

Why did I eat that? Obesity and the neuroscience of food craving

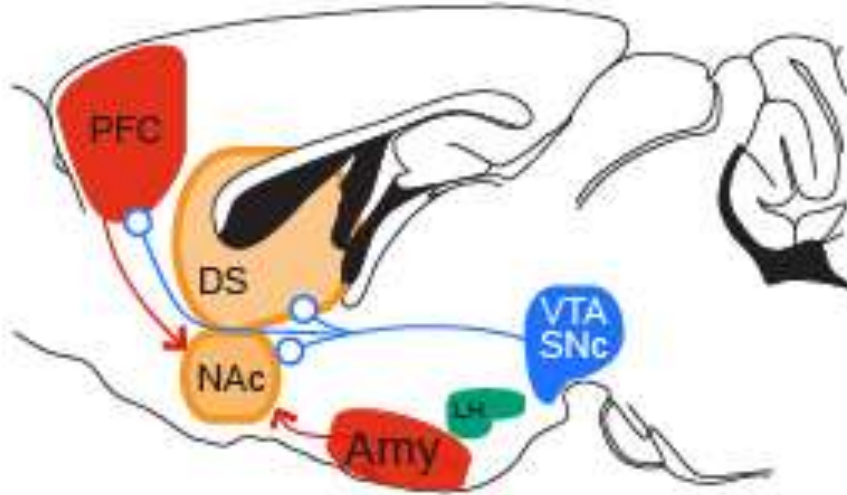
Carrie R. Ferrario, PhD

Oct 13, 2020

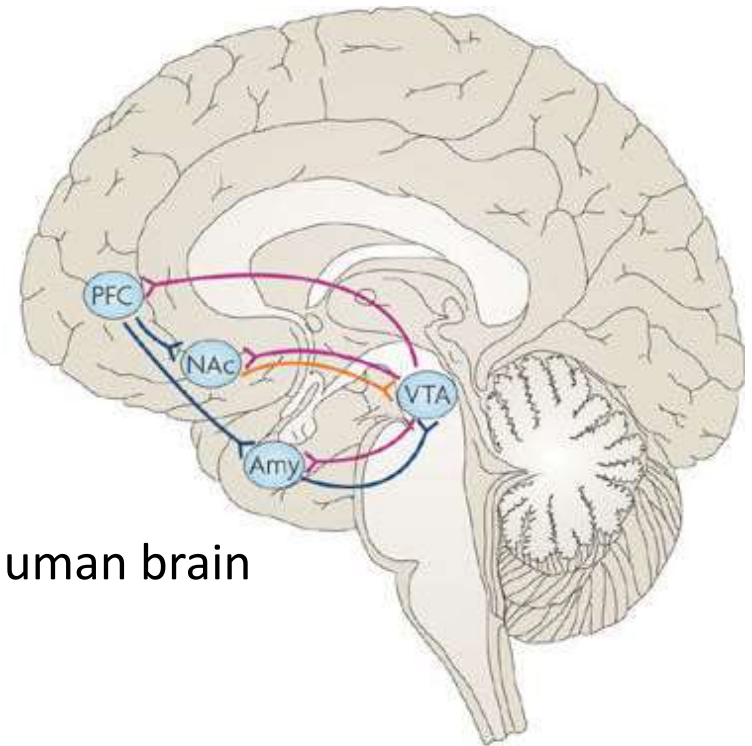
BBRF Meet the Scientist Webinar Series



Brain Systems Mediating Cue-Triggered Motivation



Rat brain



Human brain

Glutamate = excites
Dopamine = modulates

Nature Reviews | Neuroscience

Outline:

Cue-triggered motivation is stronger in obesity susceptible rats *before* obesity.

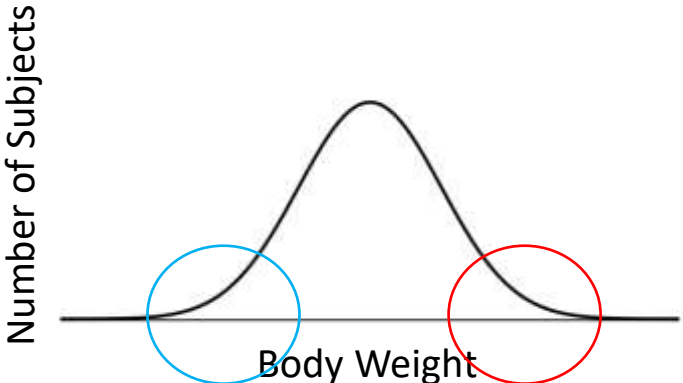
- Food-seeking
- Approach

Effects of sugary,
fatty “junk-foods”

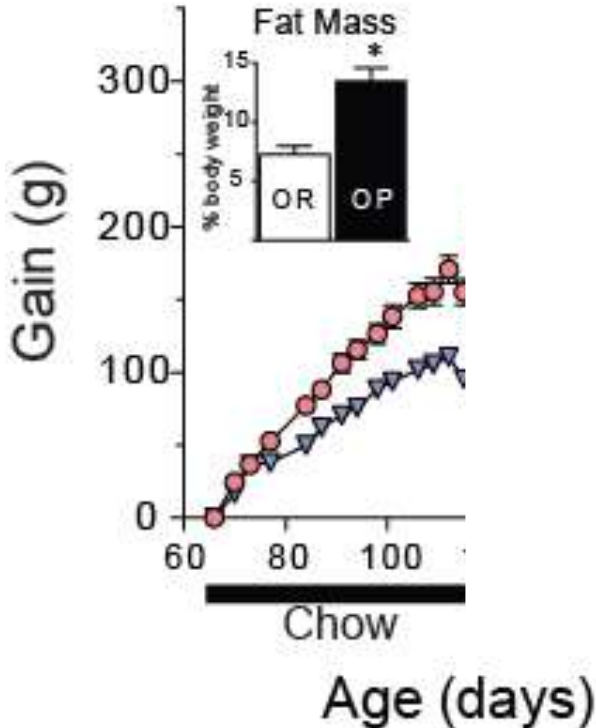


Rodent models:

Selectively bred rat model

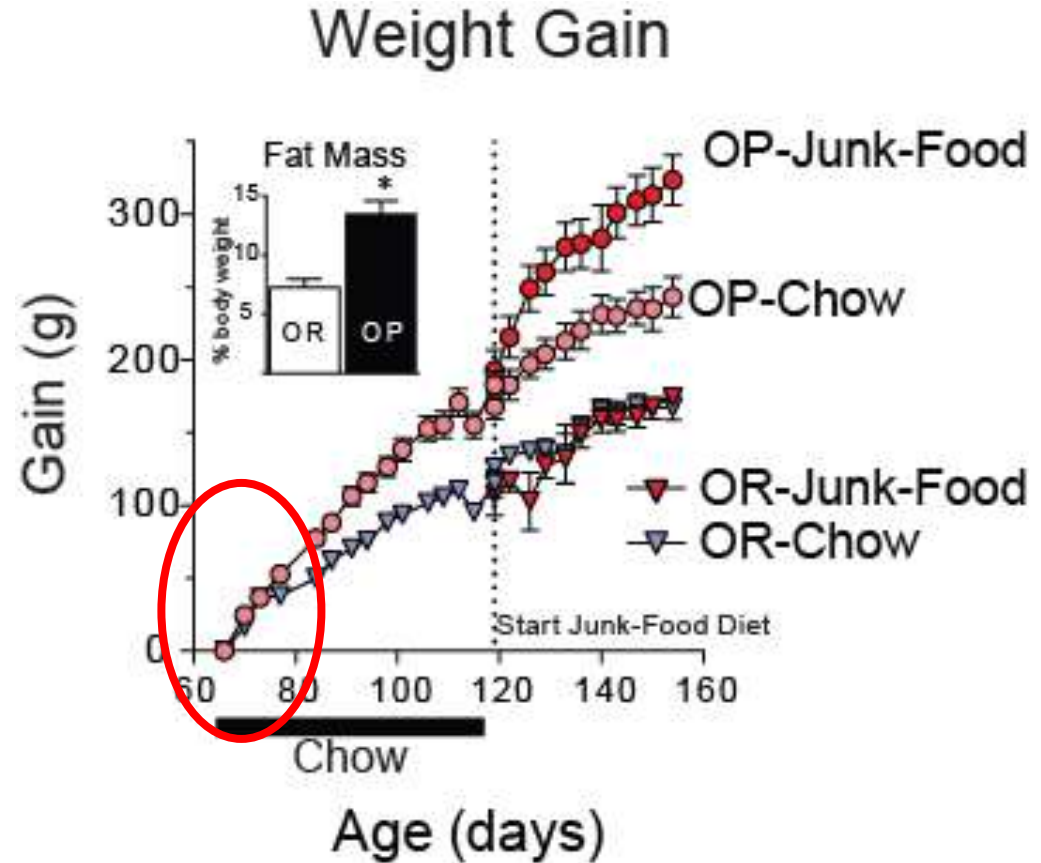
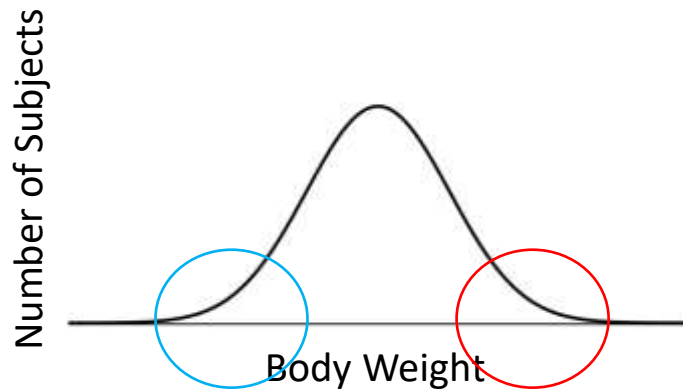


Weight Gain



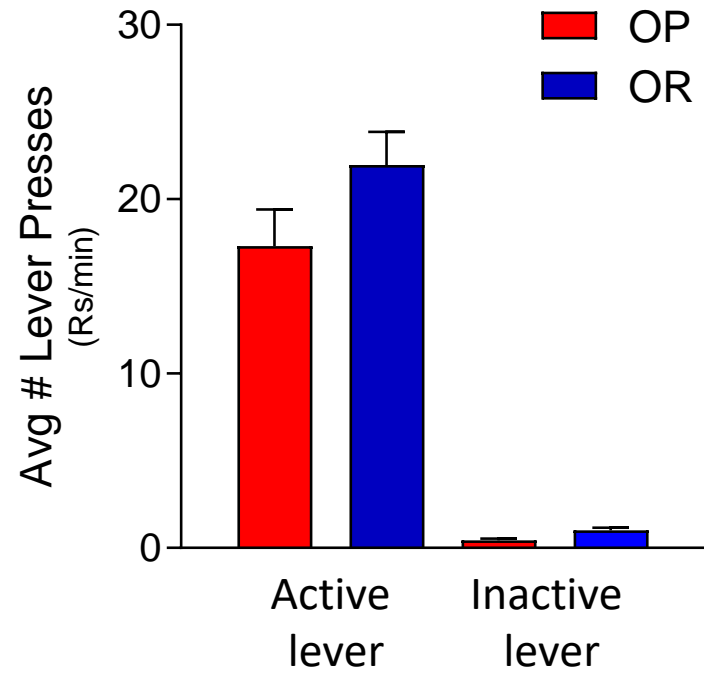
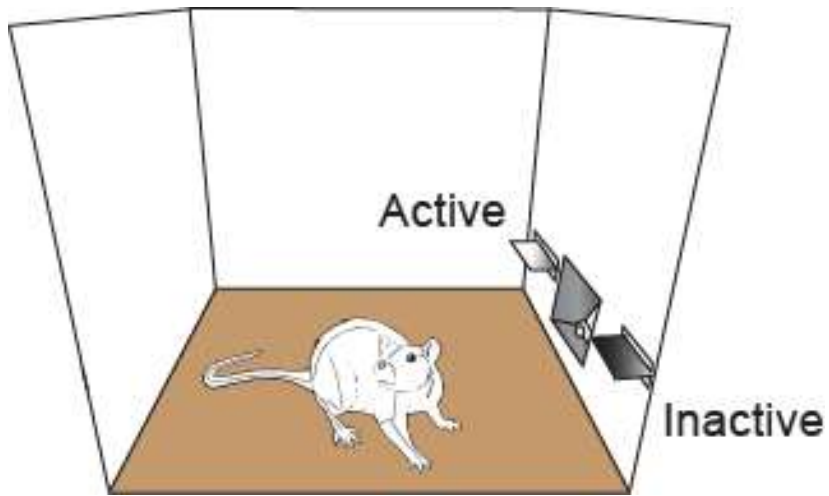
Rodent models:

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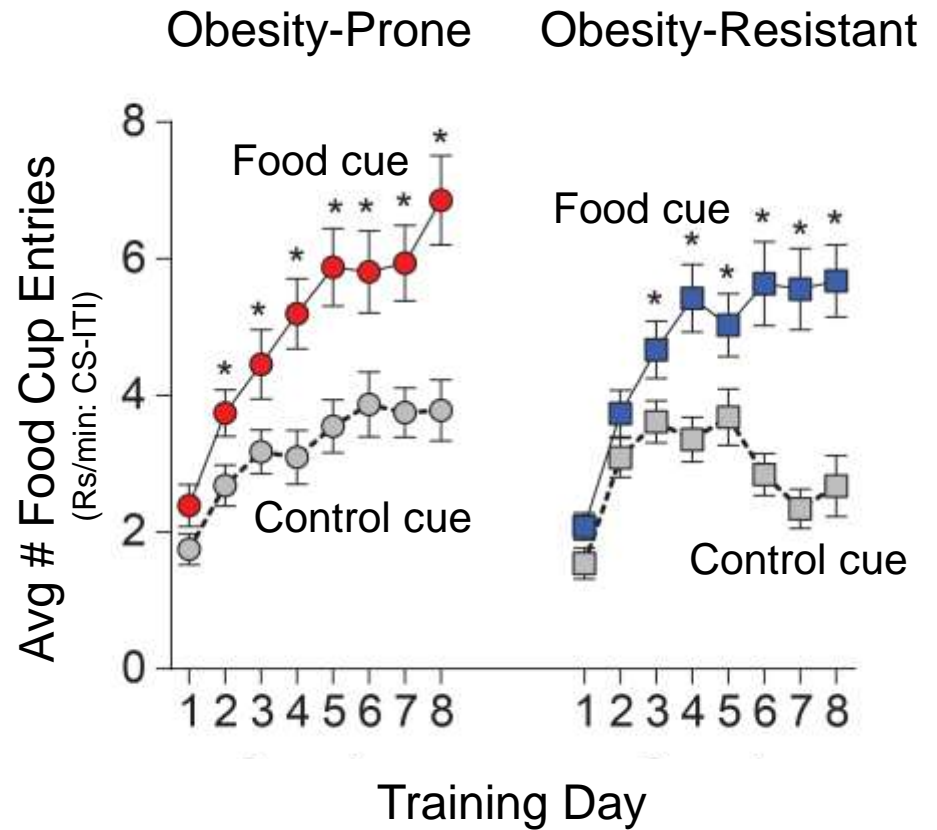
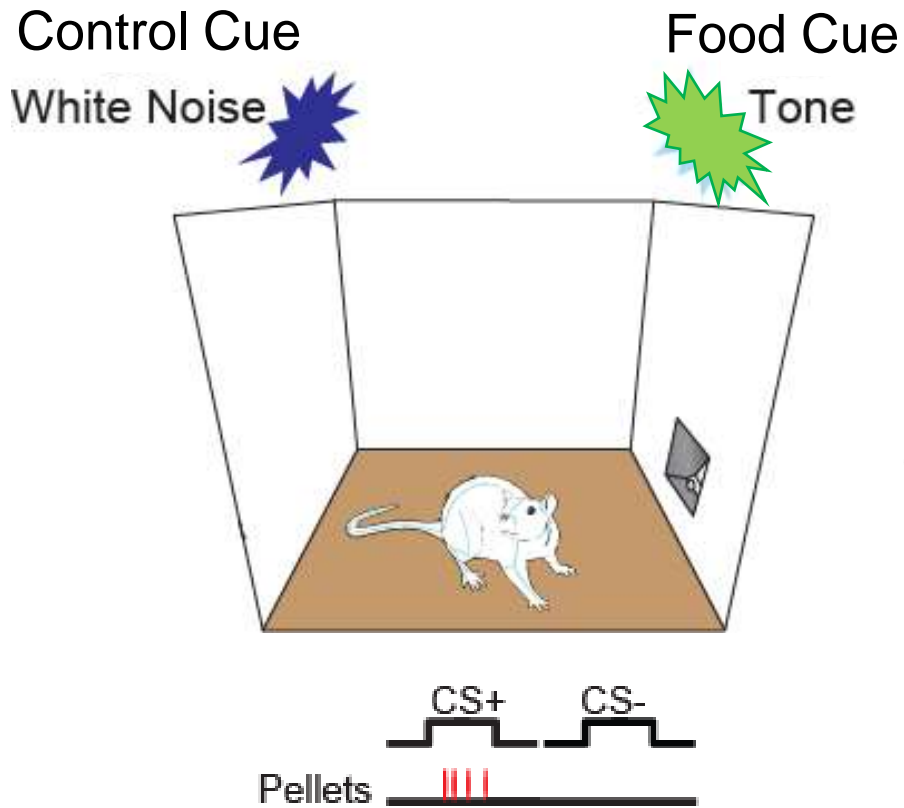


Is cue-triggered food-seeking enhanced in obesity-prone rats?

Lever Press for Food (Food-Seeking)



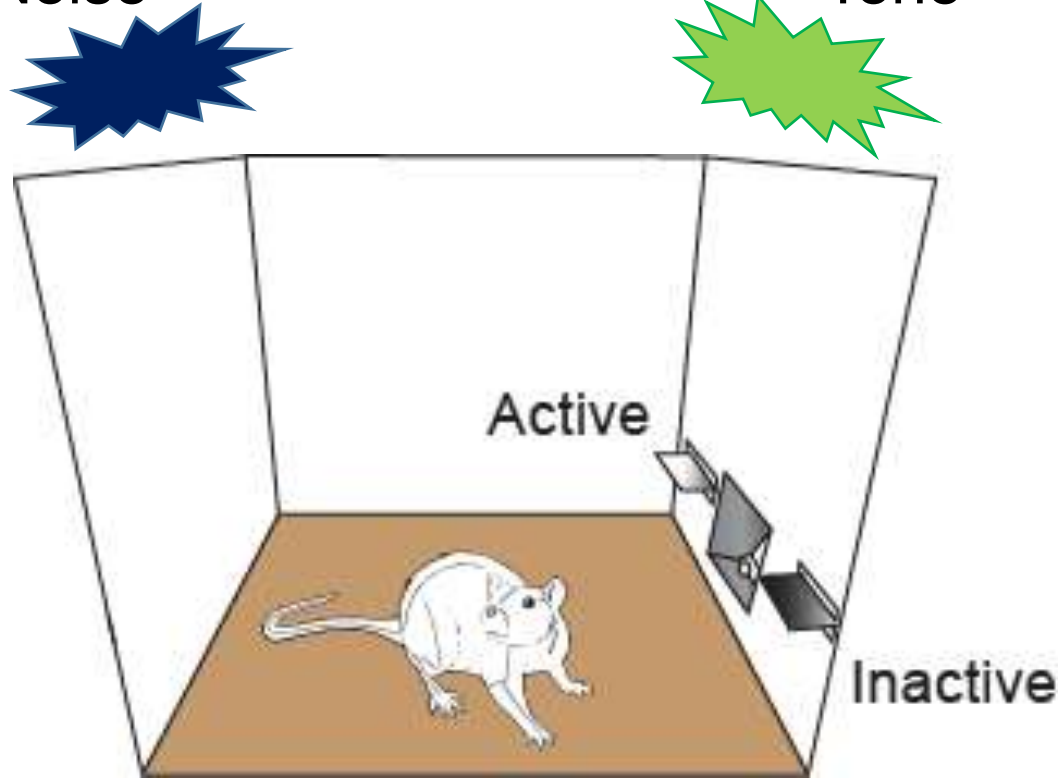
Learn Food/Cue Relationship



Test: Does the food cue enhance food-seeking?

Control Cue
White Noise

Food Cue
Tone



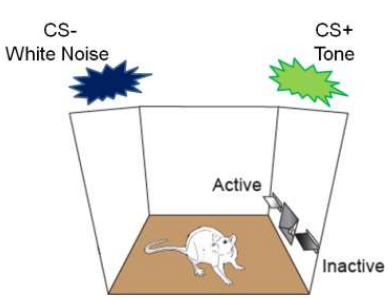
No Food Given

CS- (Control Cue)

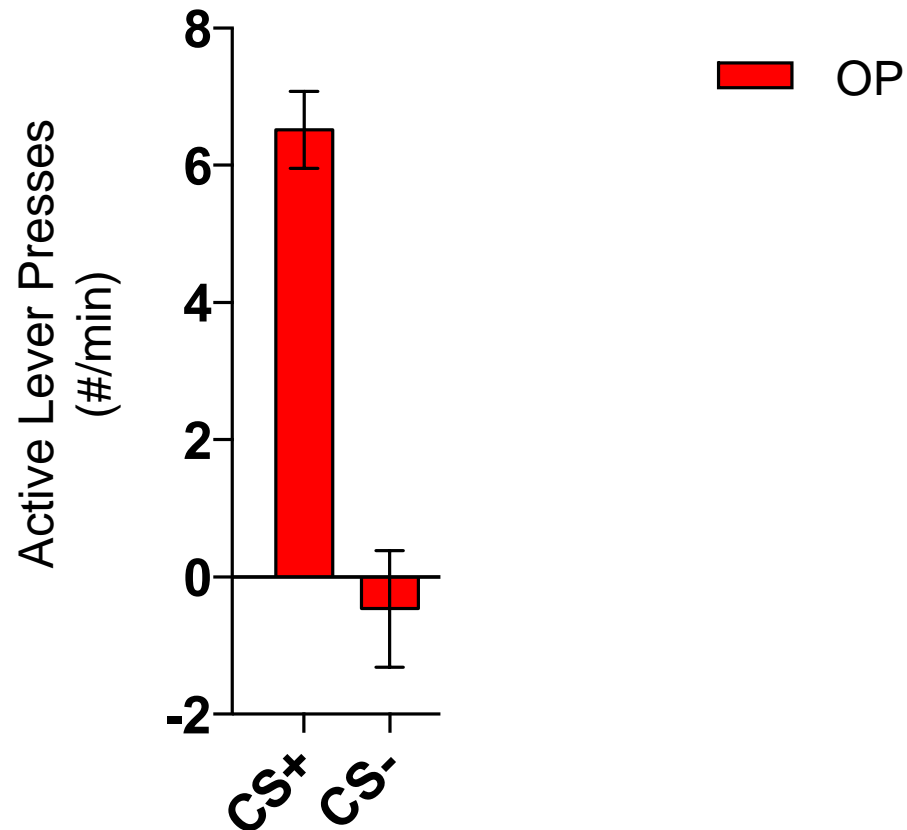


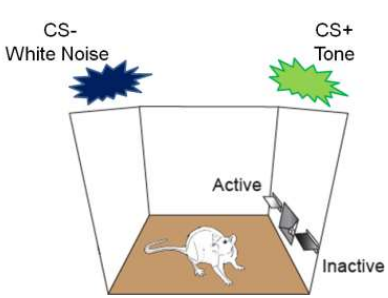
CS+ (Food Cue)



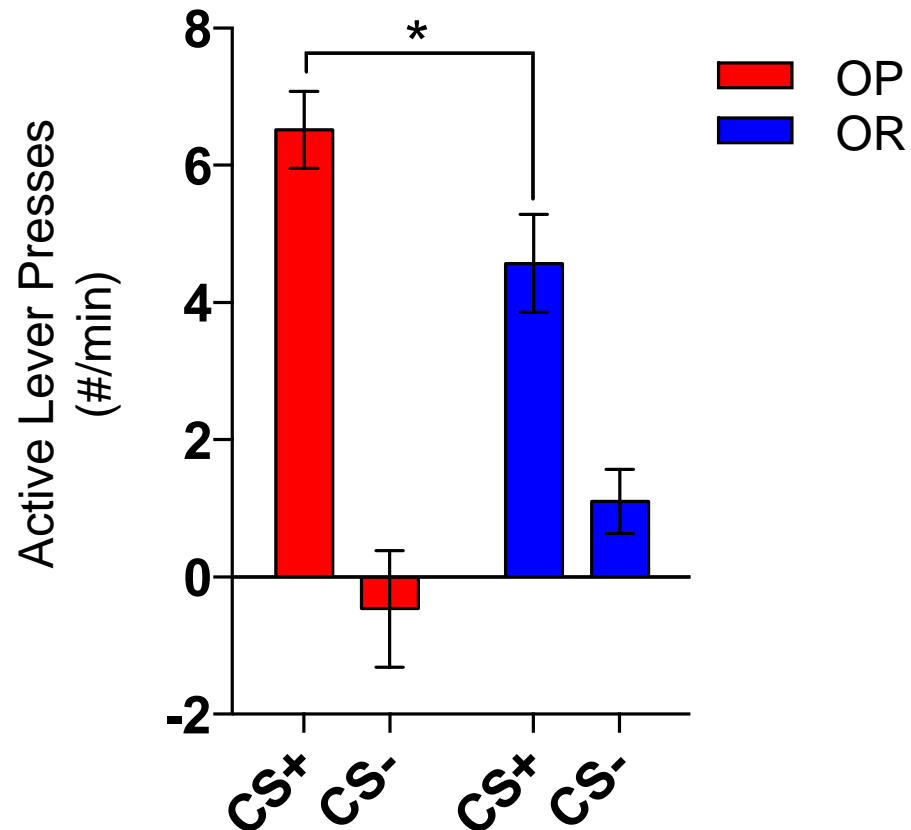


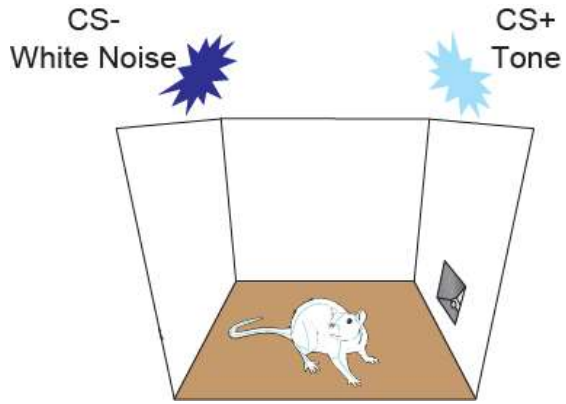
Greater cue-triggered food-seeking in obesity-prone rats



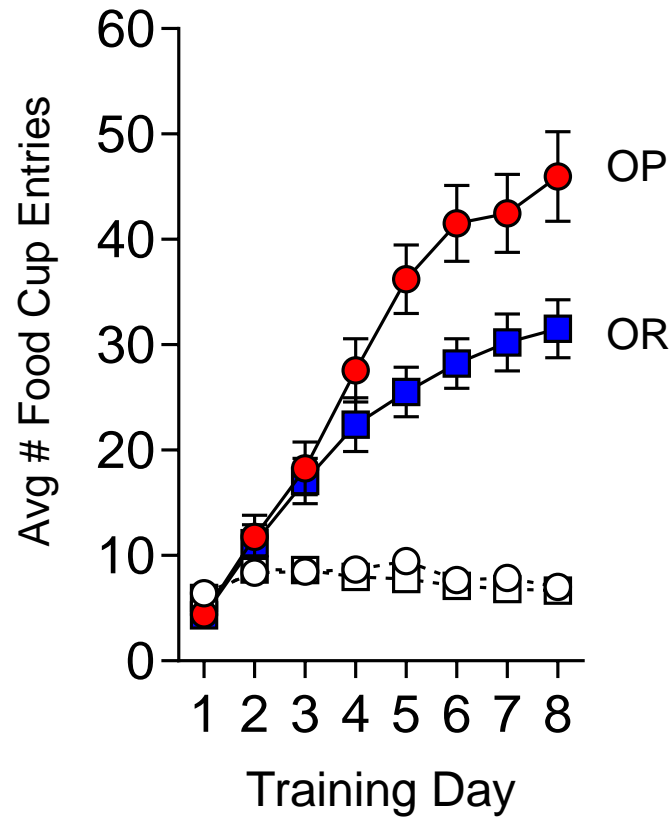


Greater cue-triggered food-seeking in obesity-prone rats



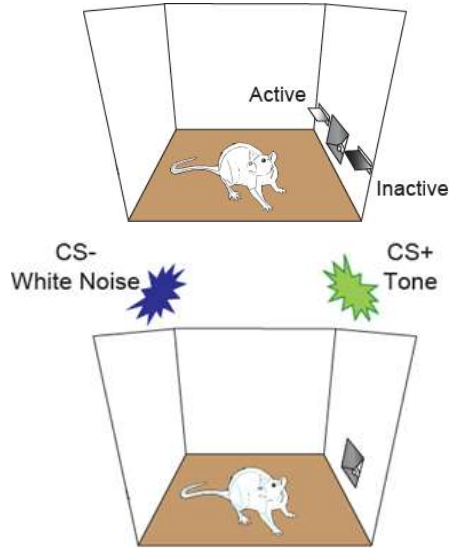


Cue-triggered Approach

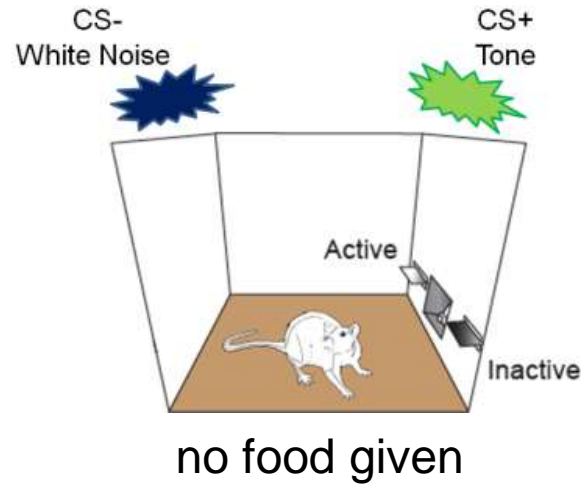


Standard Rats:

Training



Cue-triggered food-seeking

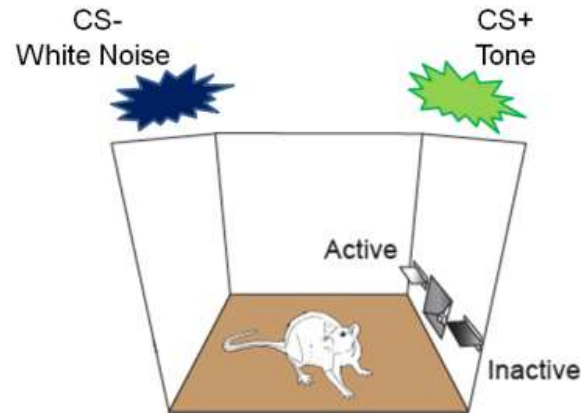


Junk-Food

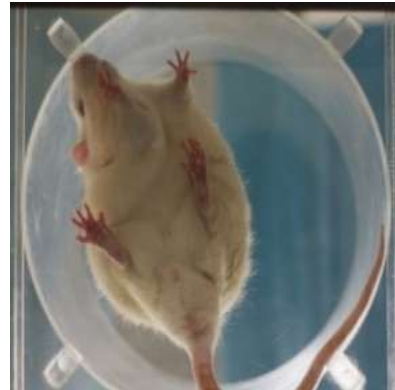
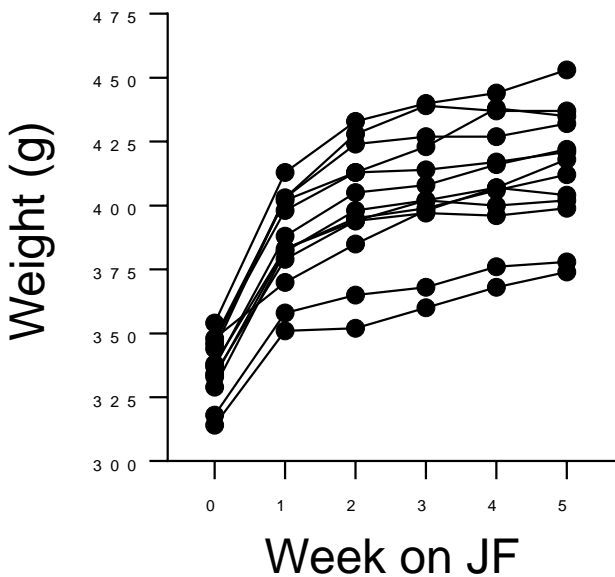
	Purina Lab Chow	Junk-Food Mash
Fat	4.5%	19.6%
Protein	23%	14%
Carbs	48.7%	58%
Calories	4 kcal/g	4.5 kcal/g

Standard Rats:

Cue-triggered food-seeking



Junk-Food

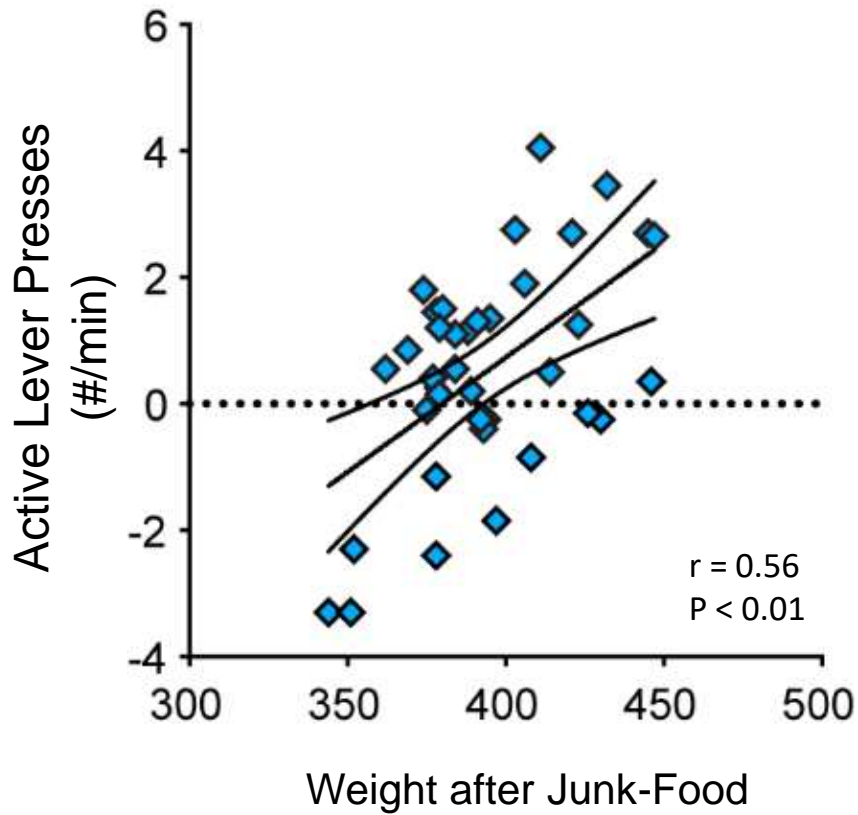


Gainer

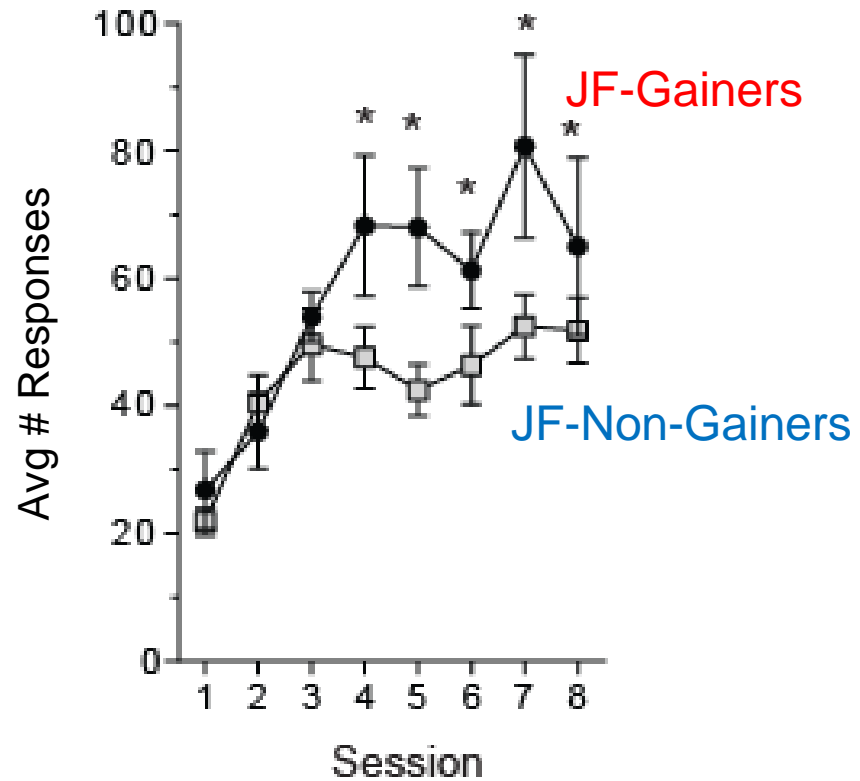


Non-Gainer

Cue-triggered Food-Seeking



Cue-triggered Approach

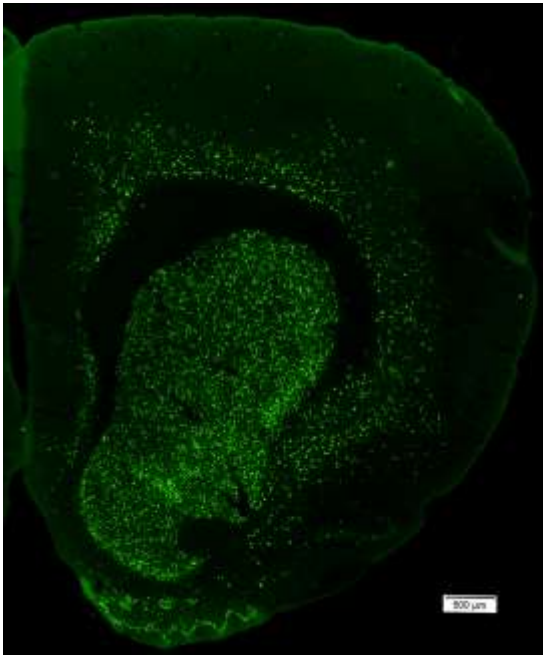


Take-homes 1:

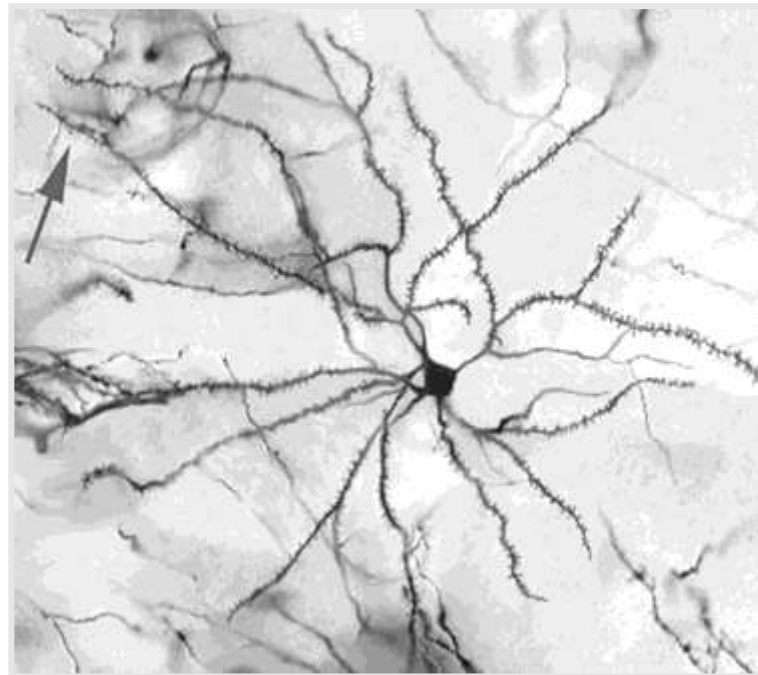
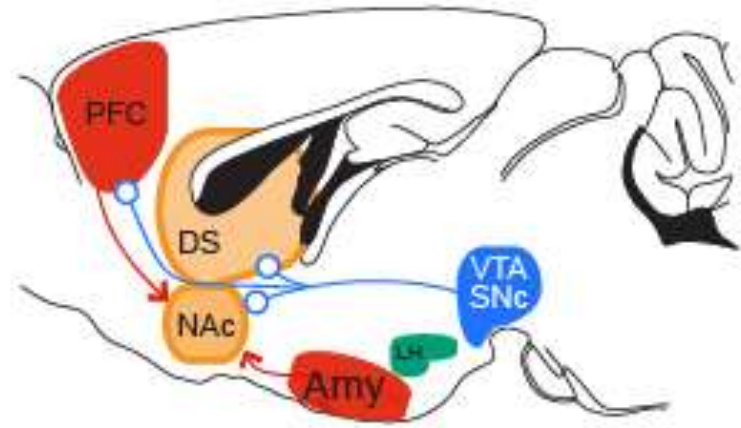
1) Vulnerability factor in humans

2) Provides a useful tool



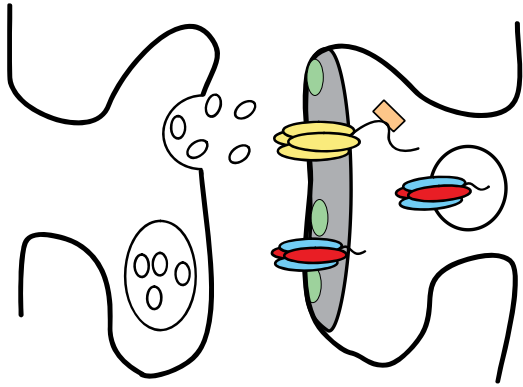


Green=DRD1-CRE+ cells, rat



MSN image by Grazyna Gorney, Kolb lab

Glutamate Synapse



“Typical” AMPA Receptors

Majority of AMPARs

Allow Na^+ into cell (excitation)

“A-typical” CP-AMPA Receptors

Very few in adult brain (~10%)

Selectively blocked by NASPM

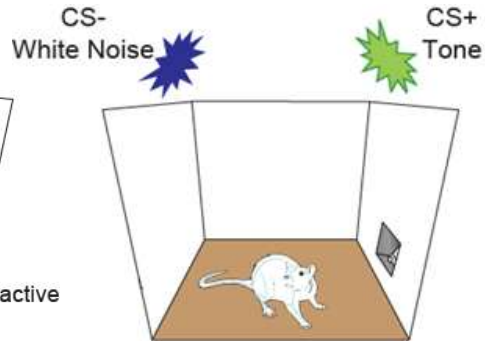
Allow Ca^{2+} into cell (stronger excitation)

Do CP-AMPA Receptors mediate cue-triggered food-seeking?

Training

Lever Press
for Food

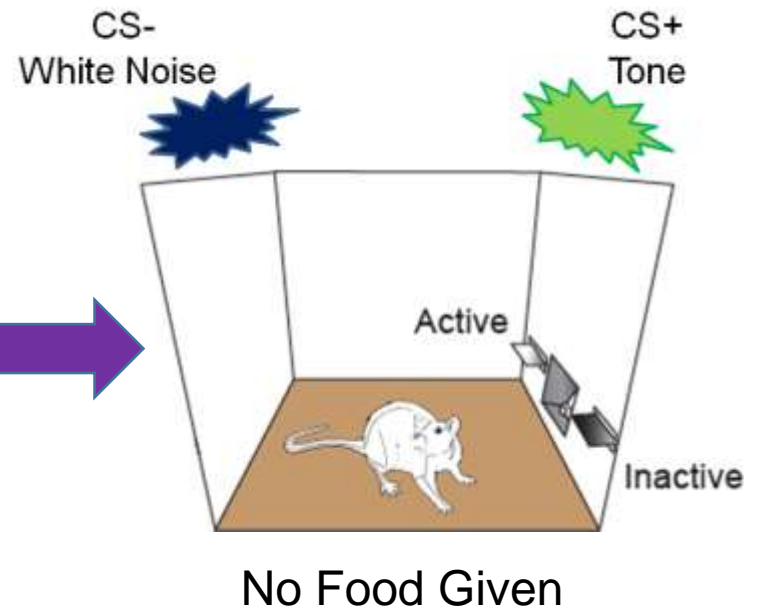
Food Cue
Training

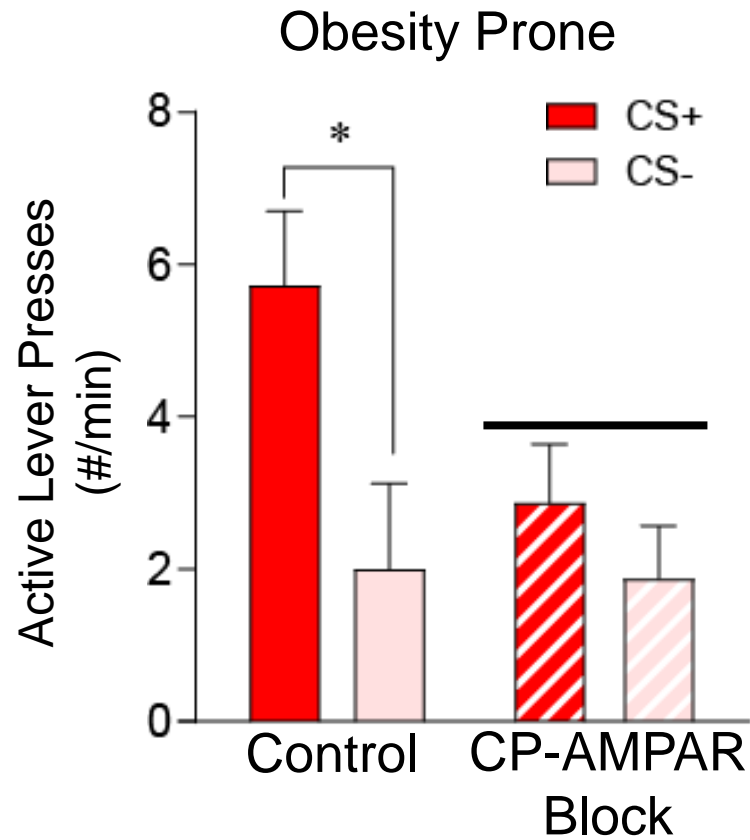


CP-AMPA Blockade During Test

Intra NAc infusion of:

- Control
- NASPM (blocks CP-AMPA)





Activity of CP-AMPARs is needed for cue-triggered food-seeking.

Does eating junk-foods enhance AMPARs?

Do effects differ in obesity-prone & obesity-resistant rats?

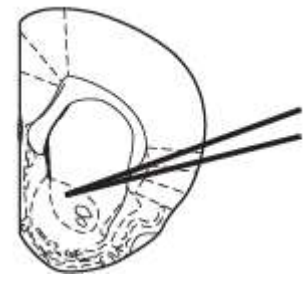


Standard Rats:

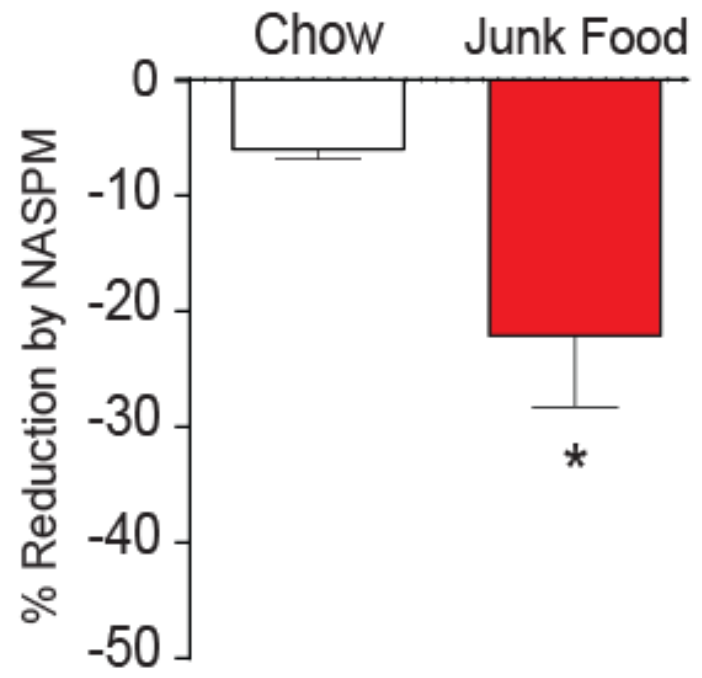
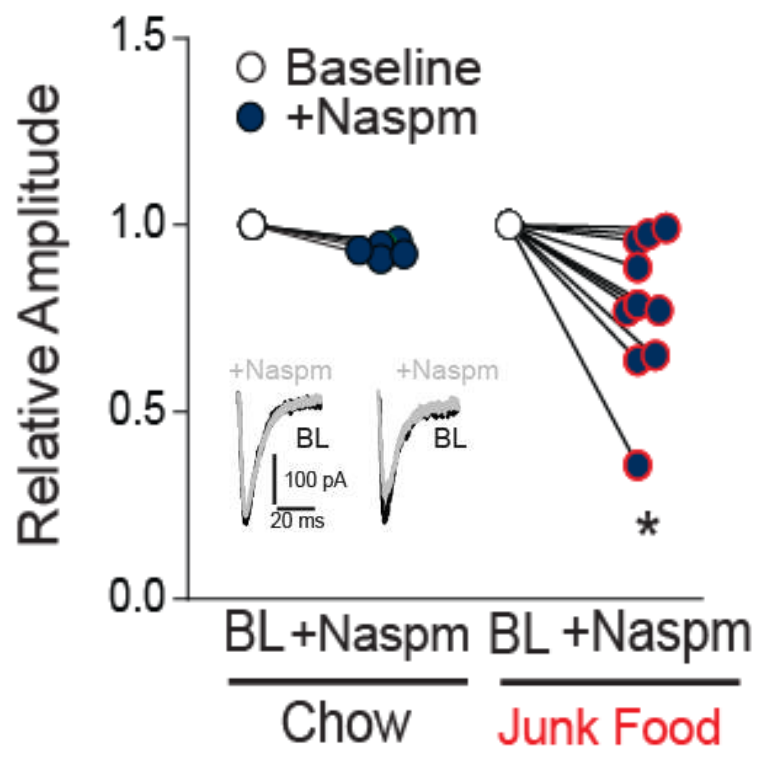


3 months

Chow (3 weeks)
JF-Deprivation



Junk-food increases CP-AMPA function



Selectively bred obesity-prone and obesity-resistant rats



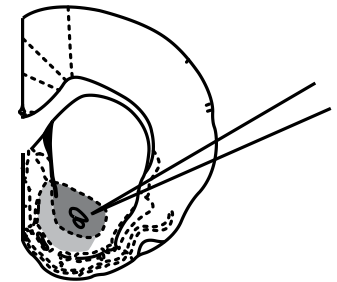
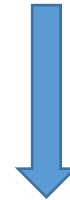
10 days



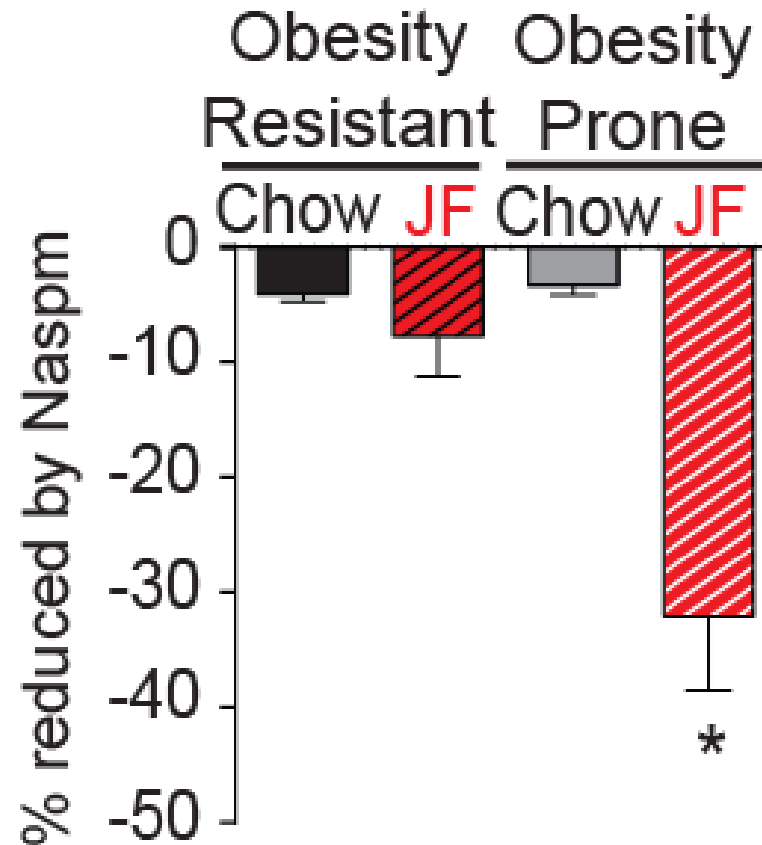
Chow

Chow (2 weeks)

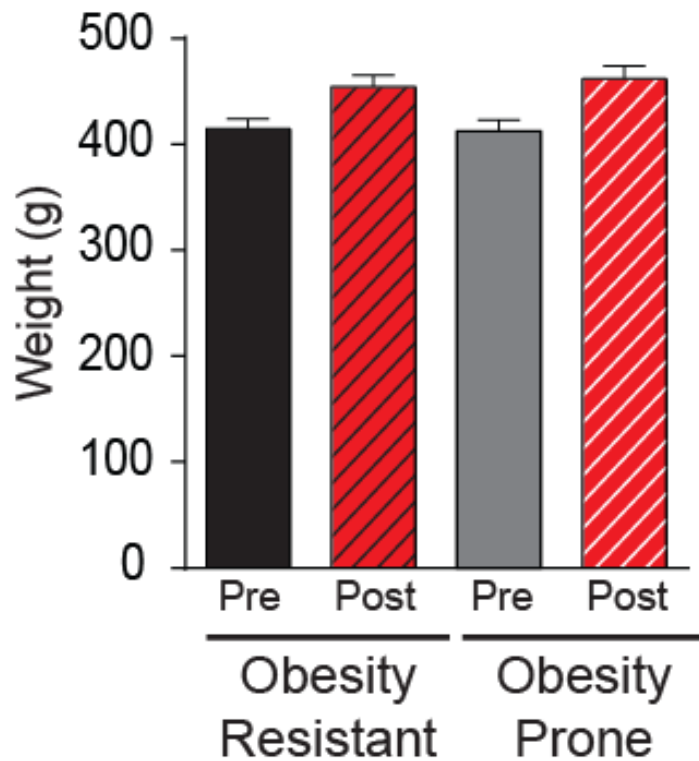
JF-Deprivation



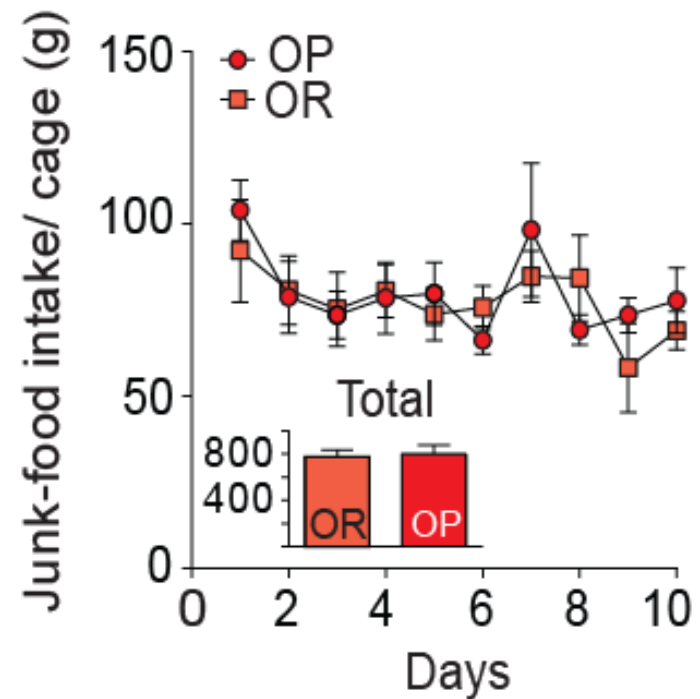
Junk-food increases CP-AMAPRs in obesity-prone but not obesity-resistant rats



Weight gain is similar between groups



Amount of Junk-food eaten is similar between groups

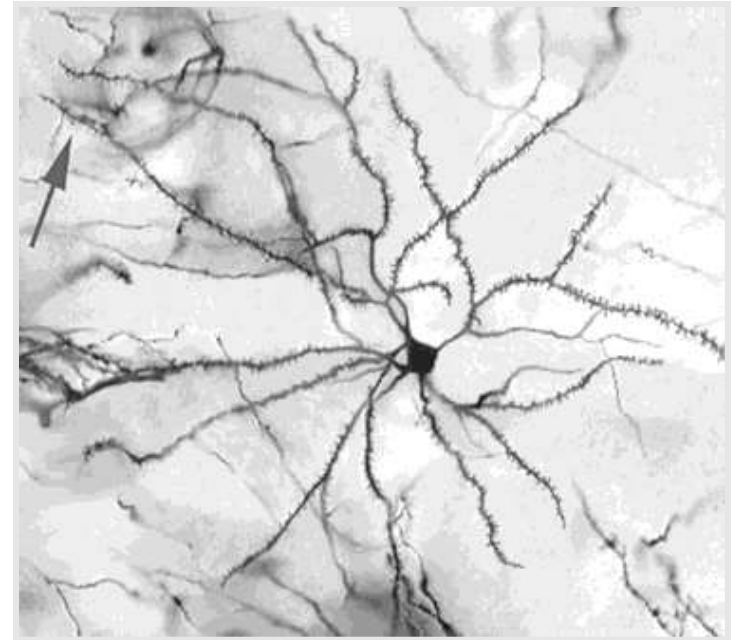
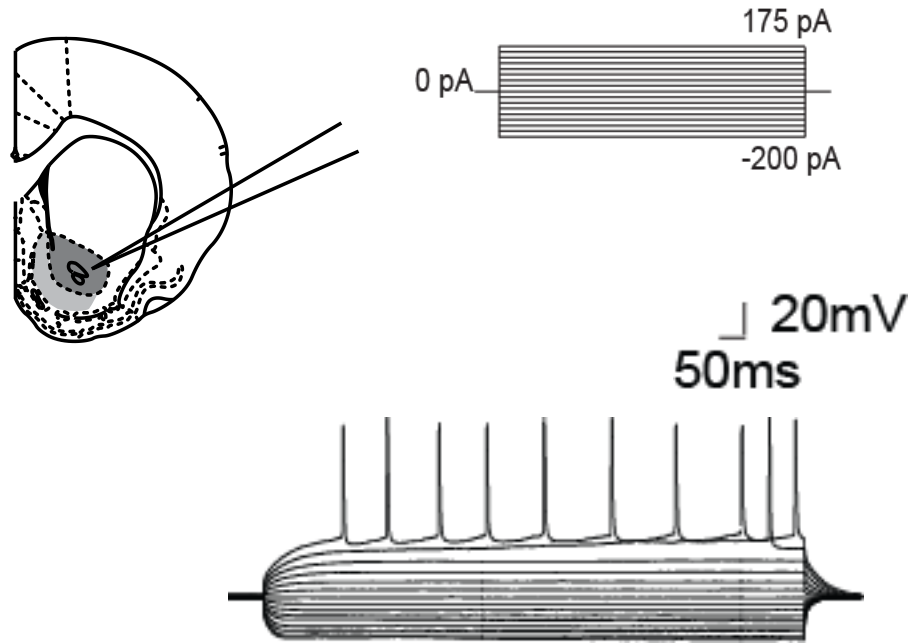


Take-homes 2:

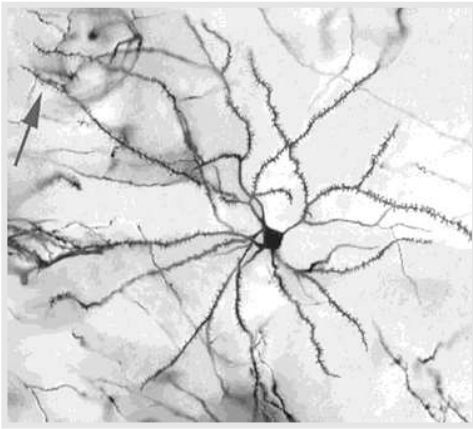
- 1) Changes in brain function occur in response to eating junk-food
- 2) Obesity-prone more sensitive to these effects

Why different behavioral sensitivity & neural changes?

Inherent enhancements in Medium Spiny Neuron function

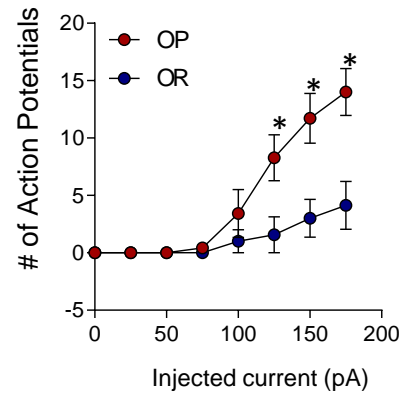


MSN image by Grazyna Gorney



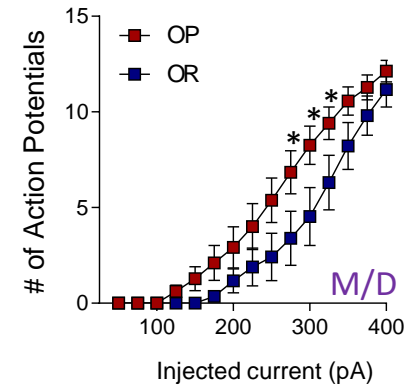
Males

MSNs fire more easily

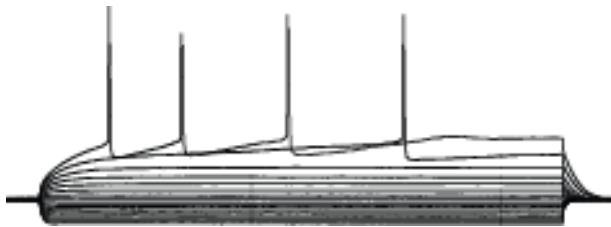


Females

MSNs fire more easily

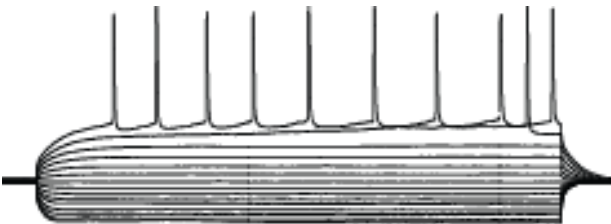


Obesity-Resistant

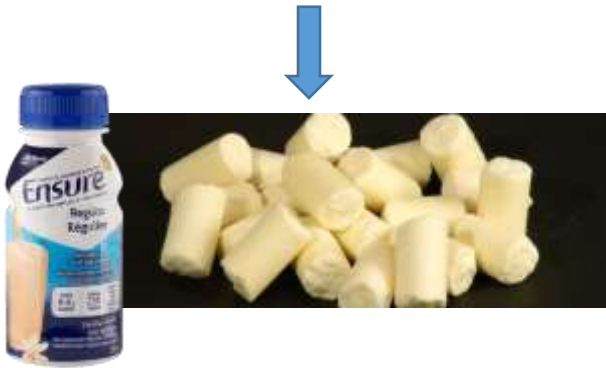


Obesity-Prone

20mV
50ms



Outbred SD Rats



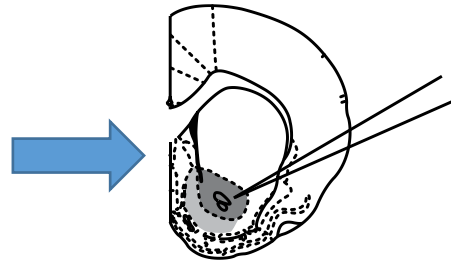
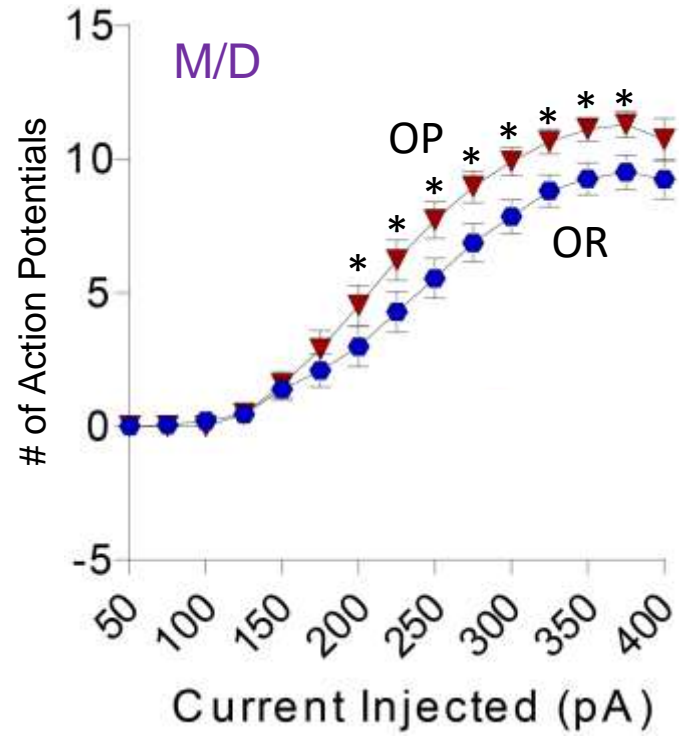
OR



OP

Female F1
OR

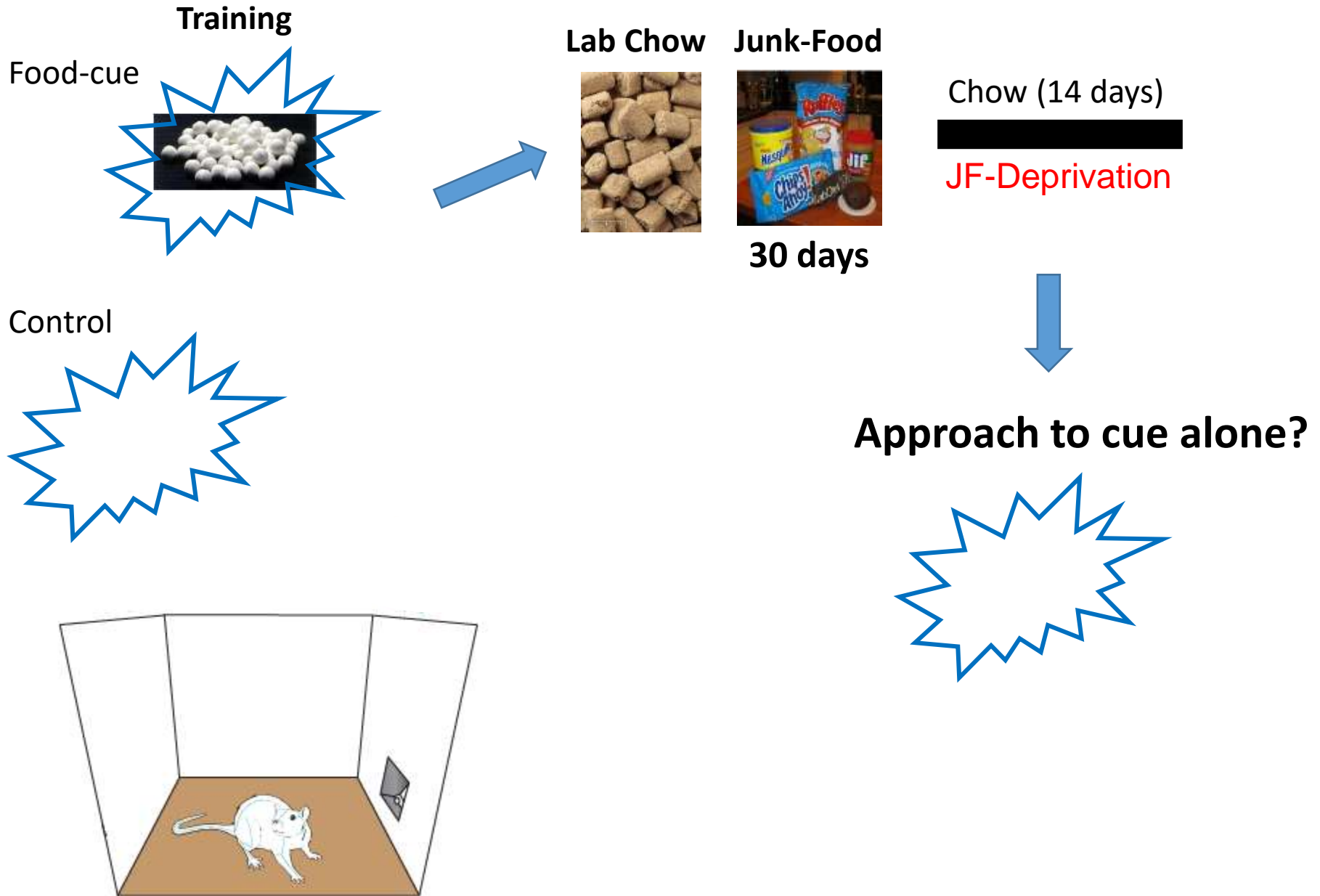
Female F1
OP

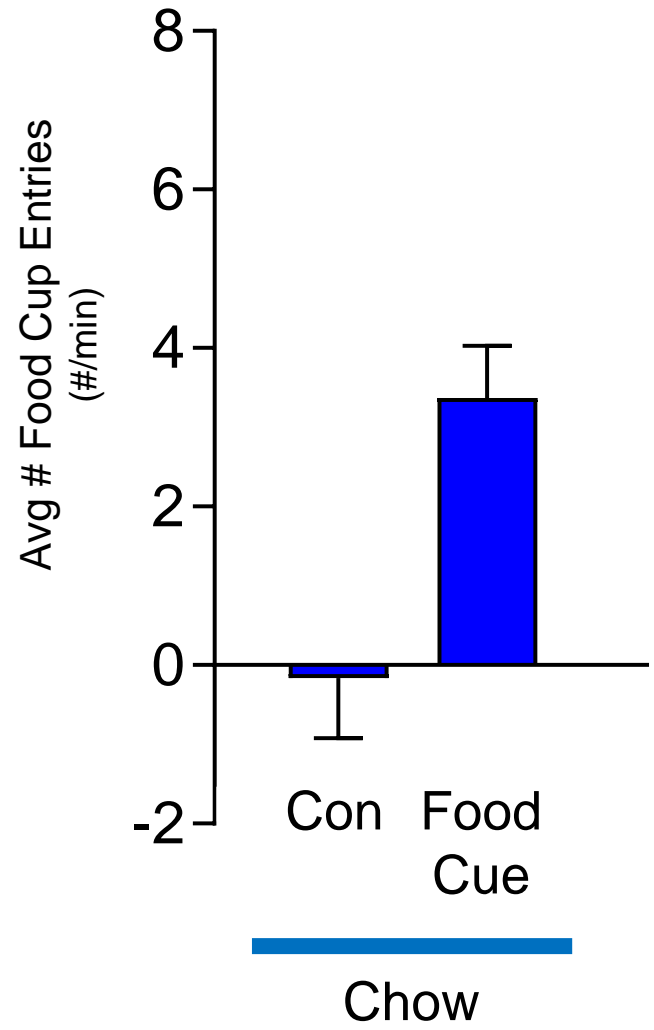


Why different behavioral sensitivity & neural changes?

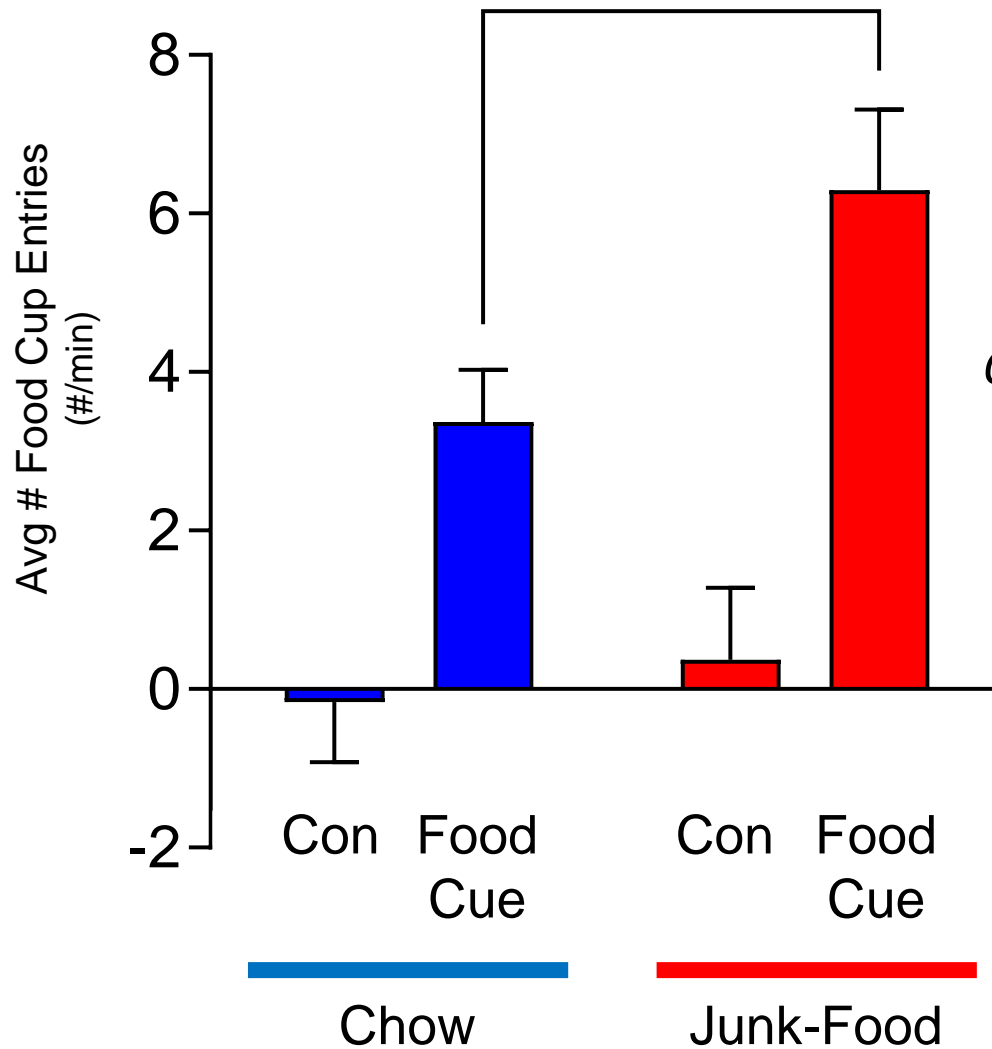
Fire more easily, easier to induce changes in cell function.

Does junk-food enhance cue-triggered motivation?

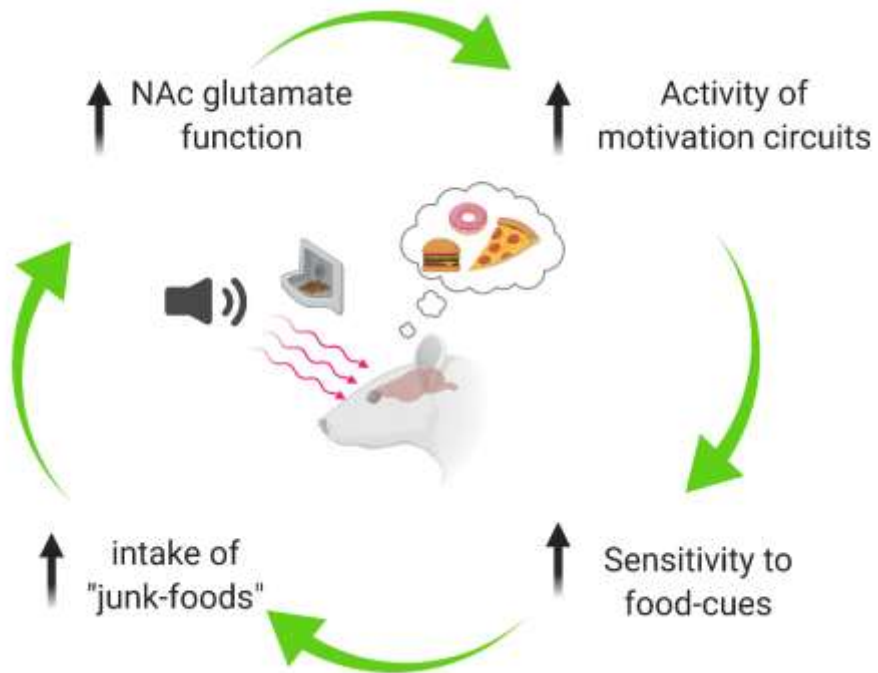


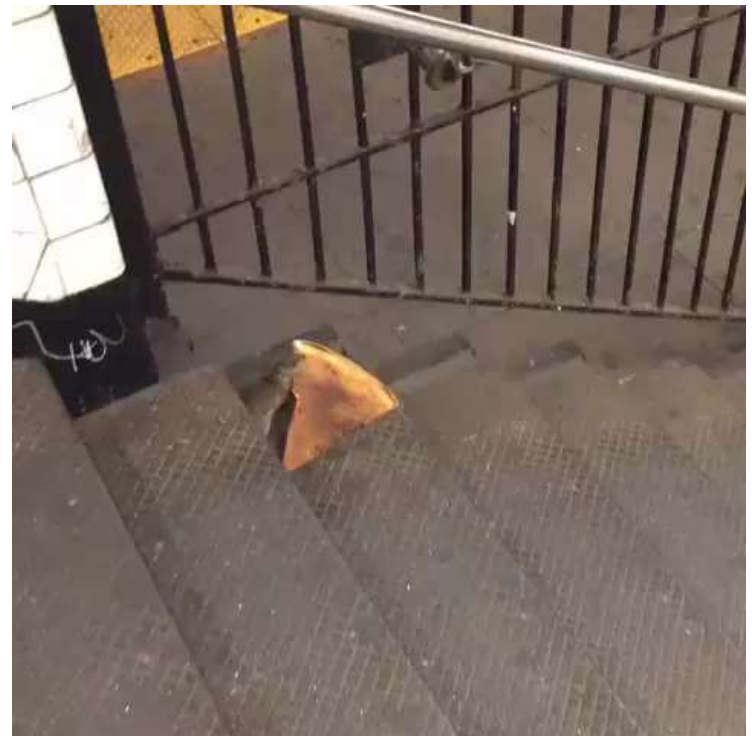
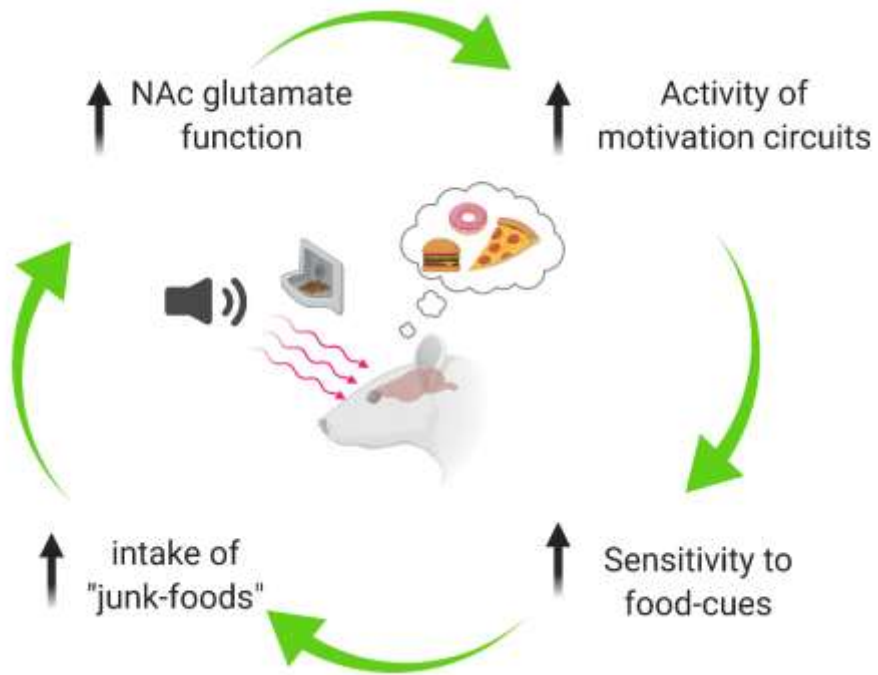


Junk-food enhances cue-triggered approach



*Outstanding Questions:
Effects greater in OP vs OR?
How long lasting?
Mechanisms?*





Current Lab Members:

Tracy Fetterly, PhD[#]

Julie Finnell, PhD

Megan Wickens, PhD

Amanda France

Jacob Ormes

Allison Nieto

Anish Saraswat

Sophia Dunlap

Rachel Springsdorf^{\$}

Ongoing Collaborations:

Travis Brown (U WY)

Monica Dus (UM)

Terry Robinson (UM)

Past Lab Members:

Yanaira Alonso-Caraballo, PhD[@]

Rebecca Derman, PhD⁺

Peter Vollbrecht, PhD[#]

Max Oginsky, PhD^{#,*}

Emma Bergman

Cameron Nobile



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*F32DK112627A, #T32DA007268,\$T32DA007281

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DA044204; R21-DA045277; Brain & Behavior Foundation

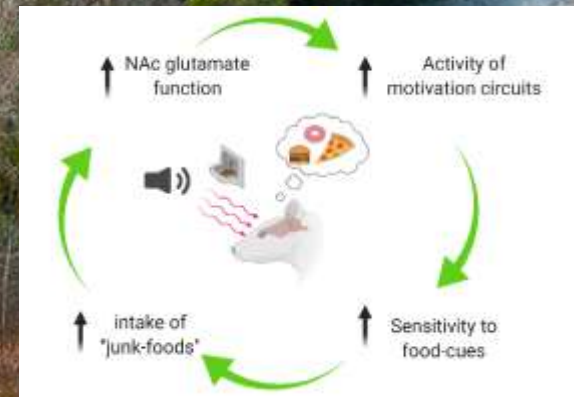
Take-homes:

1) Junk-food changes in brain function *before* obesity

2) Obesity-prone more sensitive to junk-food & cues

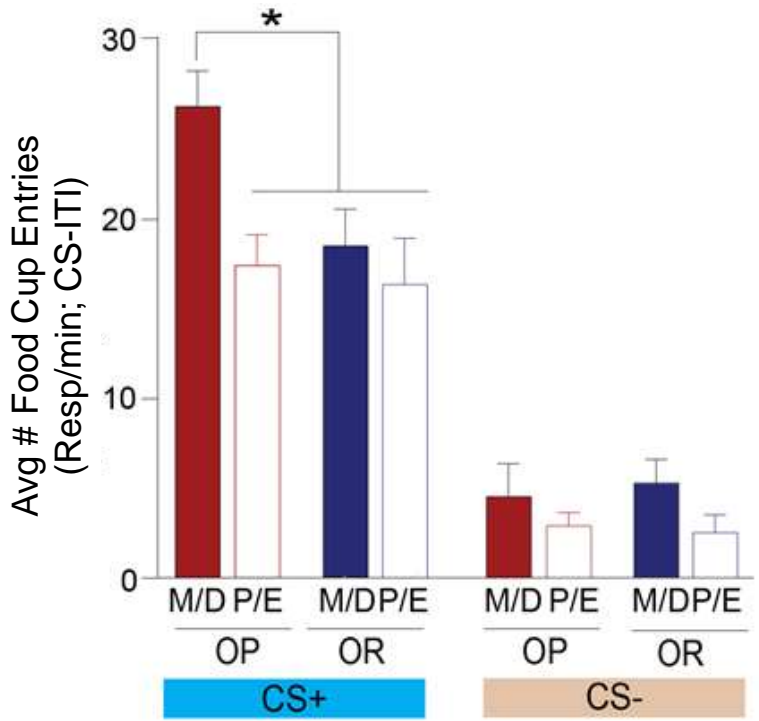
3) Vulnerability factor

4) Rodent models are useful tools

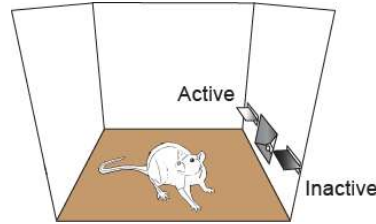
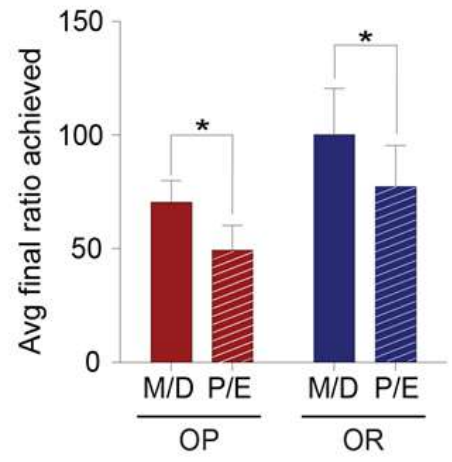


Cue-triggered motivation is greater in obesity-prone females & varies with the cycle in obesity-prone, but not obesity-resistant rats.

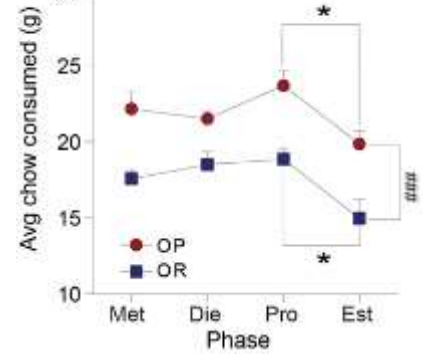
Cue-triggered Approach



Work for Food



Food Intake



MD= Metestrus/Diestrus
PE= Proestrus/Estrus