

# Effects of Chemogenetic Inhibition of the Infralimbic Cortex on Recovery from Frustrative Nonreward

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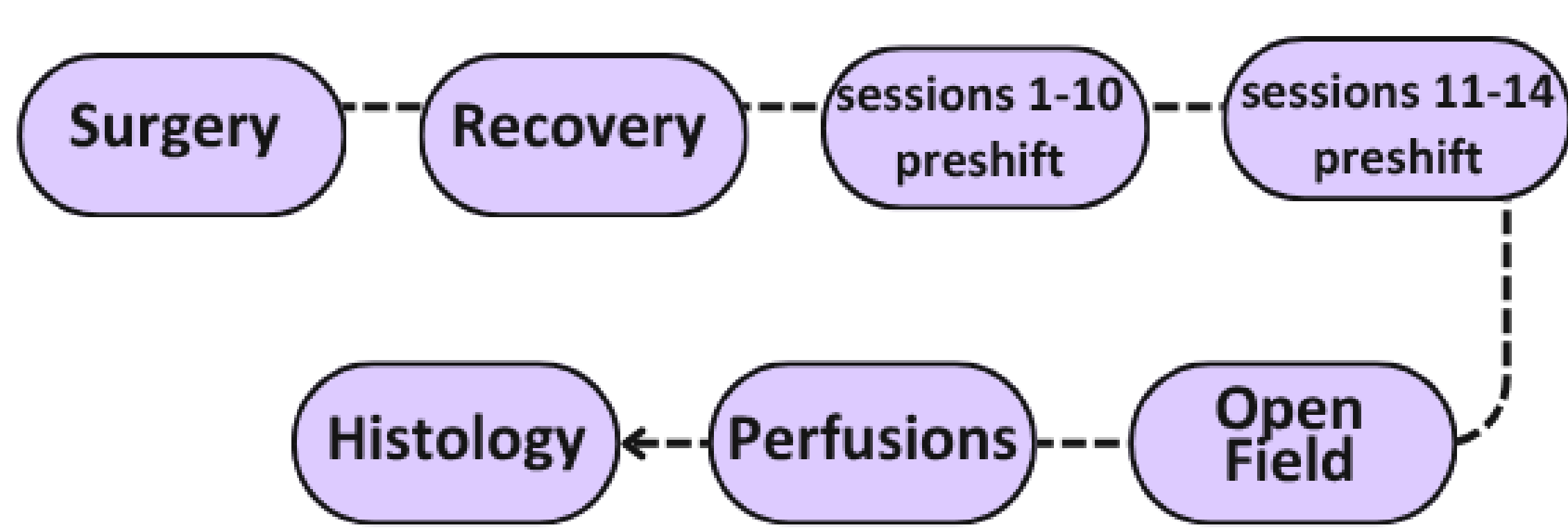


Frustrative nonreward occurs when an expected reward is reduced, producing transient behavioral suppression followed by recovery. Using a consummatory downshift task, this study examined whether infralimbic cortex (IL) inhibition alters recovery after reward downshift. Rats underwent stereotaxic surgery for viral infusion of inhibitory DREADDs targeting the IL and were shifted from 32% to 2% sucrose. Contrary to predictions, IL inhibition appeared to accelerate recovery. This effect may reflect viral spread to adjacent regions, such as the prelimbic cortex. These findings highlight a potential role for medial prefrontal circuits in adjustment to frustrative nonreward.

## Introduction

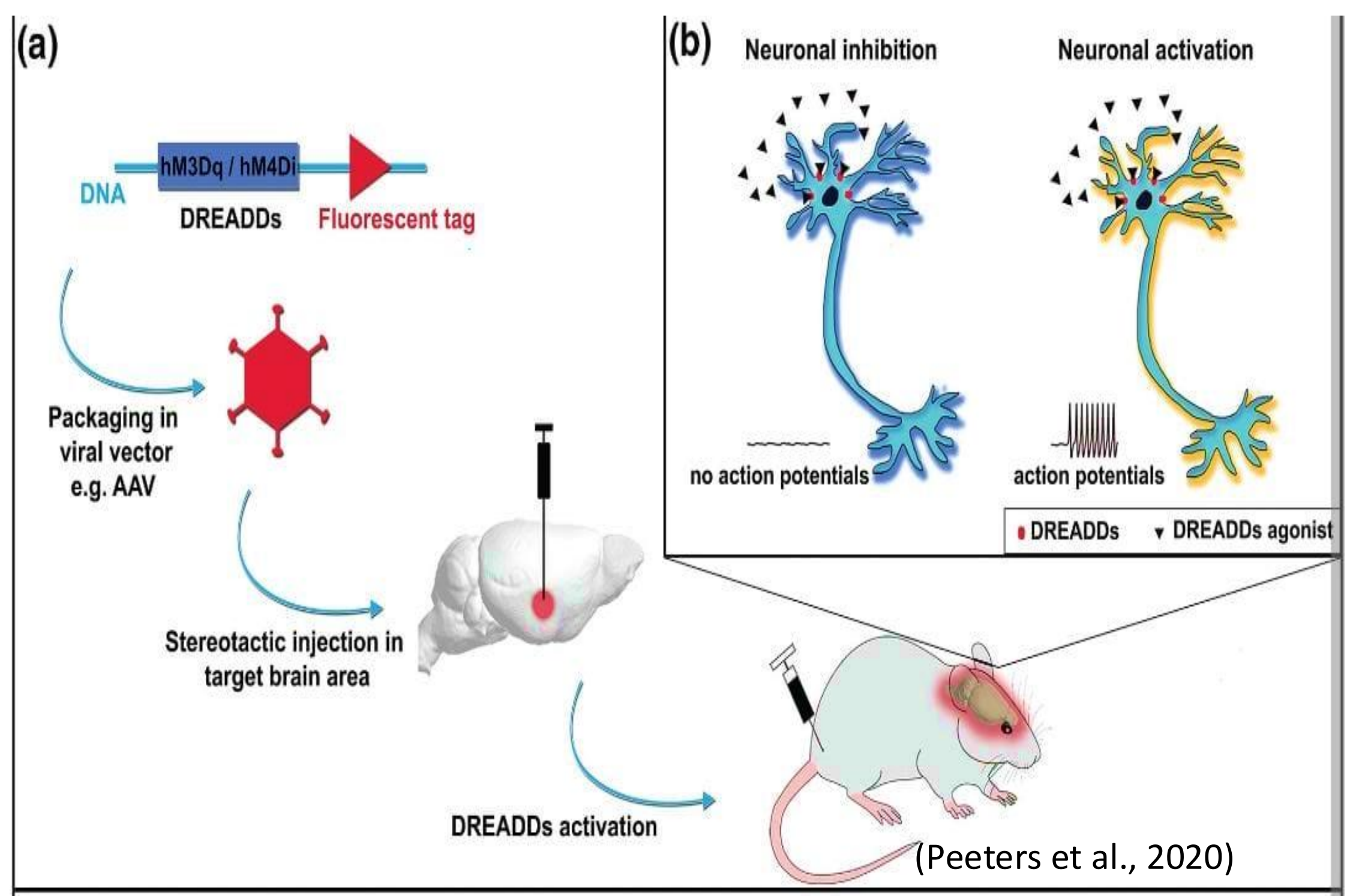
- **Frustration.** A negative emotional state that occurs when an expected reward is reduced in value (Amsel, 1992).
- **Recovery** reflects approach-avoidance conflict, memory updating, and coping with frustration (Papini, 2003).
- **cSNC.** In this consummatory successive negative contrast task, a high-value reward (32% sucrose) is unexpectedly replaced with a lower-value reward (2% sucrose).
- **Previous research** focused on subcortical regions (e.g., basolateral amygdala), but the role of cortical regions remains unclear (Guarino et al., 2023)
- **Reward downshift** leads to **behavioral suppression** followed by gradual recovery as animals adjust to the new reward.
- The **infralimbic cortex (IL)** is implicated in fear extinction (Barker, 2014).
- **Hypothesis.** IL inhibition will retard behavioral recovery after reward loss.

## Method



### Surgery and Manipulation

DREADD: designer receptors exclusively activated by designer drugs. Engineered muscarinic receptors modified to respond to CNO, rather than to their natural ligand, acetylcholine.

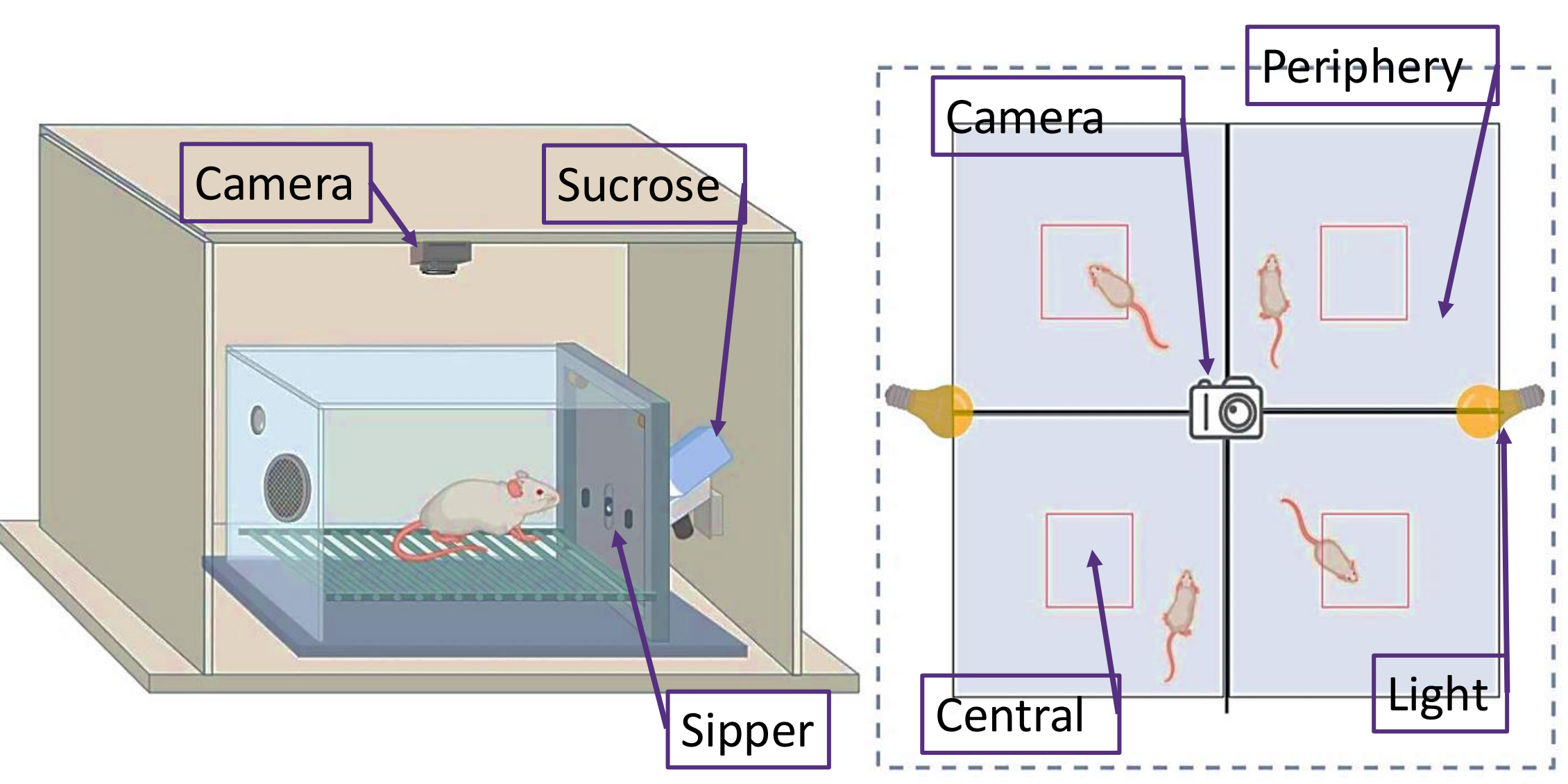


### Experimental Design

- Rats trained to consume **32% sucrose** (Sessions 1–10).
- Unexpected downshift to **2% sucrose** (Sessions 11–14).
- Licking responses recorded across sessions.

### Controls

- Animals infused with the DREADD, but receiving a vehicle injection, rather than CNO.



## Histology

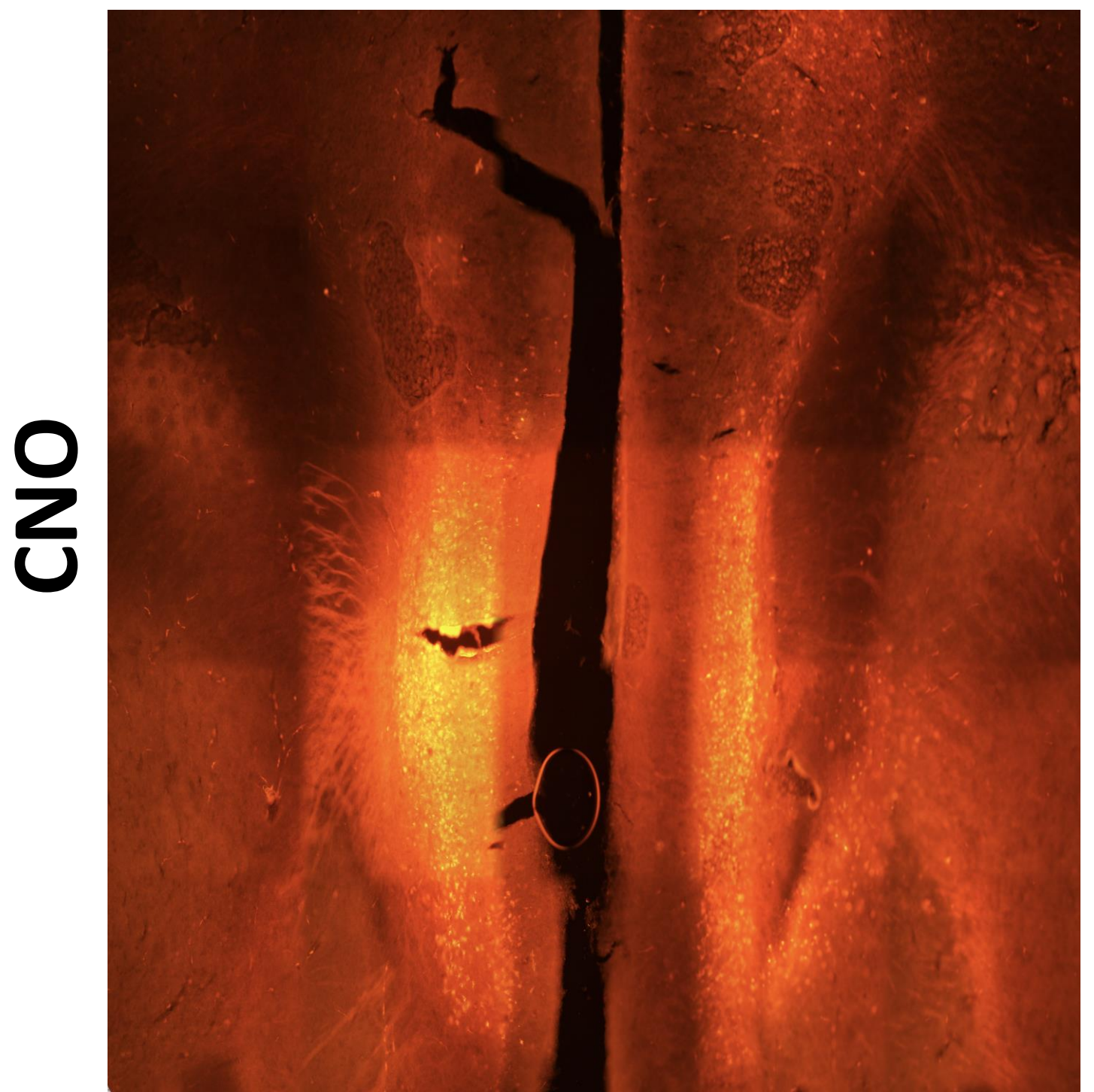
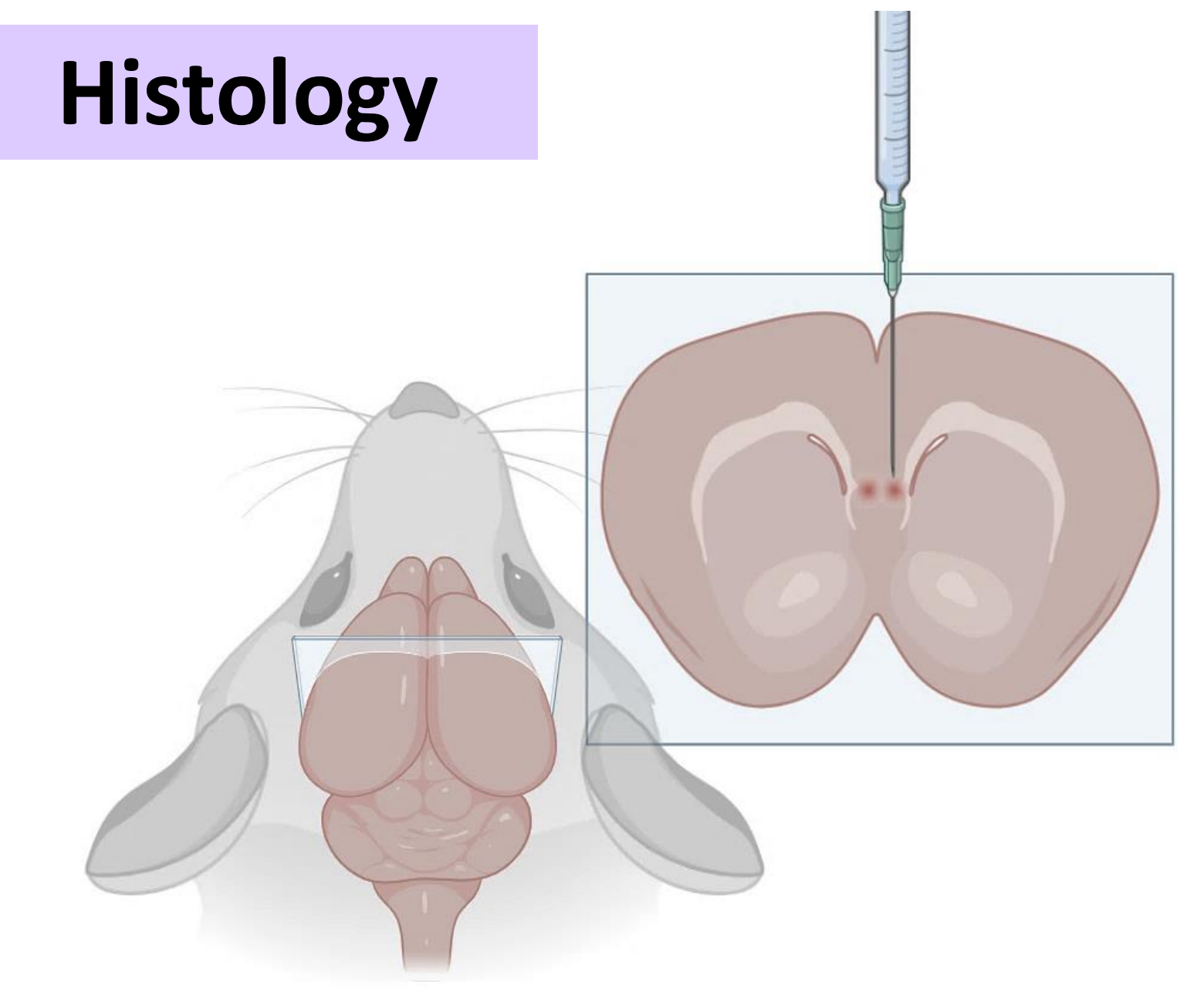


Figure 1: Brain sample of IL in CNO group

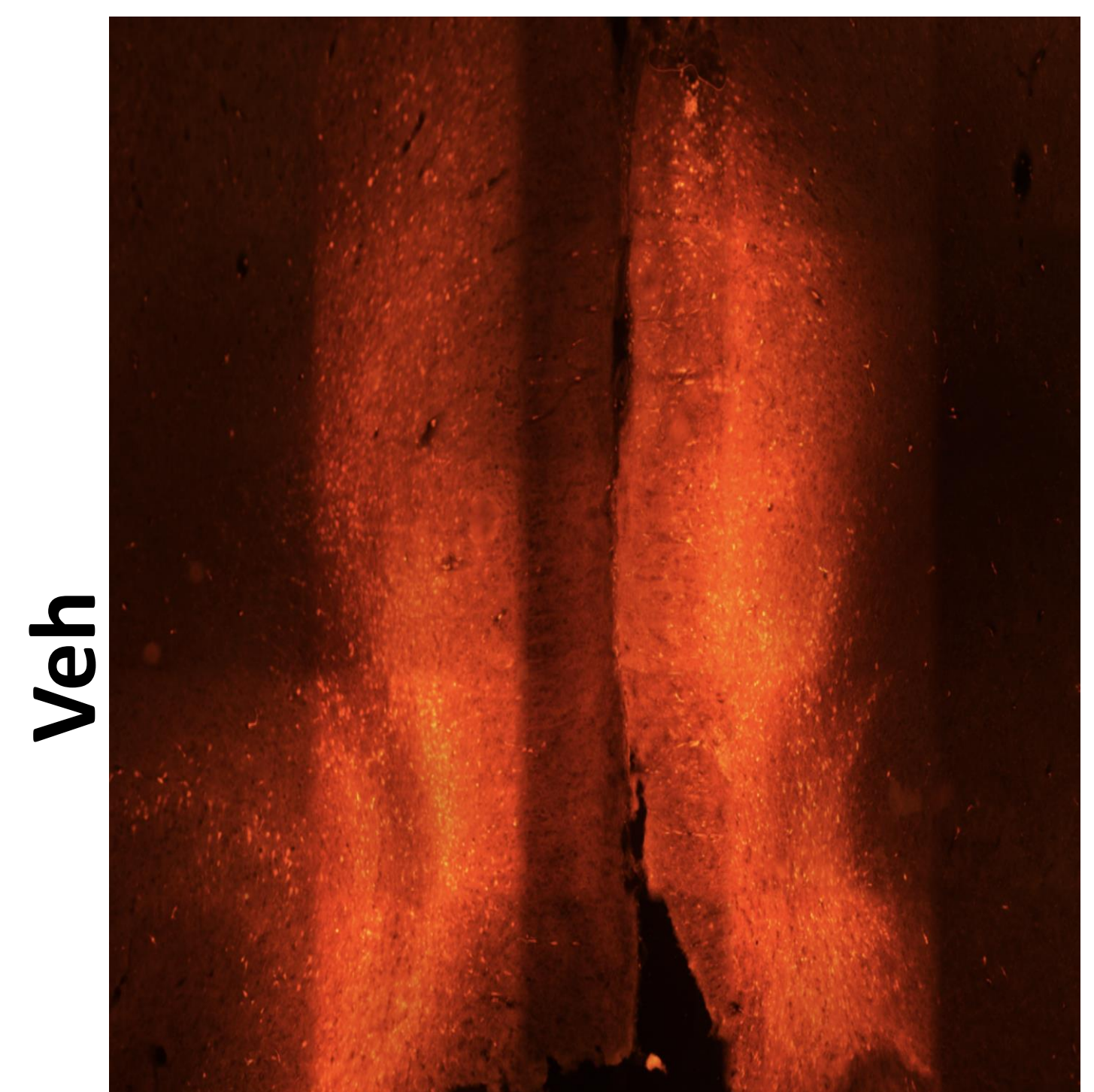


Figure 2: Brain sample of IL in Veh group

## Results

### Downshift Data

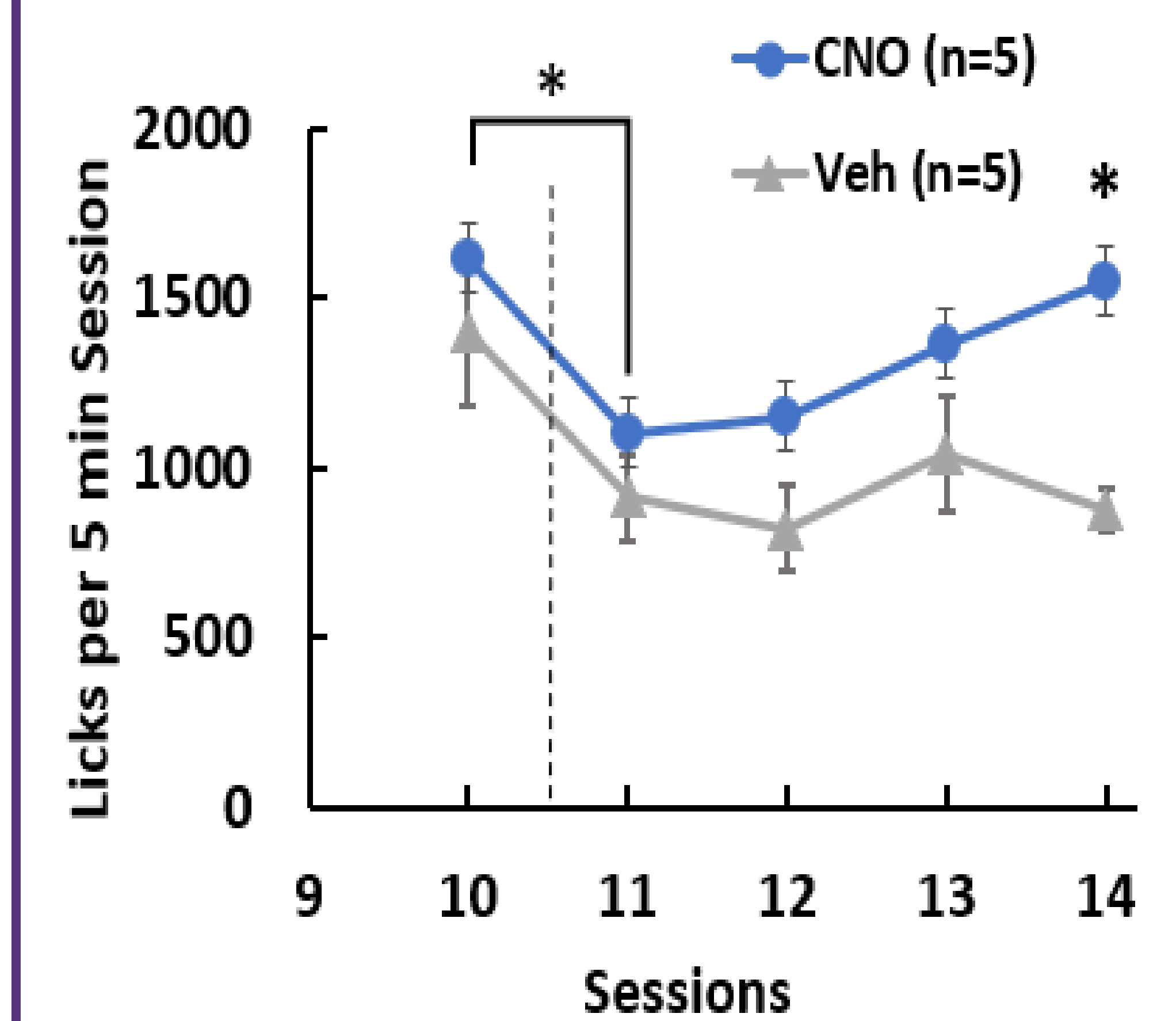


Figure 3: Lick frequency after inhibition of the Infralimbic Cortex (CNO) and control (Veh) during downshift (5 -min sessions 11-14) \* $p$ s < 0.05

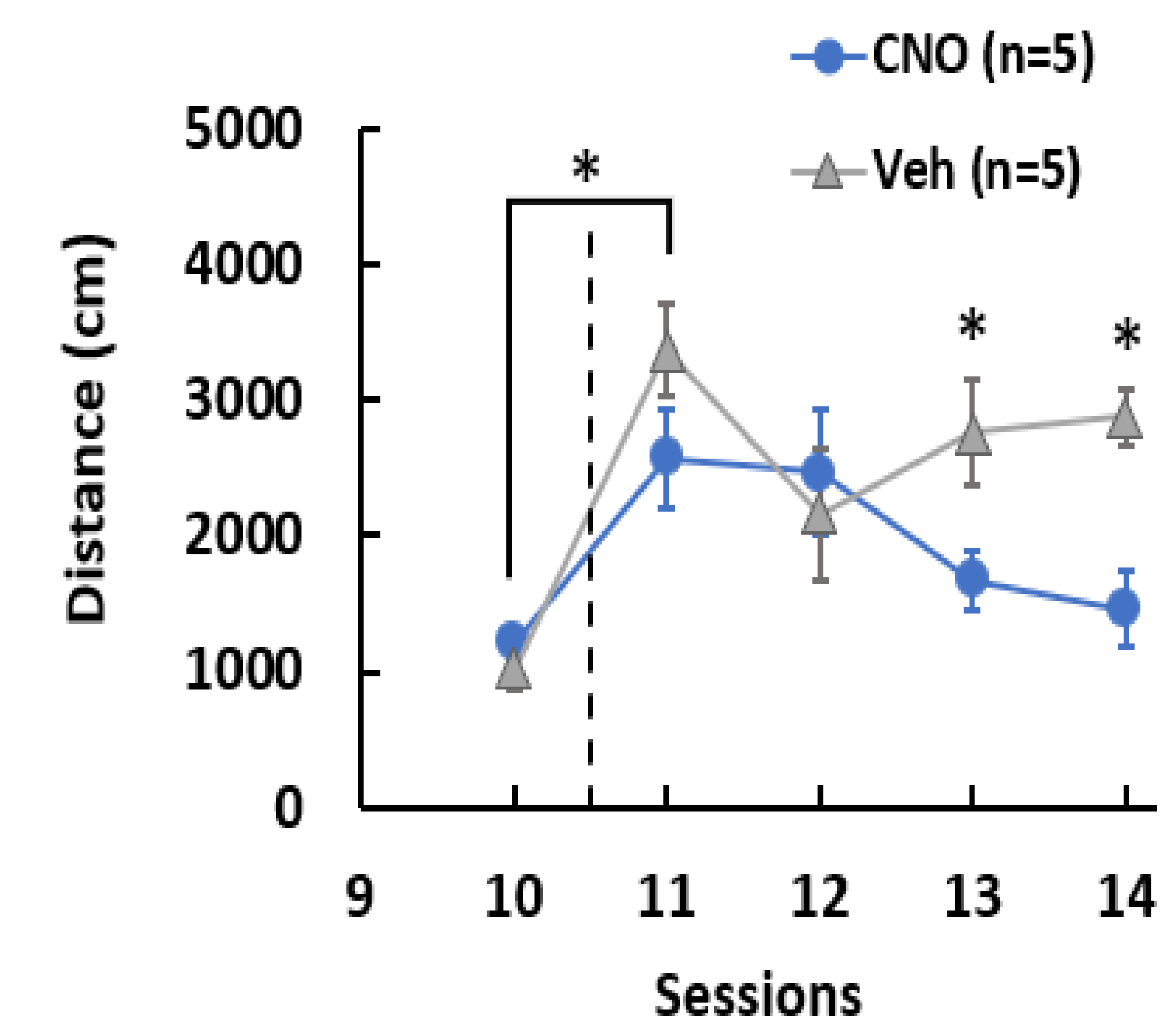


Figure 4: Distance traveled in the consummatory box during 5-min sessions 10-14 in CNO and Veh groups \* $p$ s < 0.05

### Open Field (OF)

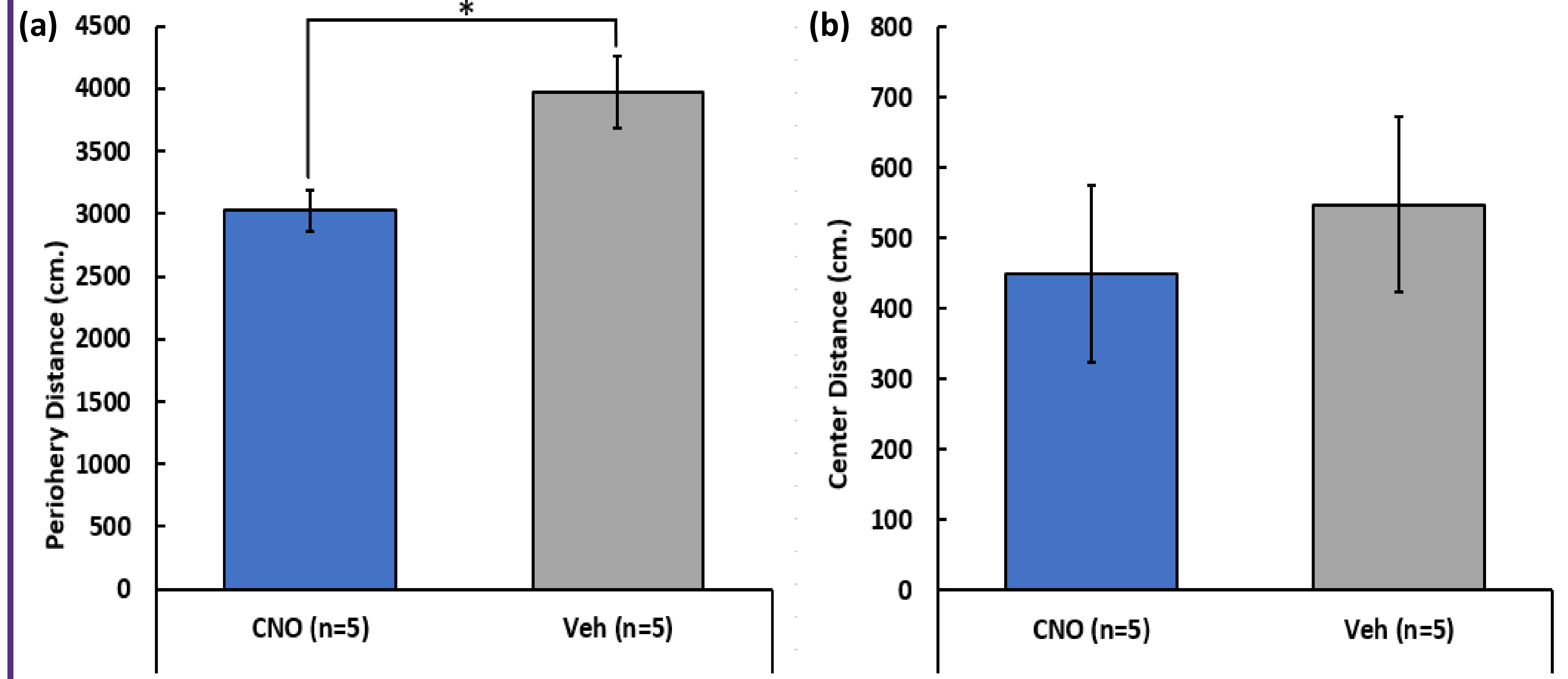


Figure 5: Distanced traveled in open field periphery (a) and center (b) during a 15 minutes session. \* $p$ s < 0.05

## Conclusions

- Unlike our prediction, IL inhibition accelerated behavioral recovery after reward loss (Figure 3).
- One possible explanation is the spread of the inhibitory DREADDs to adjacent regions, particularly the prelimbic cortex (PL), which has been linked to behavioral effects opposite to those of the IL.
- Given the small size and close proximity of IL and PL regions, diffusion of DREADD expression may influence the outcome.
- These findings suggest that recovery from reward loss may depend on interactions within these cortical circuits, rather than on the IL alone.

## References

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## Funding

