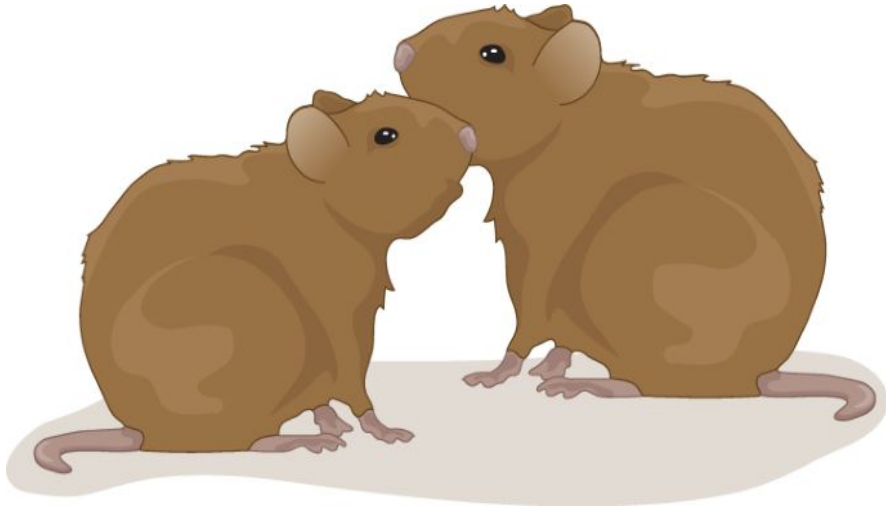


# Nucleus accumbens dopamine differentially mediates the formation and maintenance of monogamous pair bonds

Brandon J Aragona<sup>1</sup>, Yan Liu<sup>1</sup>, Y Joy Yu<sup>1</sup>, J Thomas Curtis<sup>1</sup>, Jacqueline M Detwiler<sup>1</sup>, Thomas R Insel<sup>2</sup> & Zuoxin Wang<sup>1</sup>  
2006, Nature Neuroscience

Allie Yuxin Lin and Ilana Livshits  
Mentor: Jenny Merritt  
Coordinator: Saba Shokat Fadaei

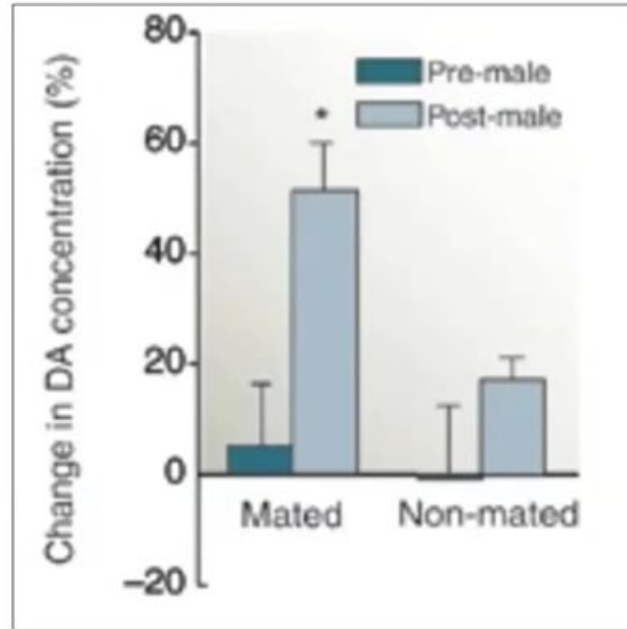
Monogamy is not the default in the animal kingdom!



# Pair bonding in monogamous prairie voles

- Pair bond is closest thing to a marital relationship in prairie voles
- Requirements for a pair bond:
  - Mating
  - partner preference
  - unfamiliar conspecifics, including potential mates, are aggressively rejected
    - selective aggression towards other “suitors”

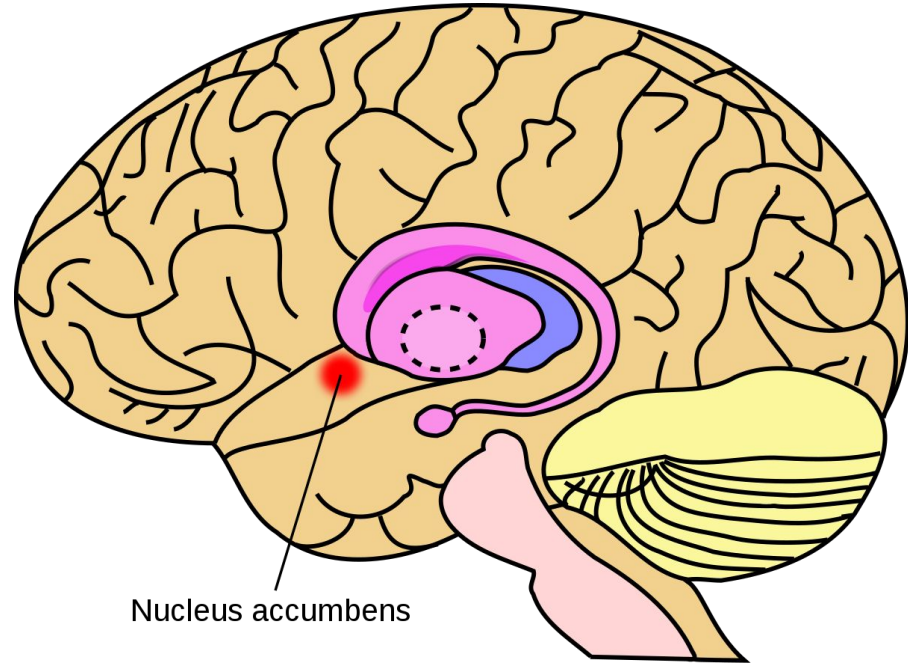
# Neurotransmitter important in pair bond formation: Dopamine



Young, L. J., & Wang, Z. (2004). The neurobiology of pair bonding. *Nature Neuroscience*, 7(10), 1048–1054. <https://doi.org/10.1038/nn132>

# Nucleus accumbens

- the neural interface between motivation and action, playing a key role on feeding, sexual behavior, reward, stress-related, drug self-administration behaviors, etc.
- part of the neural circuit that controls reward-seeking in response to reward-predictive cues



# Dopamine transmission in the nucleus accumbens

- Dopamine transmission within the nucleus accumbens mediates both approach and avoidance behaviors
- Nucleus accumbens has two dopamine receptors: D1 and D2

# Prairie Vole

[Prairie Vole Partner Preference Test Mate Choice Experiment Time Lapse \(no audio\) - YouTube](#)

- Some prairie voles (*Microtus ochrogaster*) form monogamous pair bonds, raising their offspring together
- The voles' pair bonding, sharing of parental roles and egalitarian nest building in couples makes them a good model for understanding the biology of monogamy and mating in humans.

# Formation of pair bond

Cohabitation 6h



NO mating



NO pair bond



Cohabitation 24h



mating

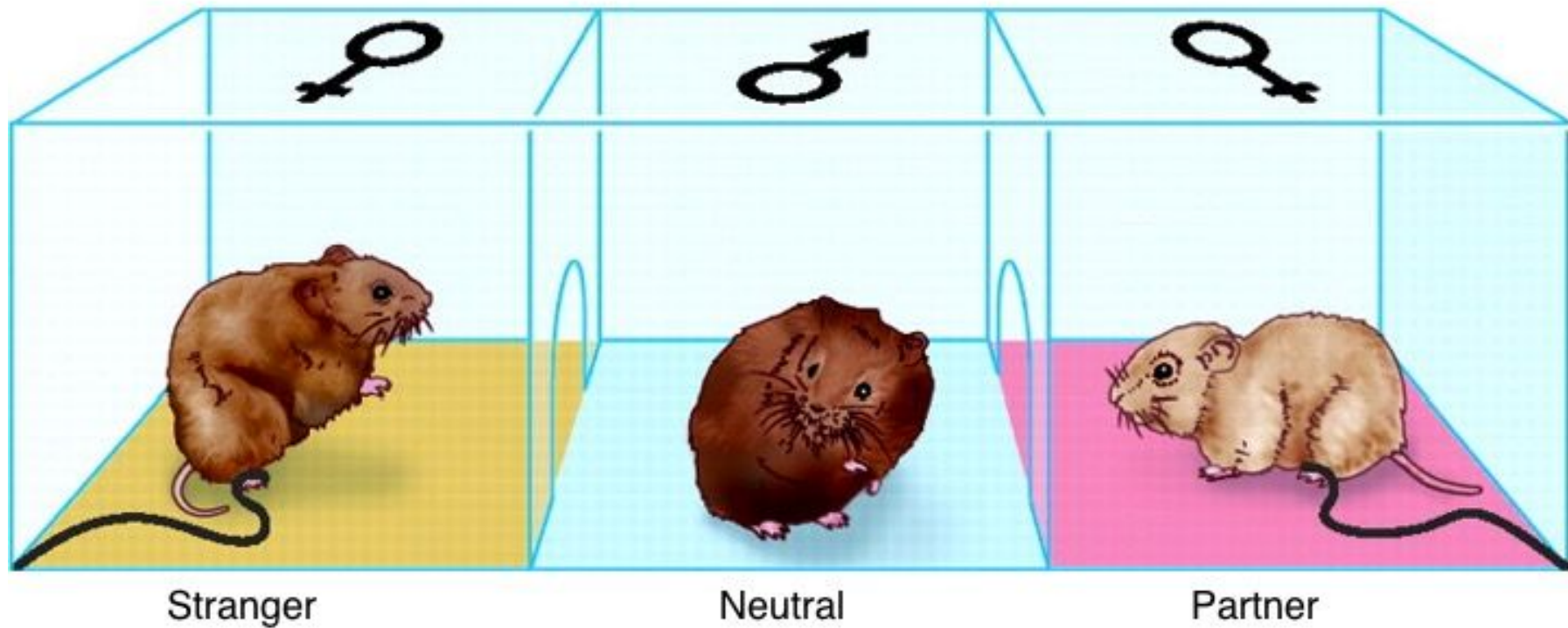


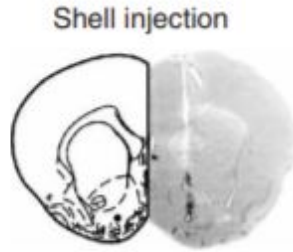
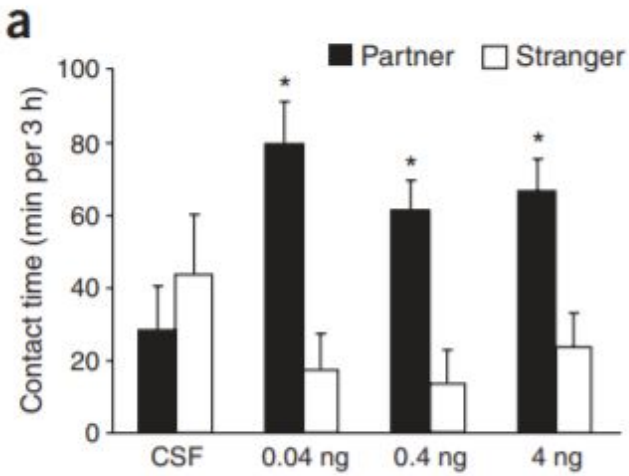
pair bond





# Partner Preference Test



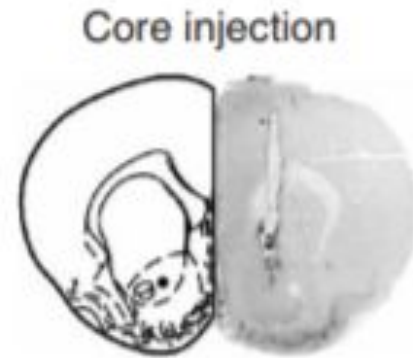
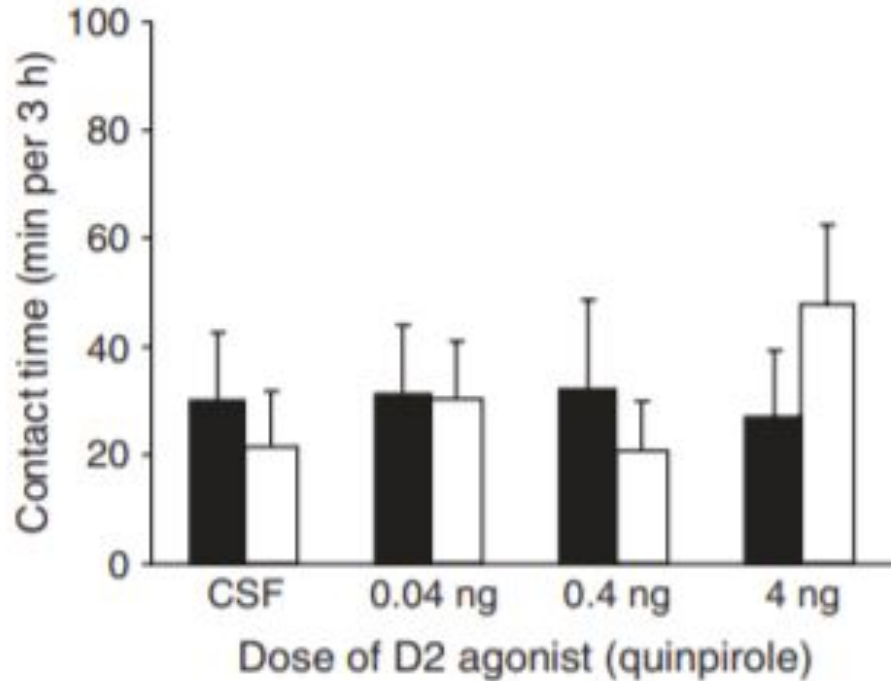


## What subregion of the nucleus accumbens does dopamine use to facilitate pair bond formation?

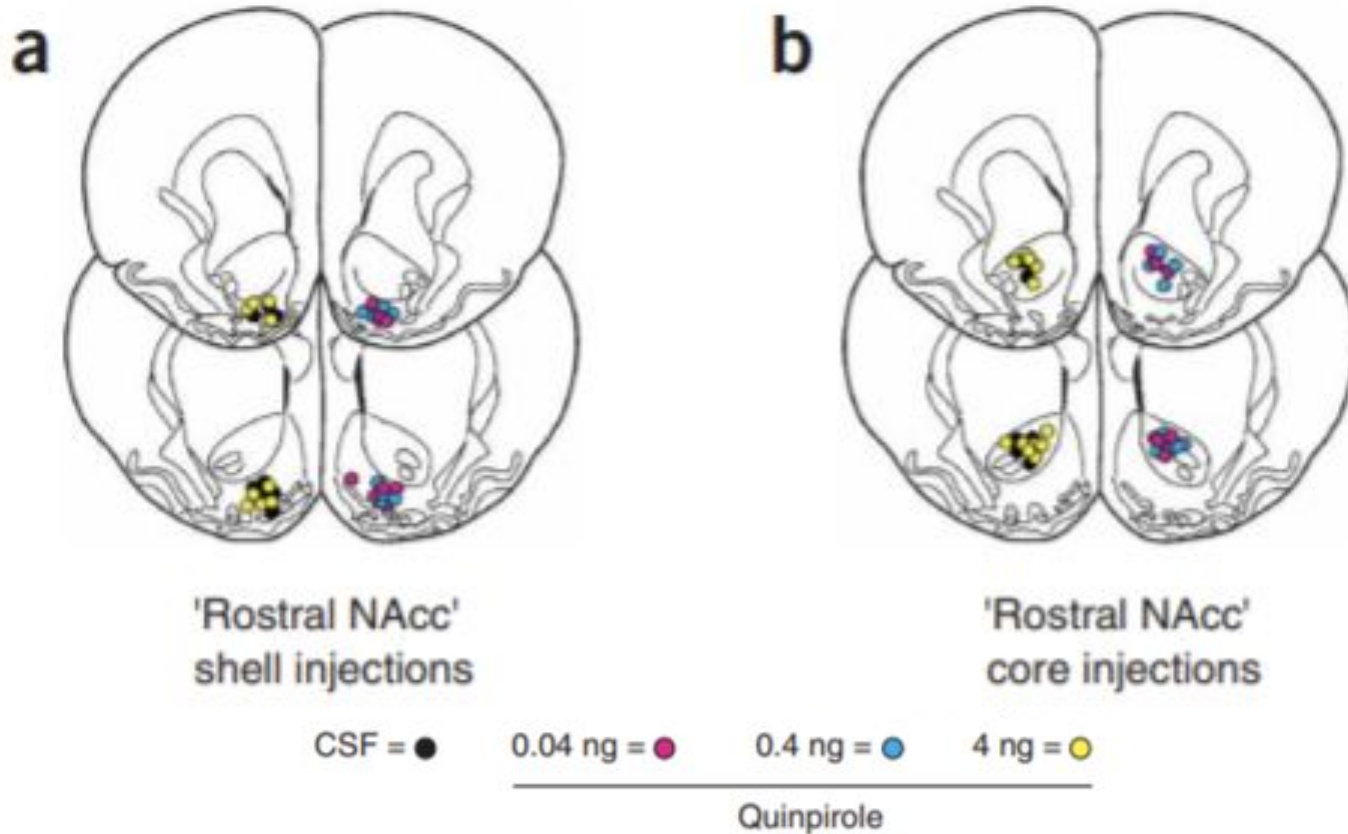
- The nucleus accumbens is composed of the core and shell
- D2-like specific agonist quinpirole is a drug known to induce partner preferences
- Males injected with CSF did not show partner preference
- Administration of quinpirole into the NAcc shell induced partner preferences in the absence of mating.

# Quinpirole core injection

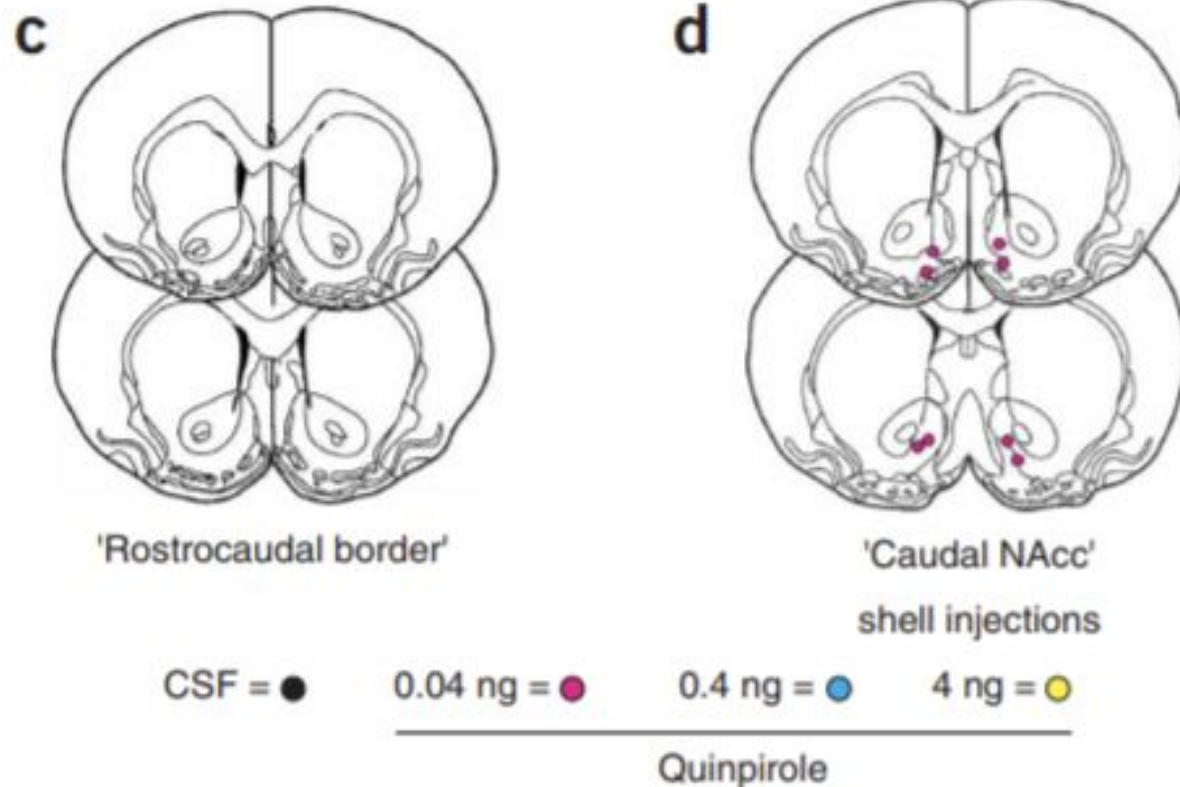
**b**



# Histological verification of injection sites for experiment 1



# Is the caudal nucleus accumbens involved in pair bond formation?



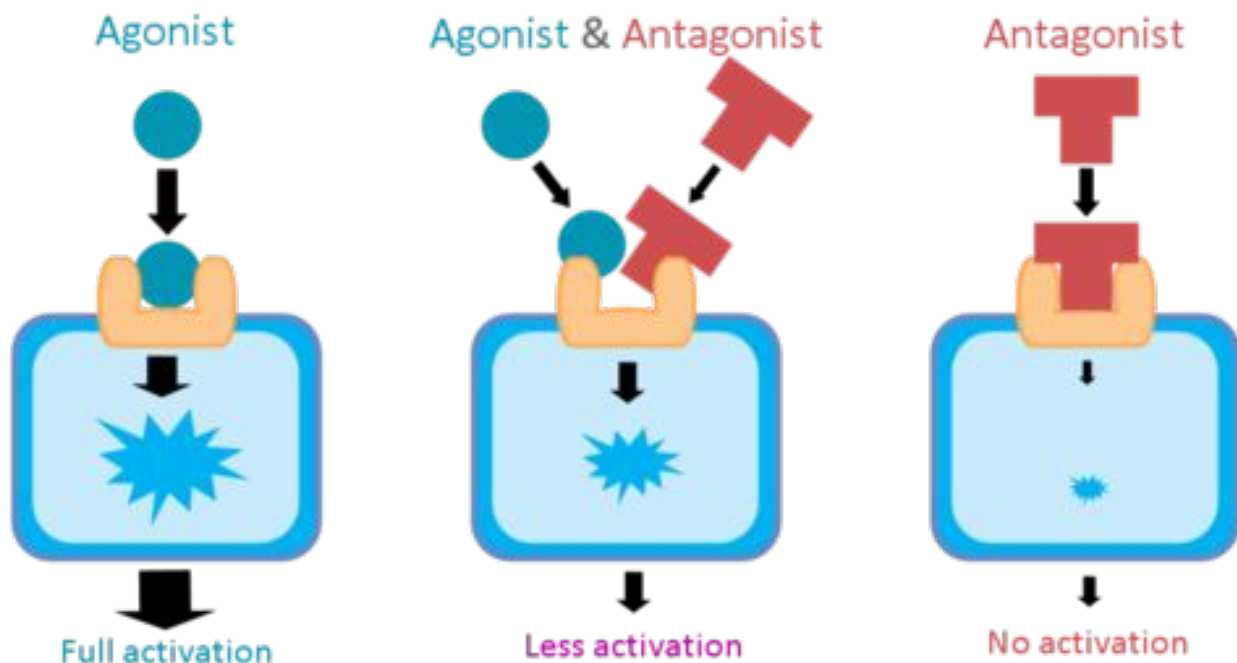
- To determine whether D2-like receptor facilitation of partner-preference formation is specific to the rostral shell, quinpirole was injected into the caudal shell.

Are D1- and D2-like receptors  
involved in pair bond formation?

# Agonists and Antagonists

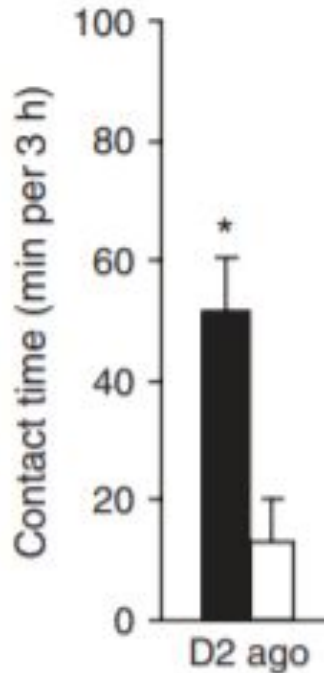
Agonists - Drugs that occupy receptors and activate them.

Antagonists - Drugs that occupy receptors but do not activate them.  
Antagonists block receptor activation by agonists.



# Opposing roles for D1- and D2-like receptors

**a** 6 h - cohabitation

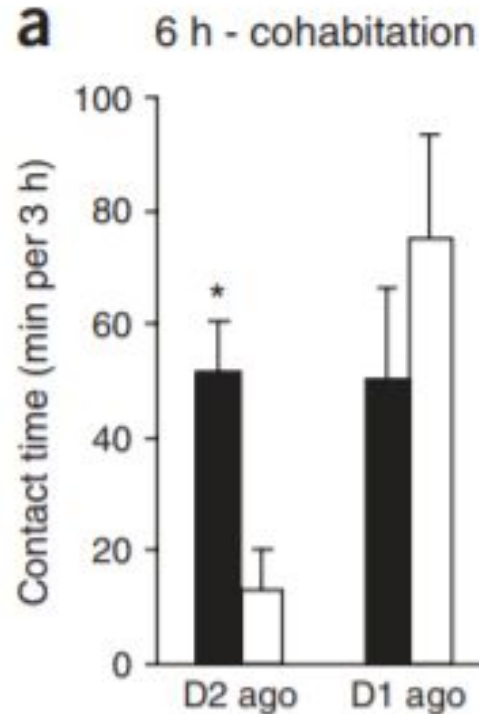


- Administration of quinpirole induced partner preferences in voles paired with a female for 6 h without mating.

■ Partner □ Stranger



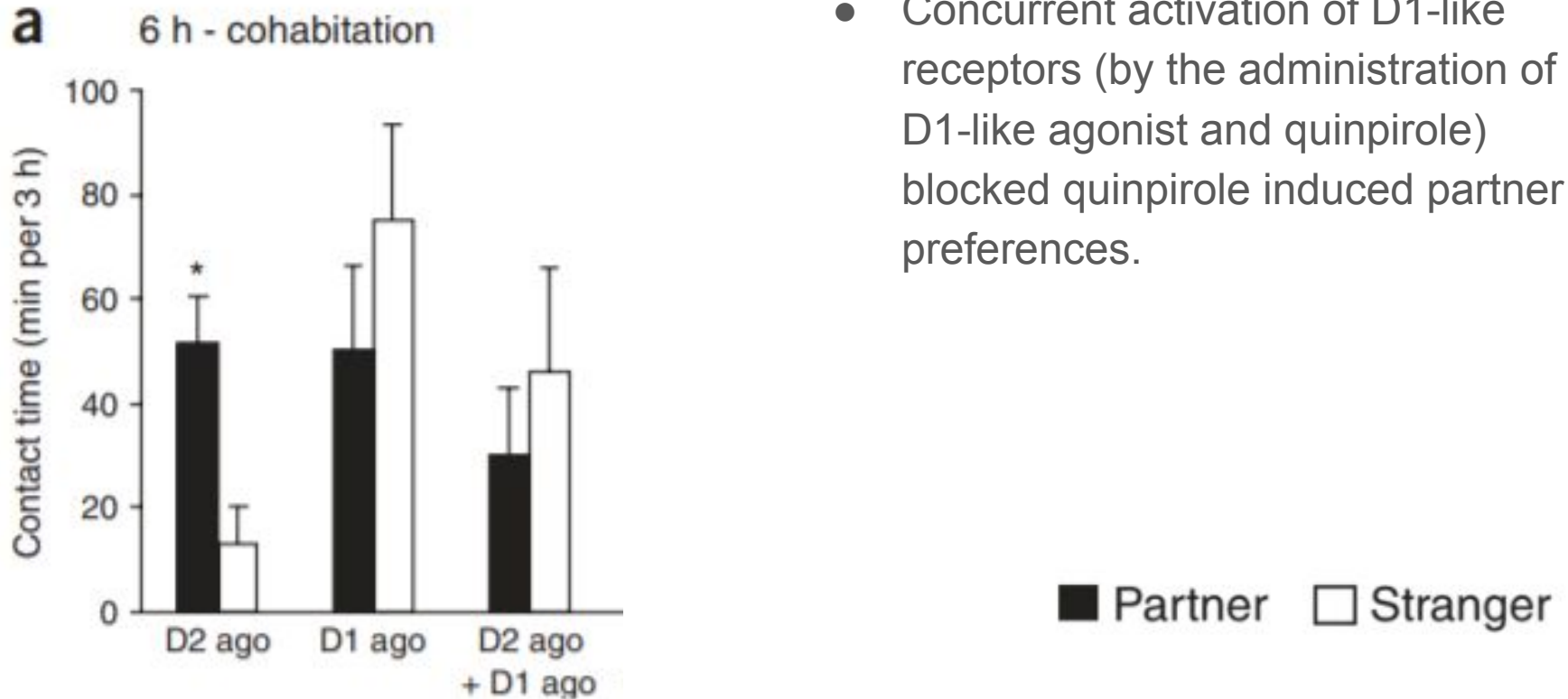
# Opposing roles for D1- and D2-like receptors



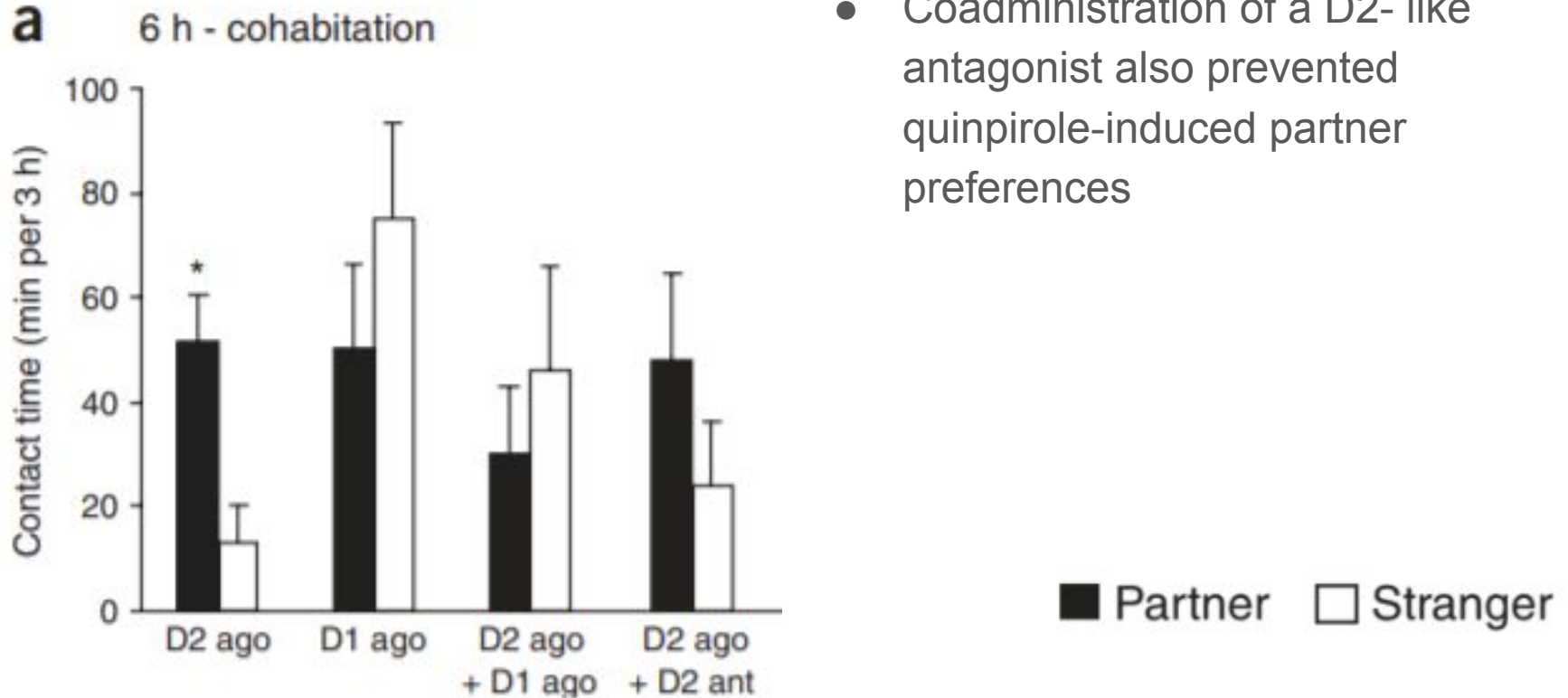
- Administration of quinpirole (bar 1), but not a D1-like agonist (bar 2), induced partner preferences in voles paired with a female for 6 h without mating.
- Therefore, quinpirole induced partner preferences served as the control group for this experiment.

■ Partner □ Stranger

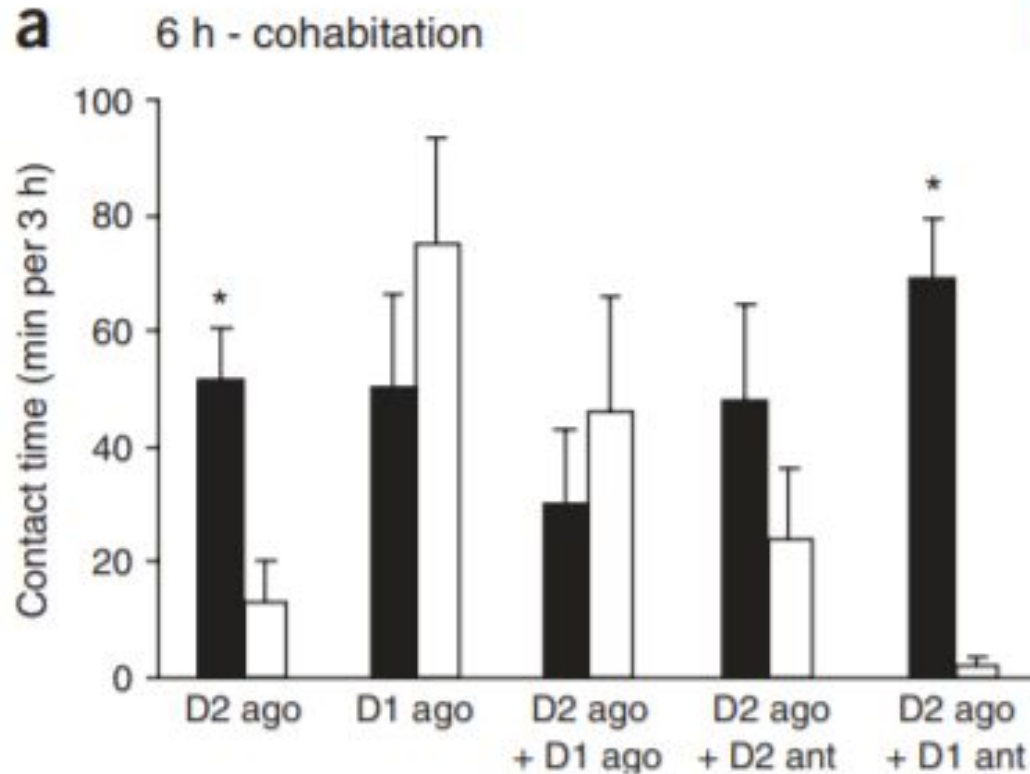
# Opposing roles for D1- and D2-like receptors



# Opposing roles for D1- and D2-like receptors

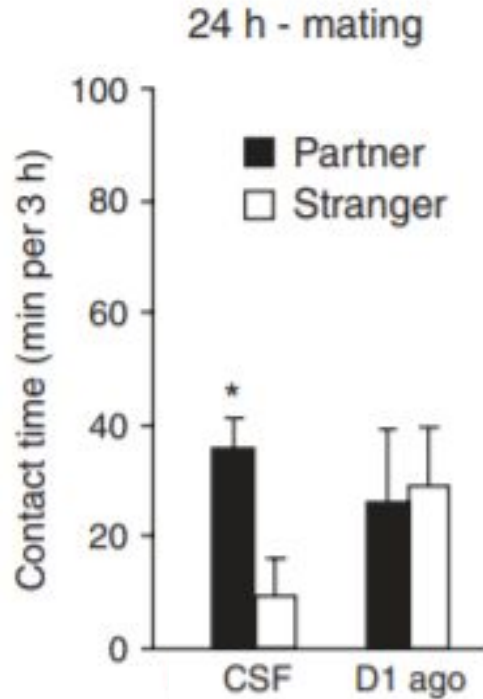


# Opposing roles for D1- and D2-like receptors



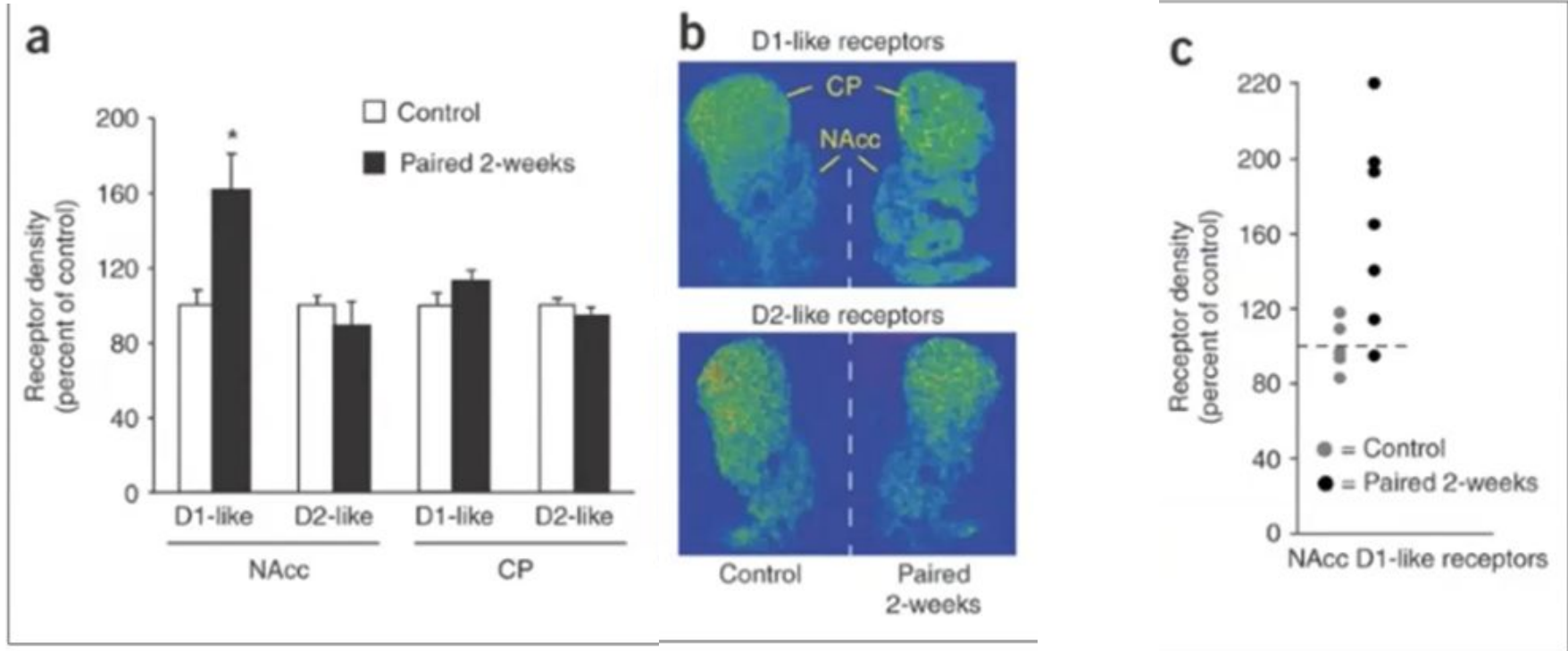
- Voles receiving both quinpirole and a D1-like antagonist showed partner preference
- The activation of D1-like receptors not only did not induce a partner preference, but also prevented the partner-preference formation induced by D2-like activation.

# Opposing roles for D1- and D2-like receptors



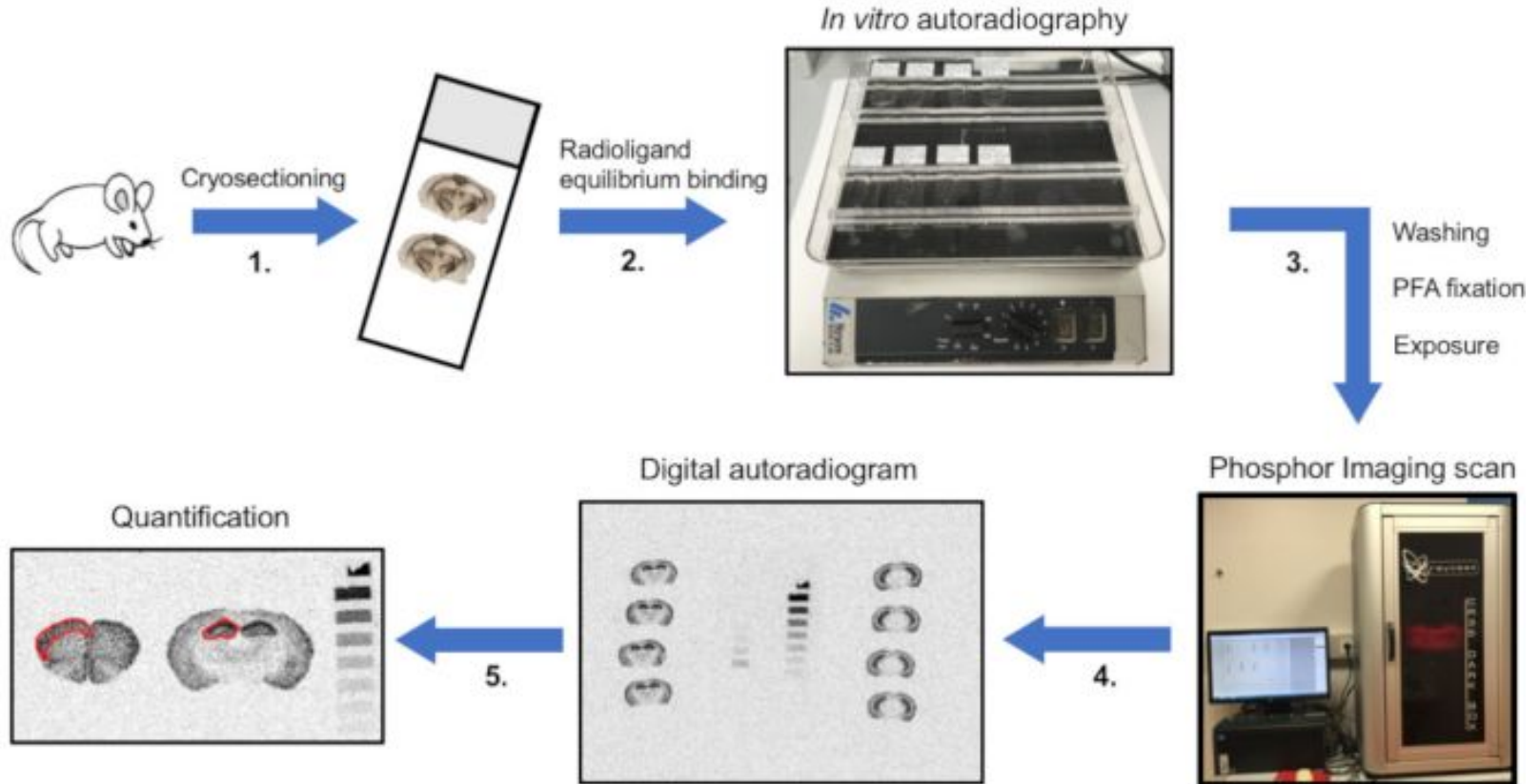
- Vehicle-injected males that mated developed partner preferences, but when injected with a D1 agonist did not exhibit partner preference.

# D1-like receptors are upregulated in well established pair bonded mates (NAcc)



How do we measure dopamine activity?

# Autoradiography



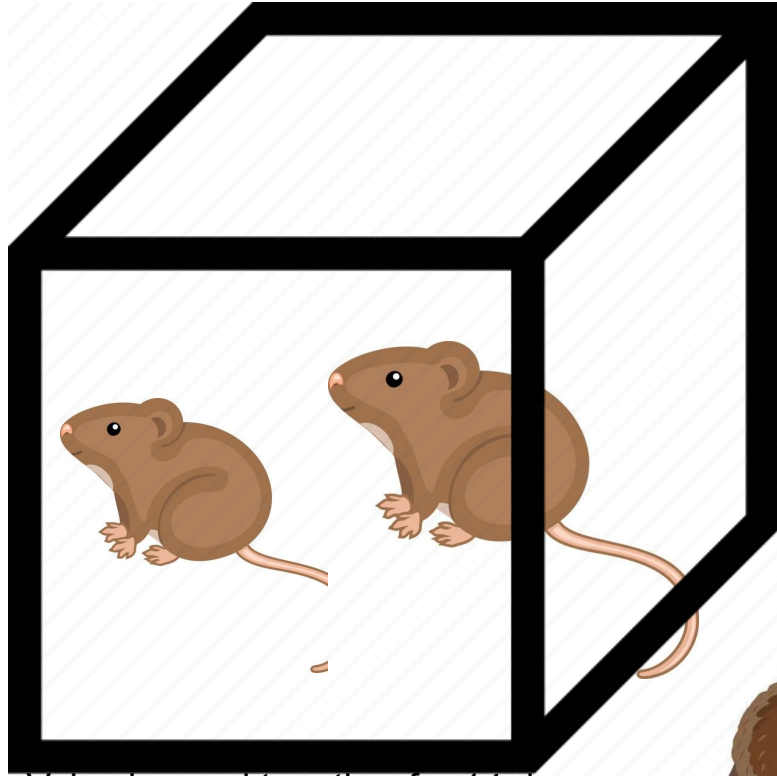


How do we measure aggressive behavior/affiliative behavior?

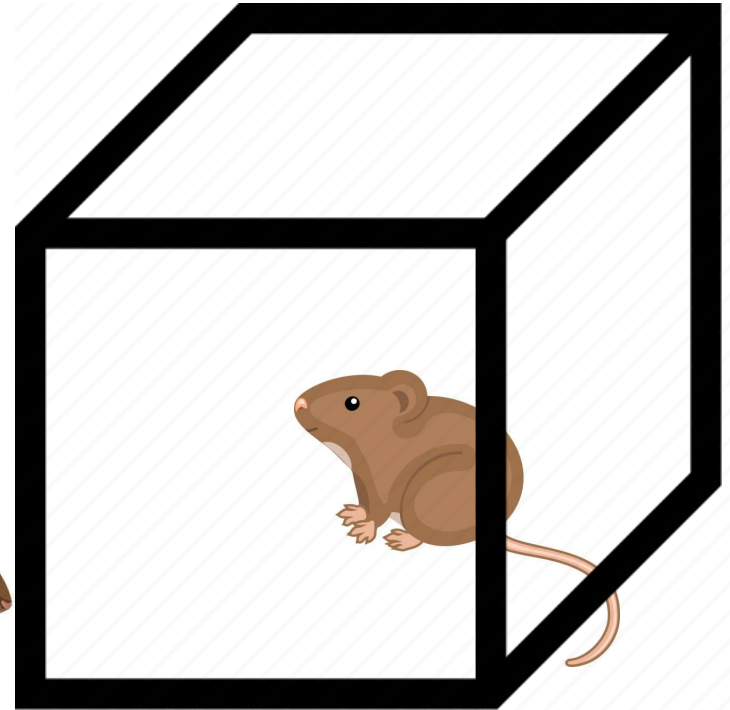
- Behavioral methodology

# Resident Intruder Test

10 Minute resident intruder task  
with 4 minutes of habituation



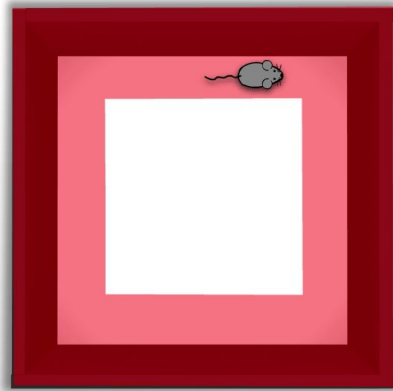
Voles housed together for 14 days



# Open field test



## Maze Basics: **Open Field**

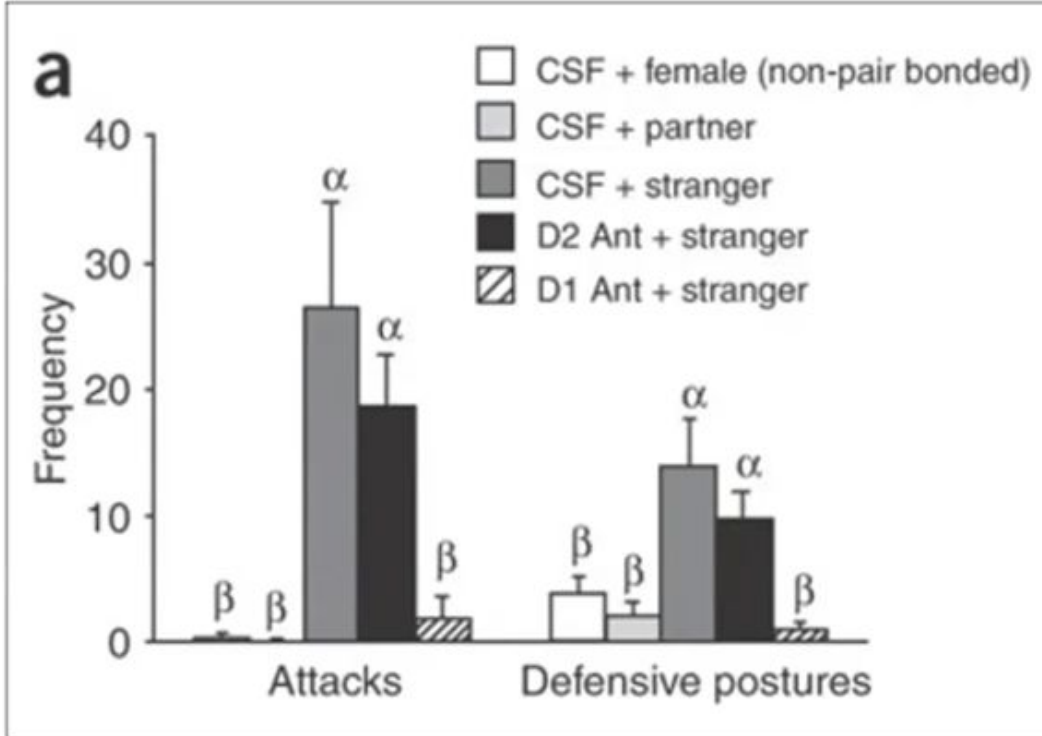


**Outer Edge**

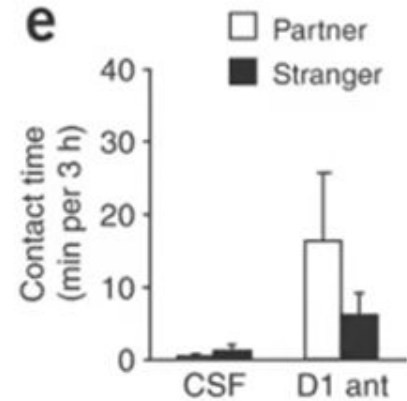
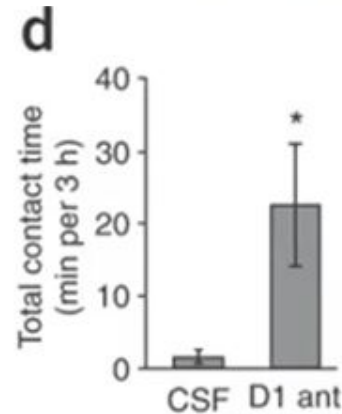
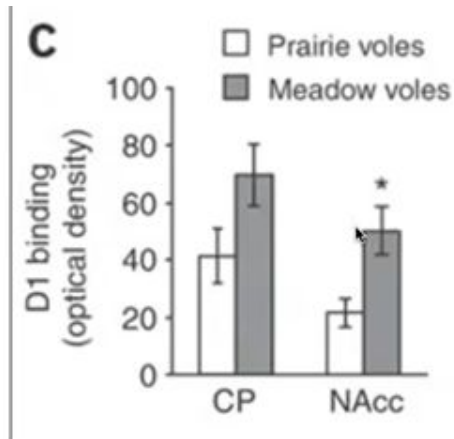
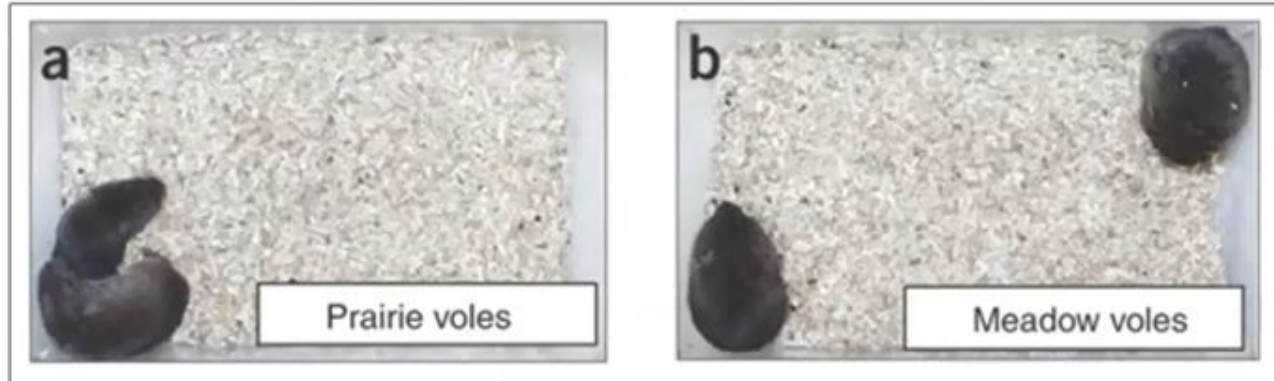


**Center**

# Upregulation of D1 receptors is critical for pair bond maintenance



# Species Differences in D1 receptor binding is consistent with species differences in social behavior



# Conclusions and Discussion

- The rostral shell is the specific subregion of NAcc where dopaminergic processing facilitates partner preference
- D2-like receptor activation is sufficient to support pair bond formation
- D1-like receptor activation is sufficient to support pair bond maintenance
- D1-like receptor binding can explain species differences in social behavior
  
- Viral gene transfer of vasopressin receptors to meadow voles showed social behavior typical of prairie voles (Lim et. al, 2004)
  - Implication: more support for the idea that D2-like receptors crucial for pair bond formation
- What do you think this means for drug addiction? Or taking it more abstractly, what do you think this paper says about the concept of love?