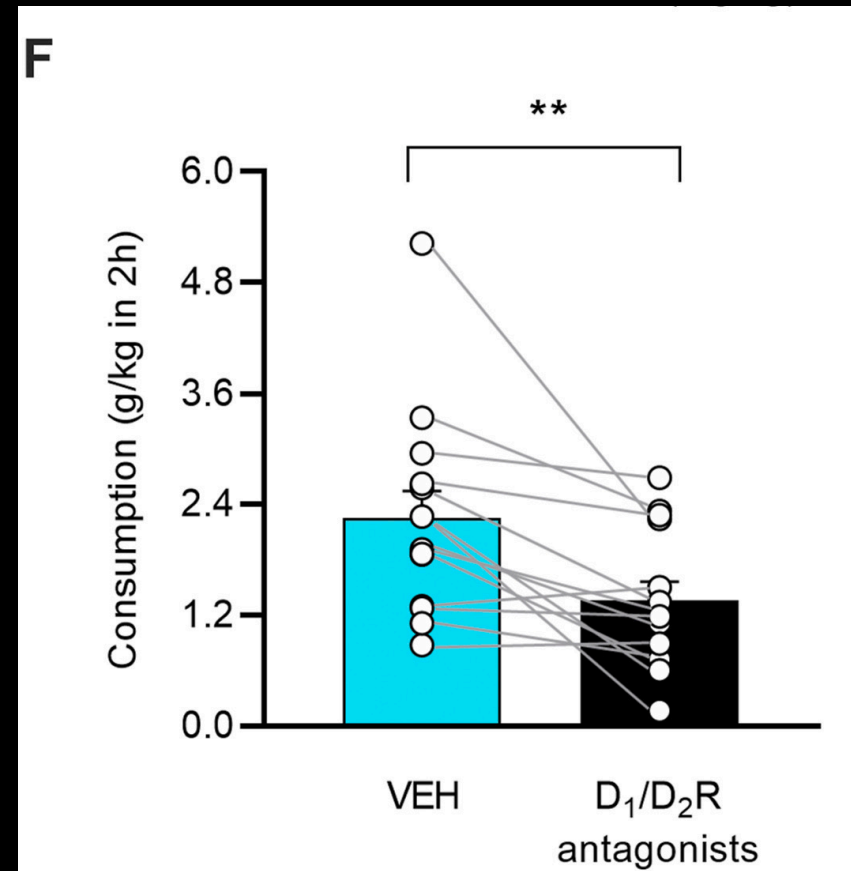
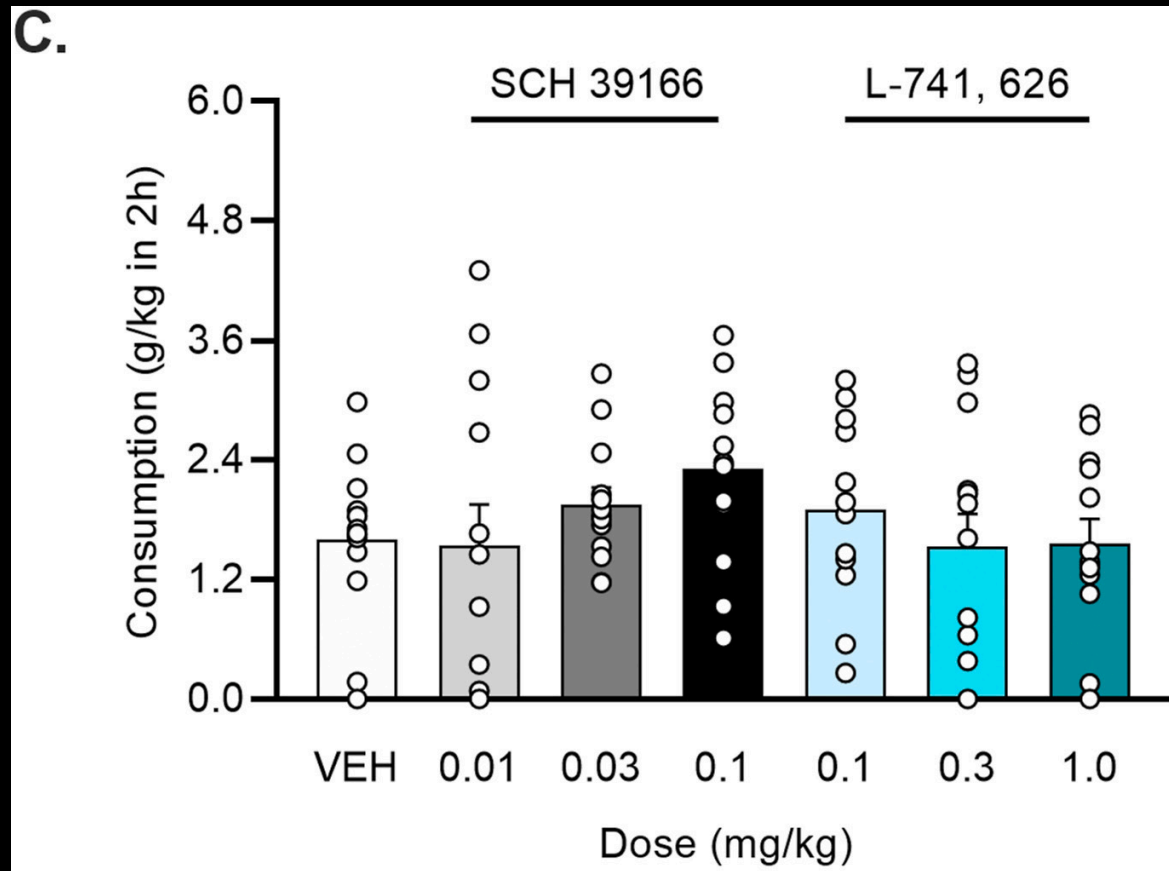




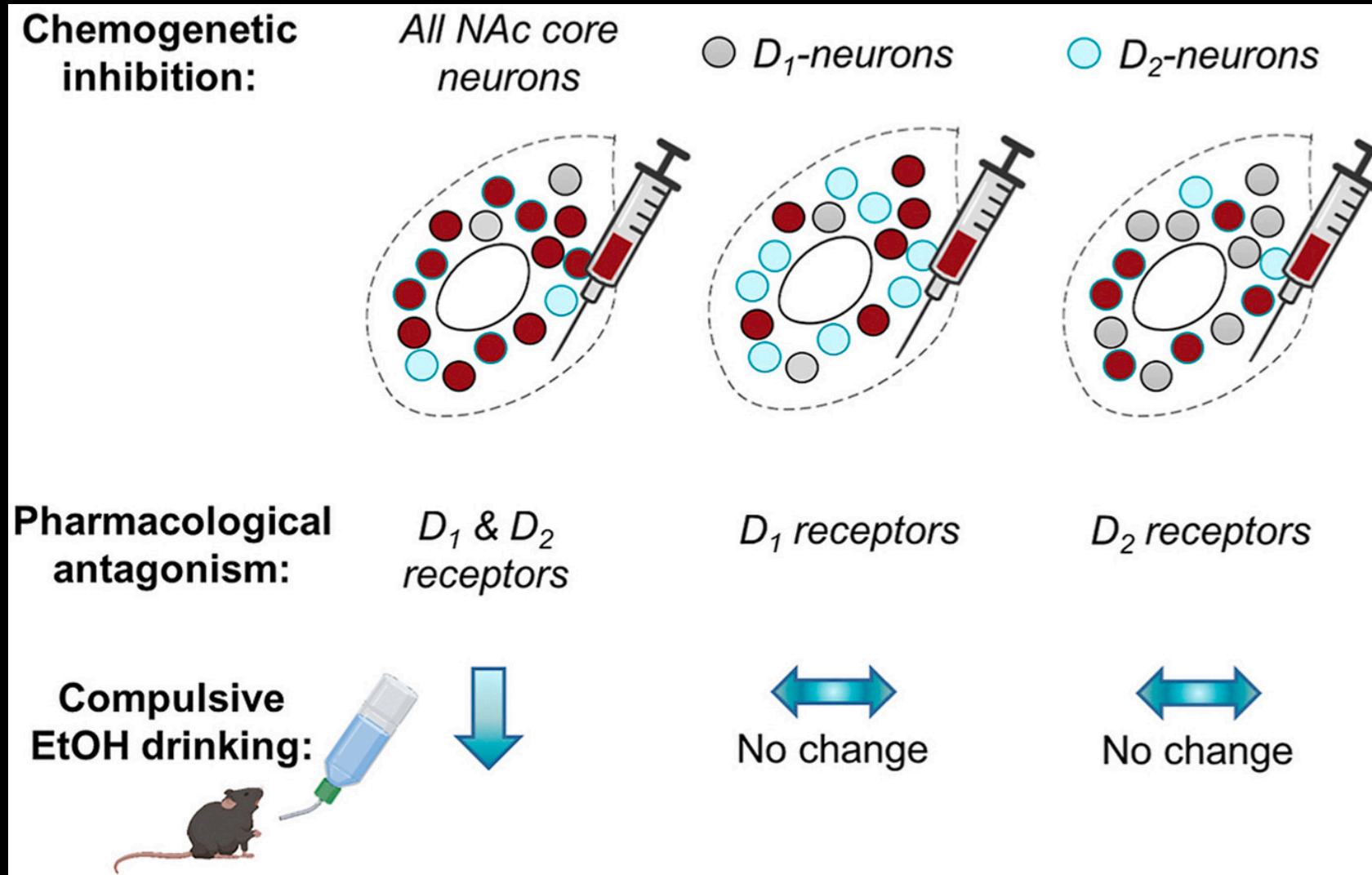
Inhibition of D₂ receptor-expressing neurons with hM4Di did not avertion-resistant intake of quinine-adulterated EtOH



Combined, but not selective, antagonism of D_1 and D_2 receptors decreased aversion-resistant intake of quinine-adulterated EtOH

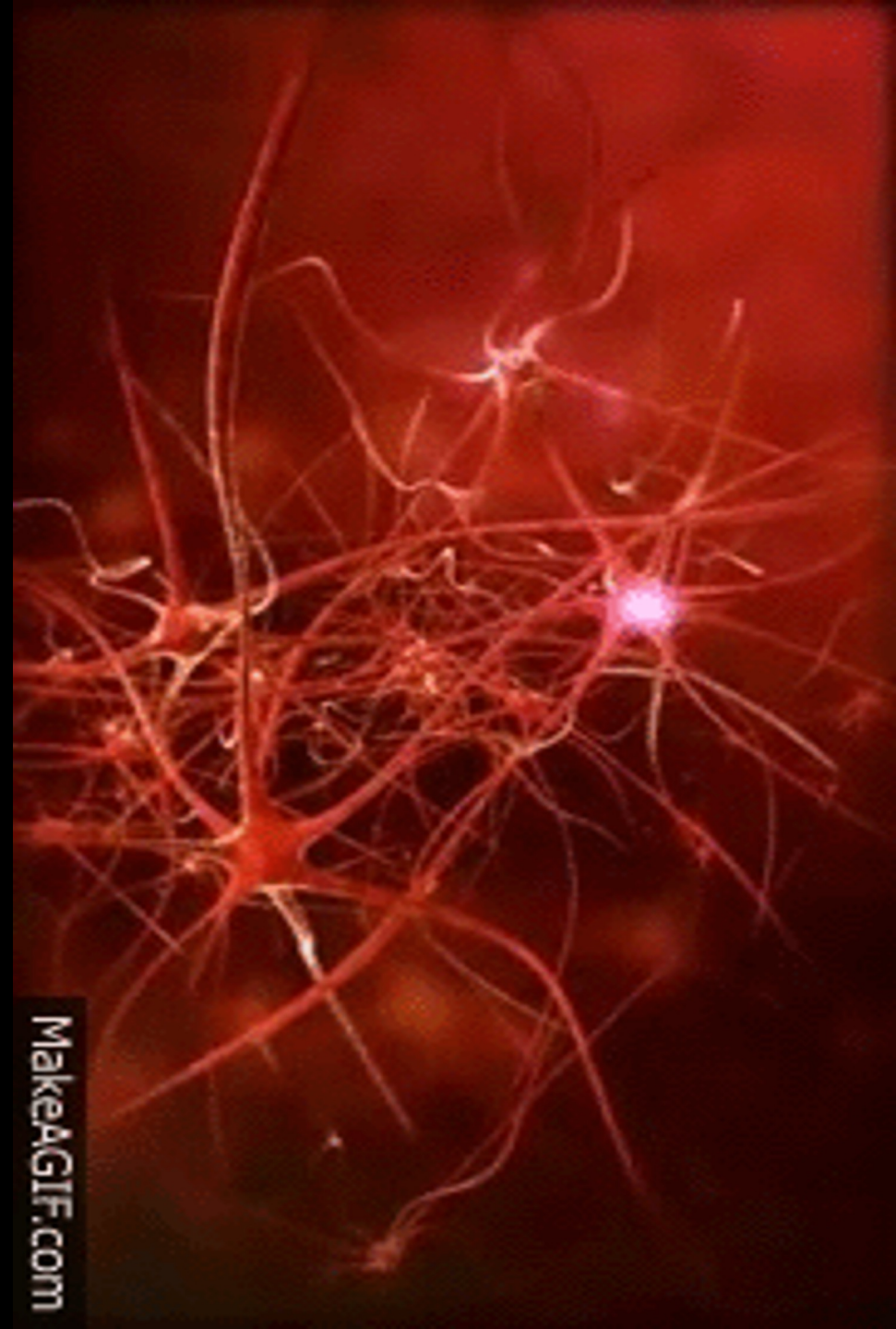


Conclusions



Why Use Chemogenetics?

- Powerful tool!
 - Noninvasive → doesn't damage tissue
- Can manipulate specific brain regions and specific cells of interest
- Can deepen our understanding of how our brain and behavior are associated



Questions?

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