



SICOM & AOCO 2024

SOMS International Conference on Obesity & Metabolism
in conjunction with Asia-Oceania Conference on Obesity

Science
JOURNALS AAAS

2024, Science

(Published)

GLP-1 Increases Cognitive Satiety via Hypothalamic Circuits in Mice and Humans

Joon Seok Park, M.D.

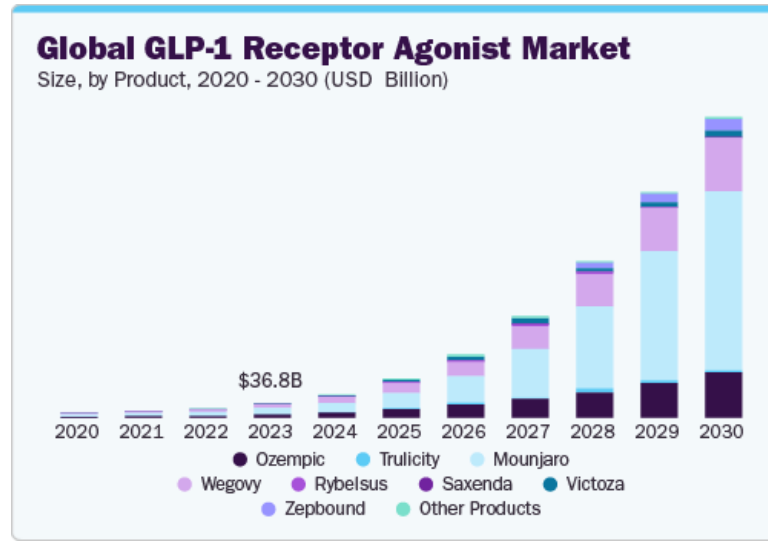
Seoul National University



Hosted by **SOMS** Society for Korean Obesity and Metabolism Studies

Co-Hosted by  Asia Oceania Association for the Study of Obesity

Obesity and GLP-1R agonists (GLP-1RA)



Novo Nordisk to launch Wegovy in South Korea mid-October

By Marian (YoonJee) Chu Oct. 7, 2024

Danish pharma giant Novo Nordisk A/S is set to launch its blockbuster glucagon-like peptide-1 therapy, Wegovy (semaglutide), in South Korea's growing obesity therapeutics market next week, a company official confirmed to *BioWorld*.



Netflix's "Culinary Class Wars" tops non-English global rankings, set for dramatic finale

Final episode of Culinary Class Wars to air on Oct. 8, revealing the ultimate winner

By Kim Yu-rim, Lee Jung-soo

Published 2024.10.07. 16:42





X 100 →



안 먹어도 될 거 같아요

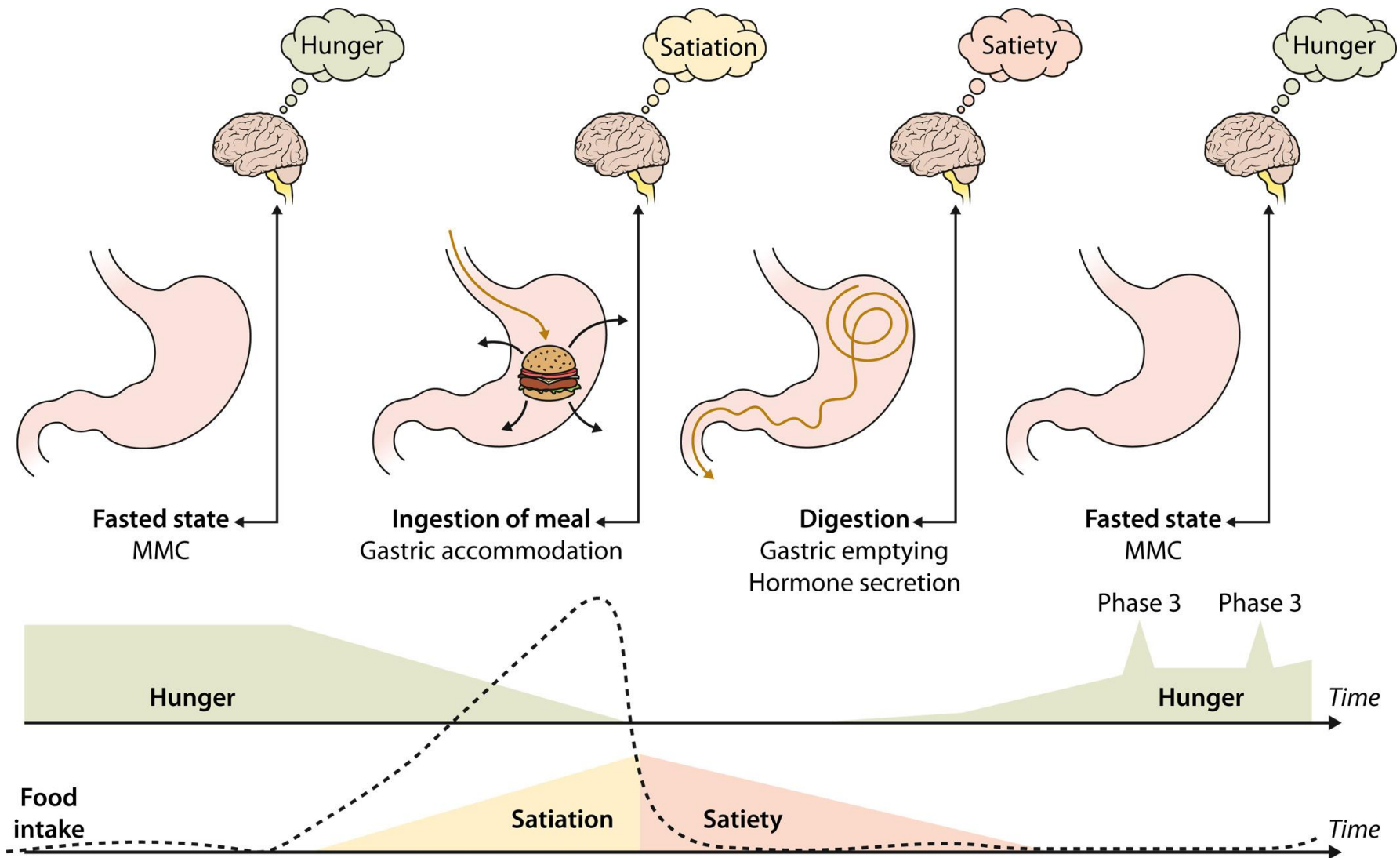
I don't think I need to eat

**이븐하지 않으면 벨는
이븐핑 안성재**

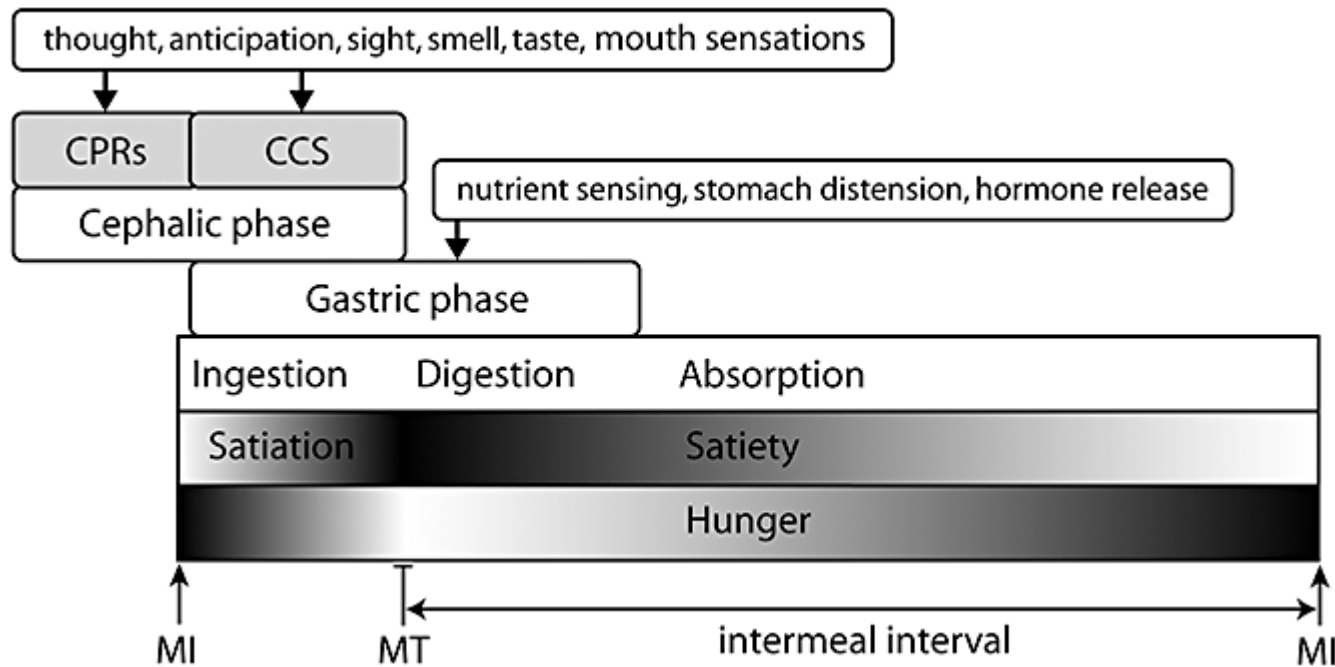


웁 (Spitting it out)

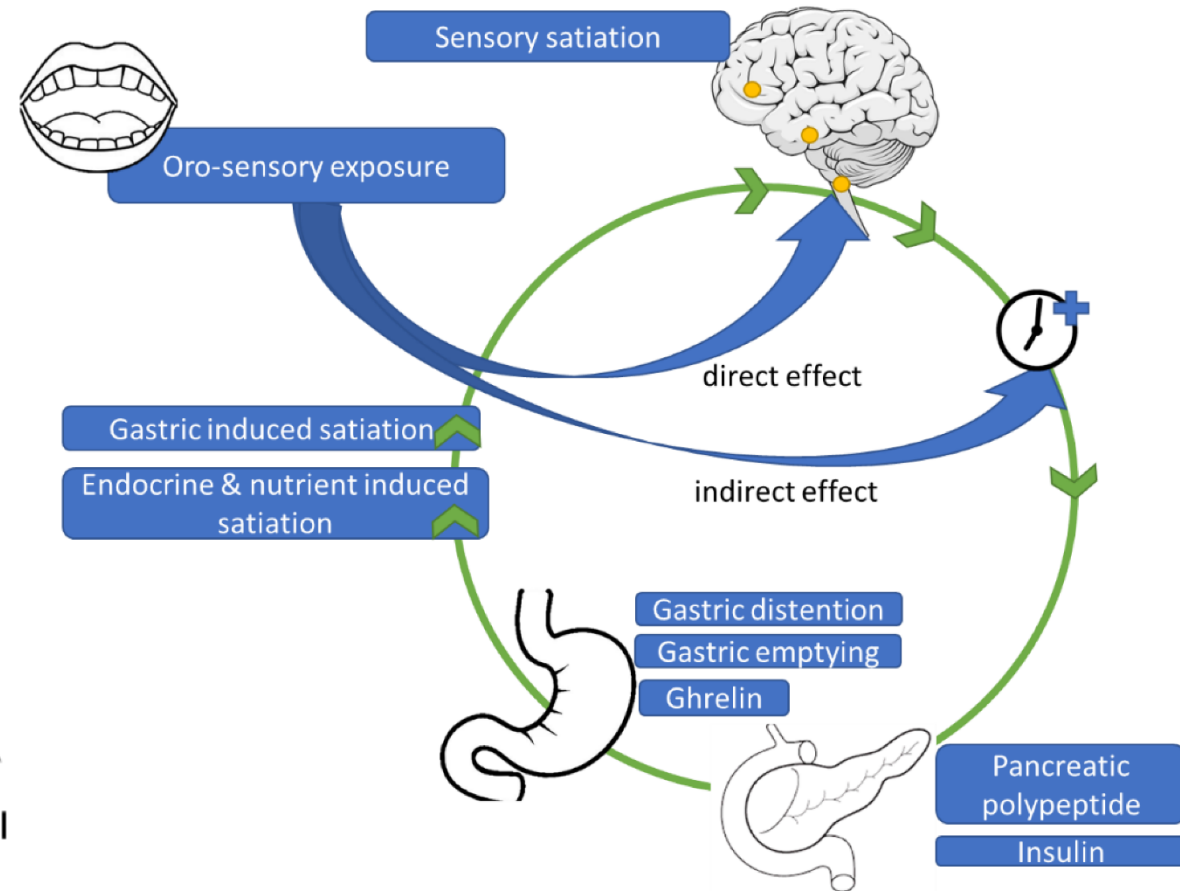
Meal termination: Cycles of hunger and satiation, satiety



Satiation can be driven by food cognition

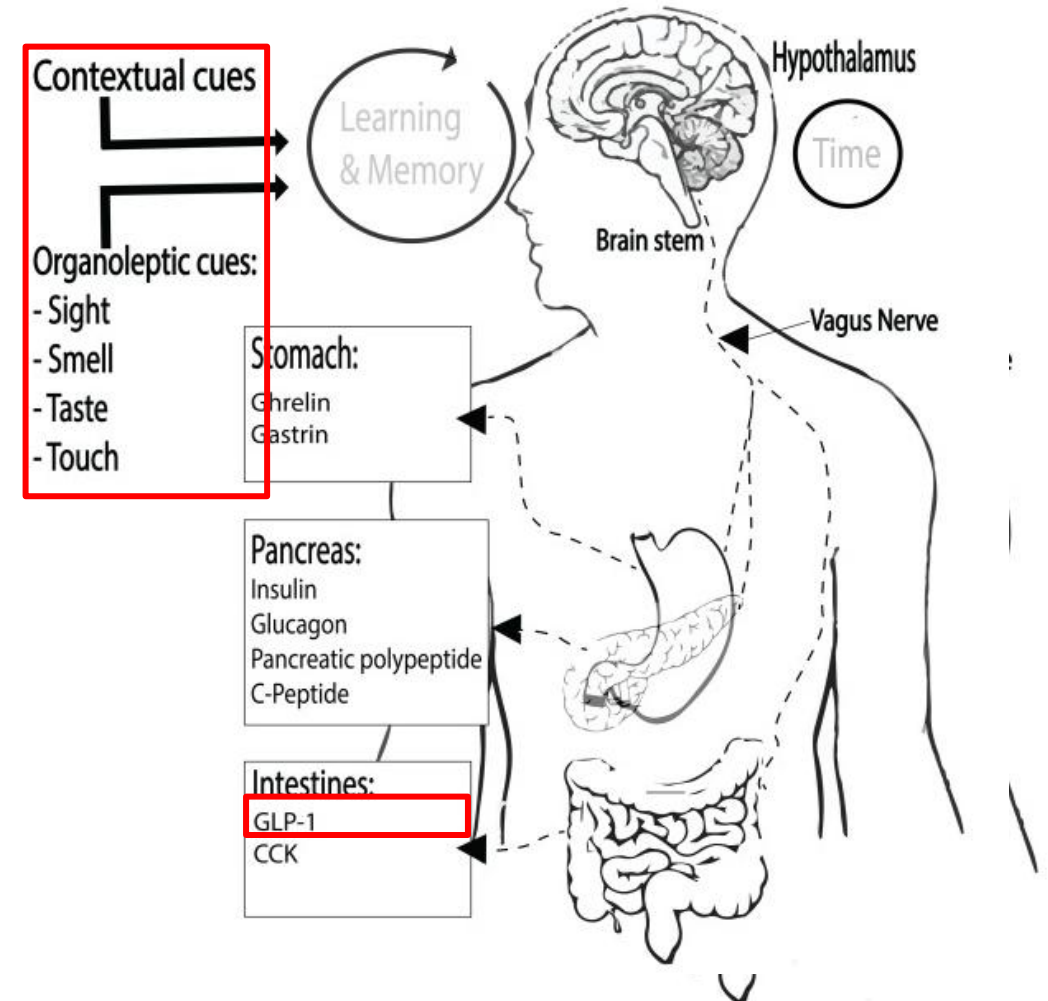
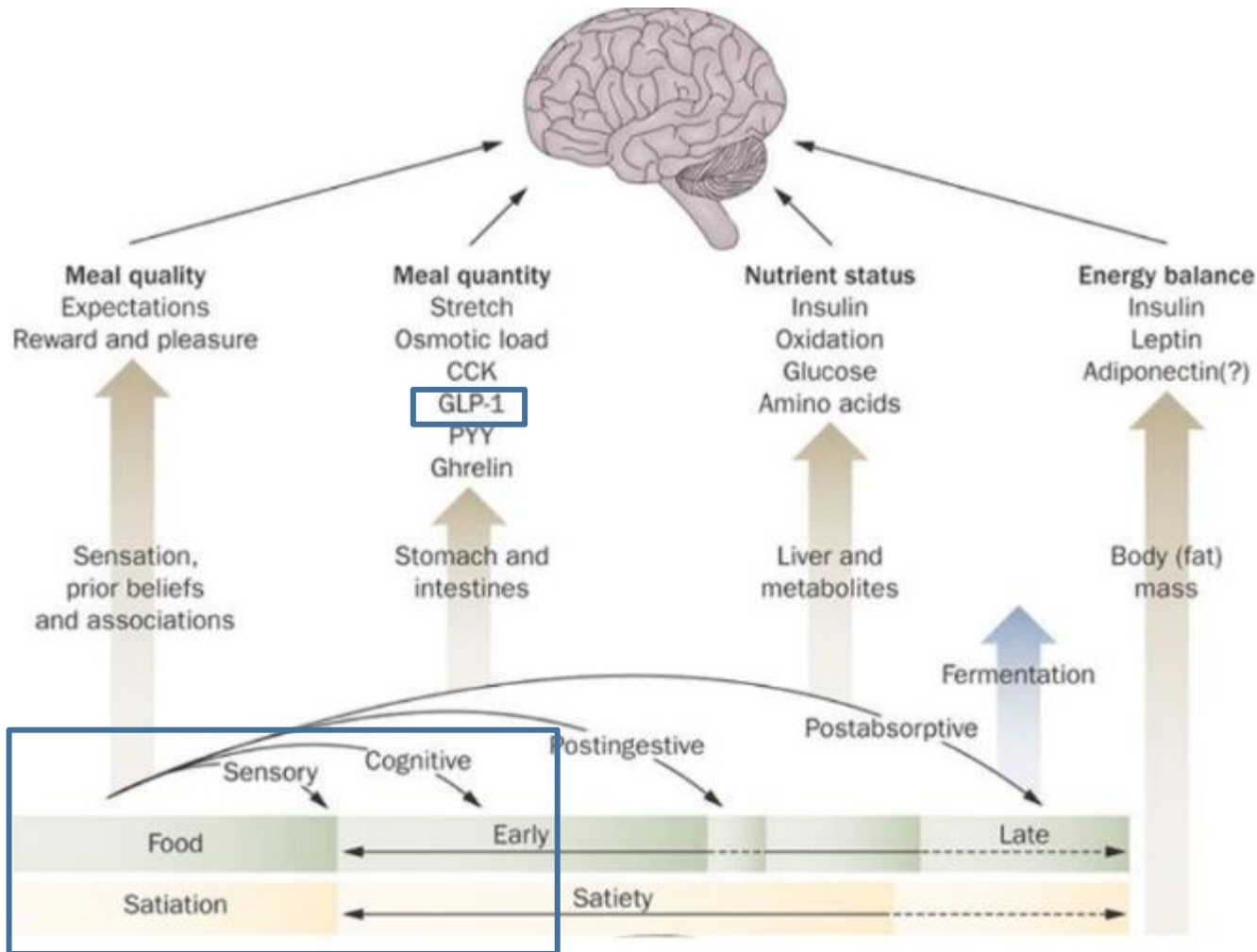


2010 Nutrition Reviews. Cephalic phase responses and appetite

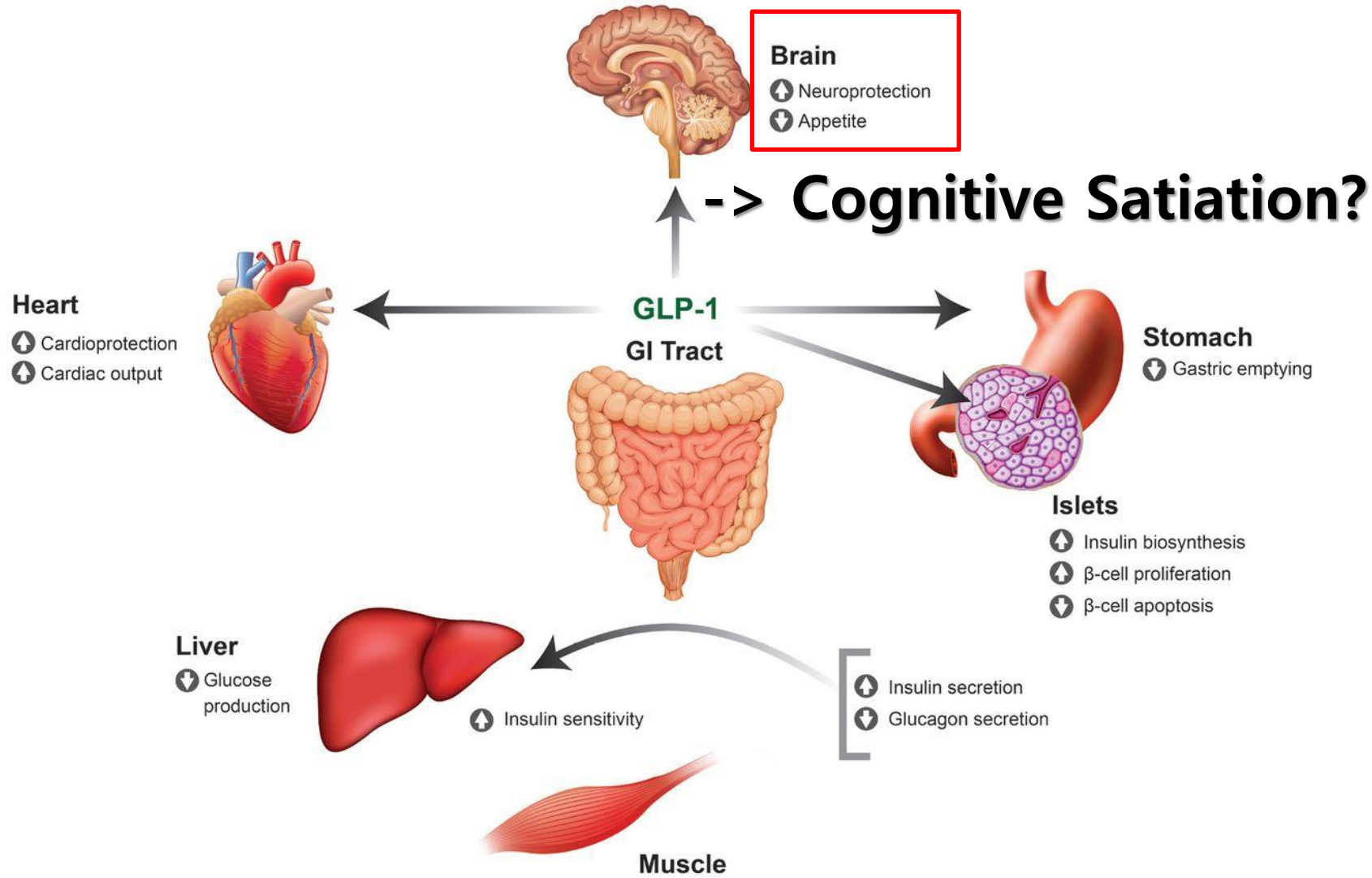


2021 Nutrients. Effects of Oro-Sensory Exposure on Satiation and Underlying Neurophysiological Mechanisms-What Do We Know So Far?

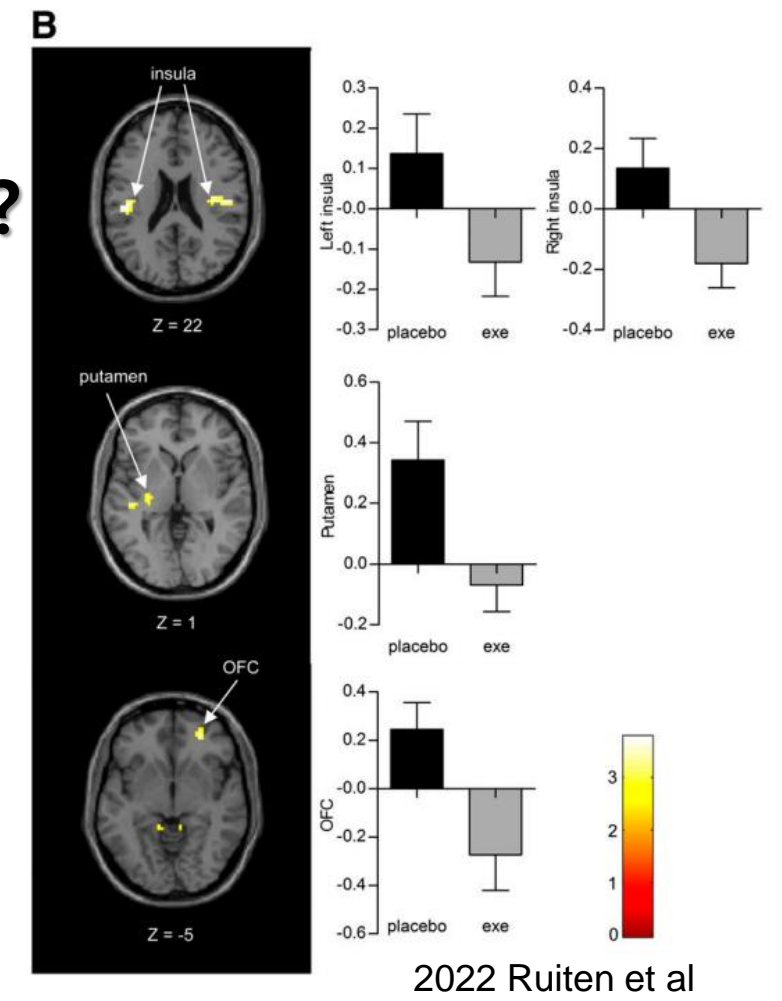
Satiation can be driven by food cognition



GLP-1R Agonists act on the Central Nervous System



fMRI changes by Food Cue post GLP-1RA



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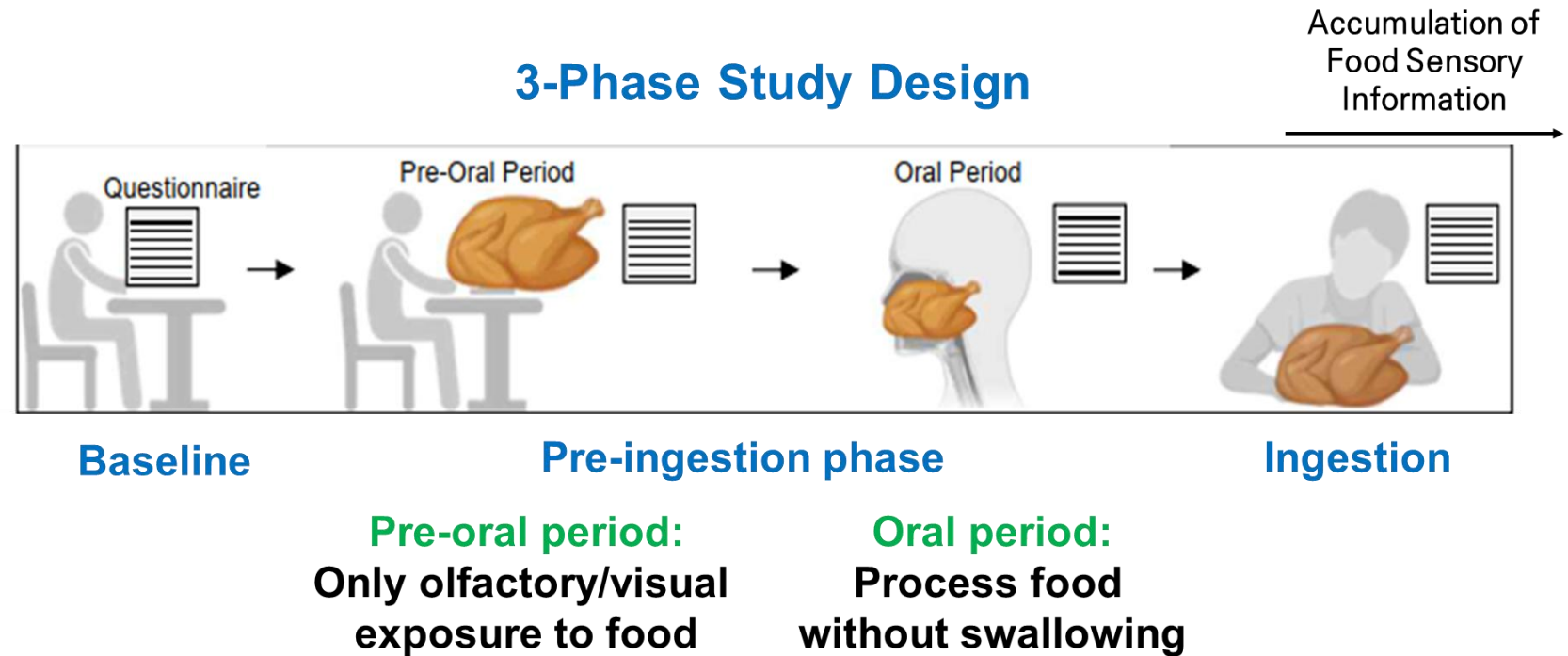
01. Clinical study

Question: Will GLP-1 injection induce cognitive satiation in humans?

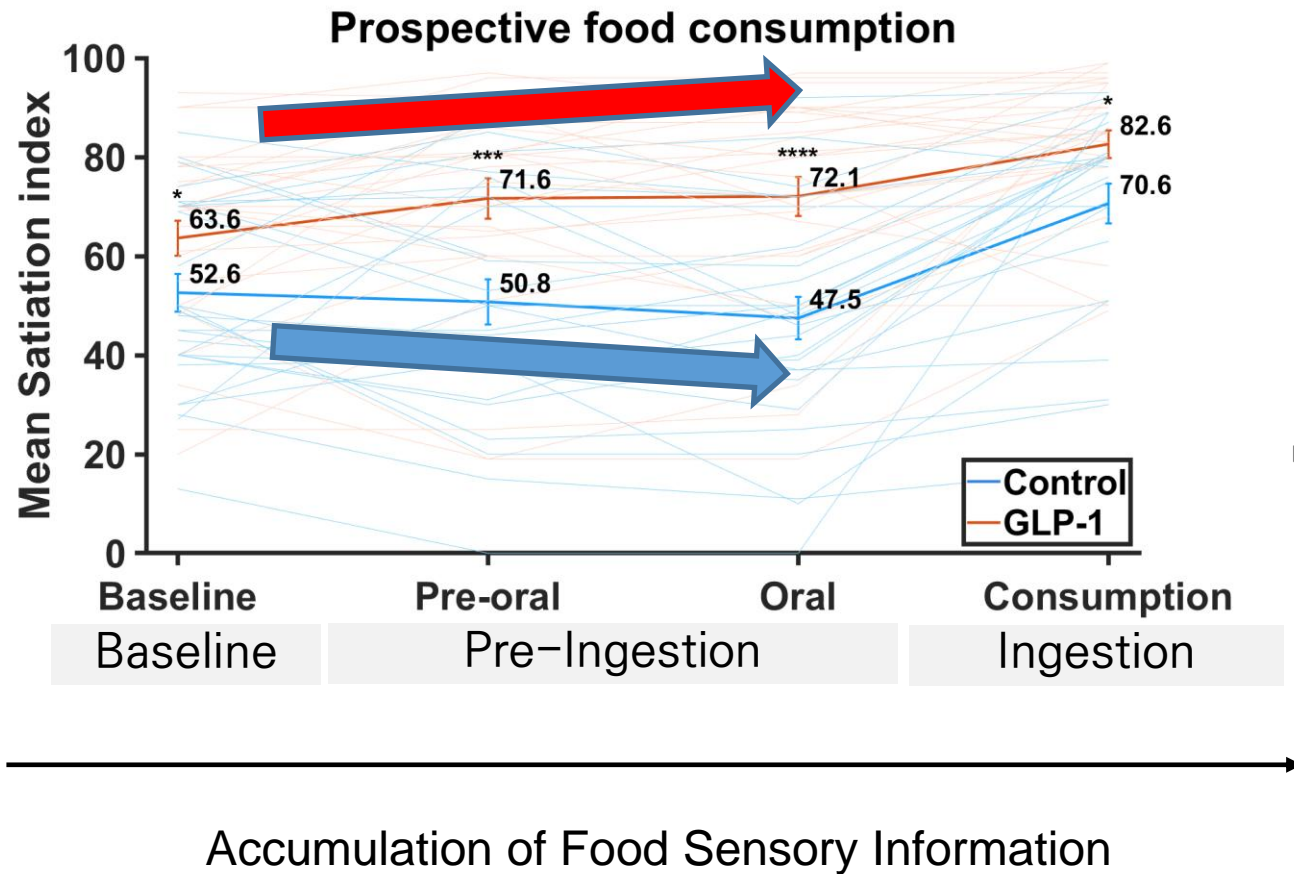
GLP-1RAs evoke cognitive satiation before food delivery in humans



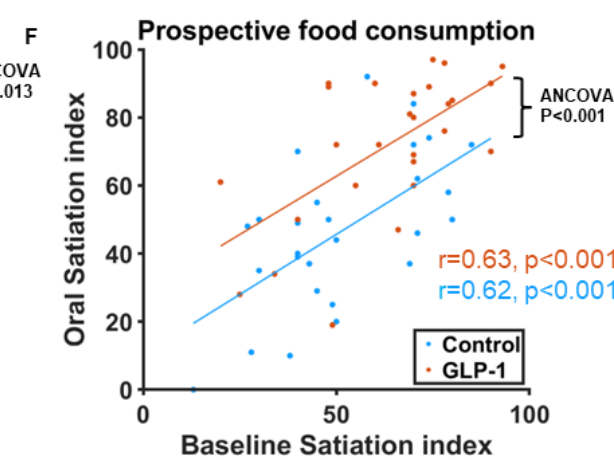
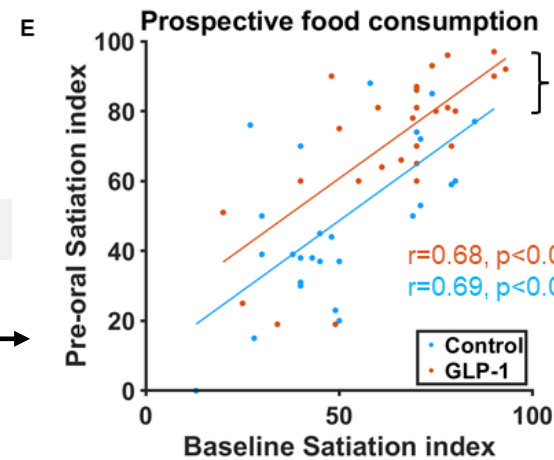
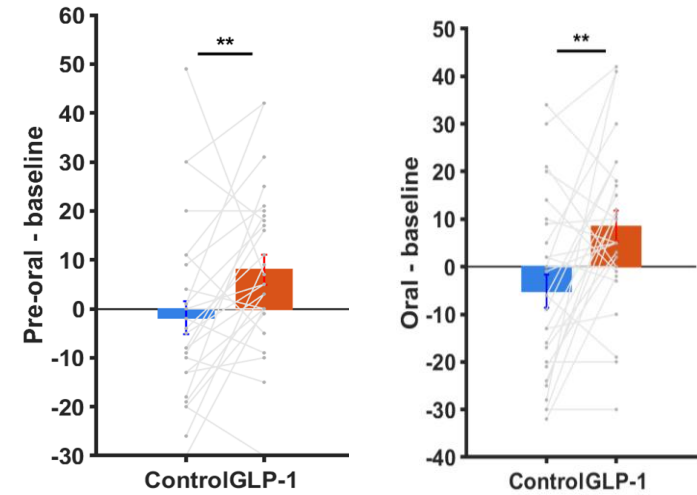
3-Phase Study Design



GLP-1RAs evoke cognitive satiety before food delivery in humans

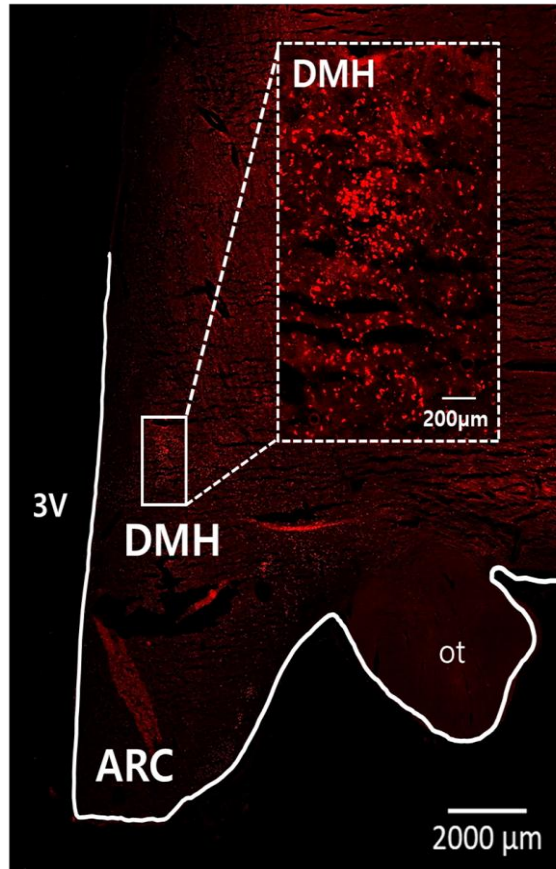


Prospective food consumption

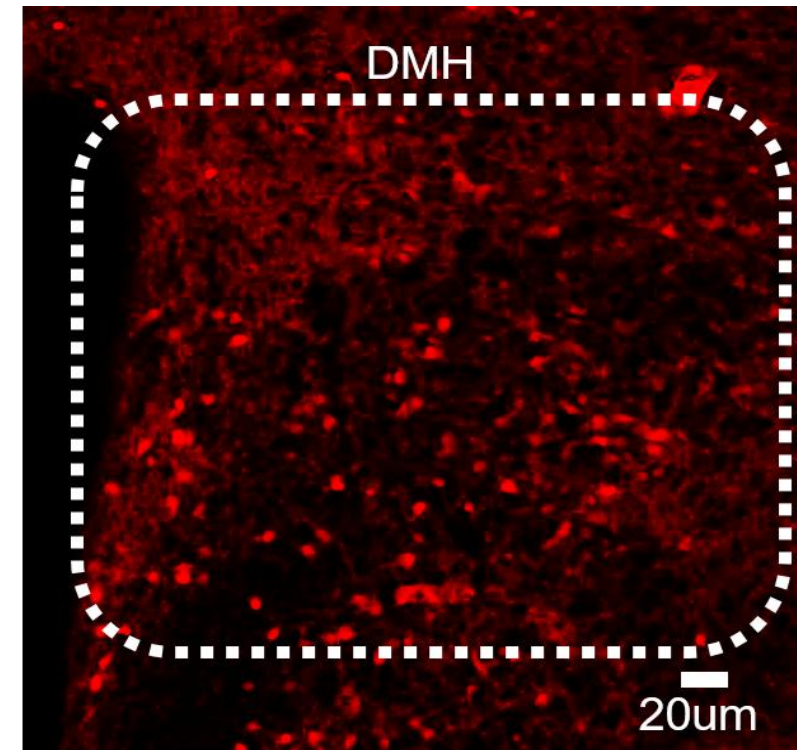
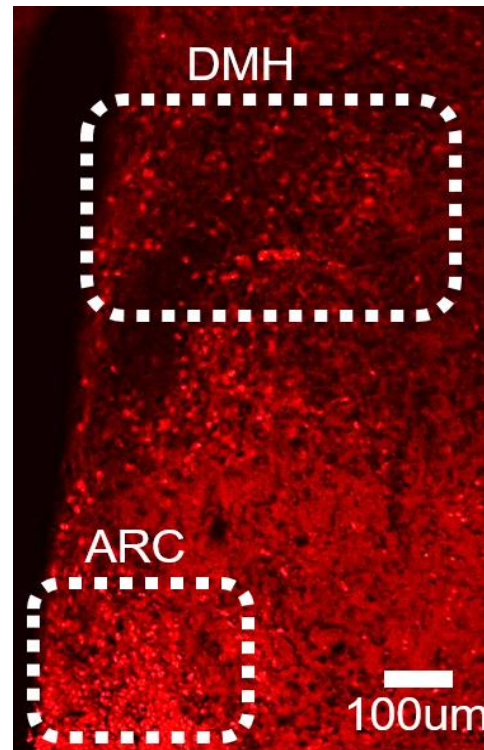


Histological Mapping of Human and Mouse Brain Reveals GLP-1R neurons in the Dorsomedial hypothalamus (DMH)

Human



Mouse



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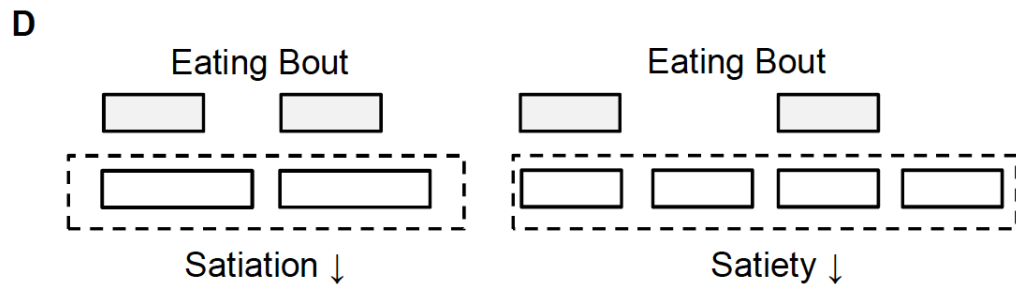
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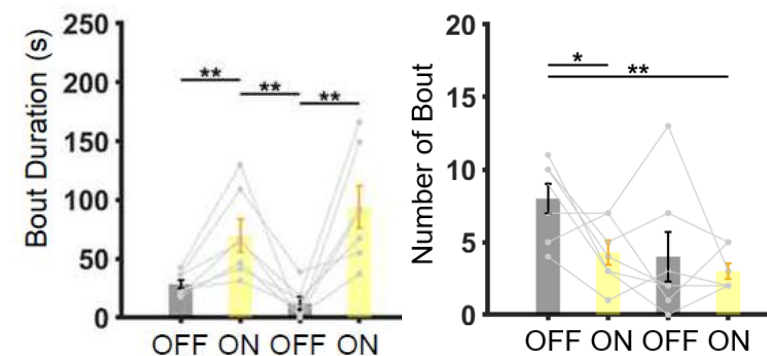
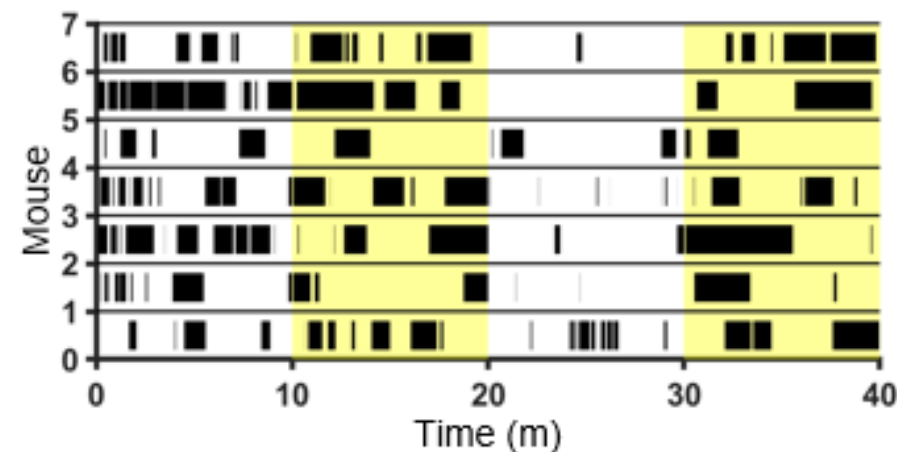
02. Neuromodulation

Question: Will Modulating DMH GLP-1R neurons lead to specific behavior change in eating?

Inhibition of DMH GLP-1R Neurons suppress satiation

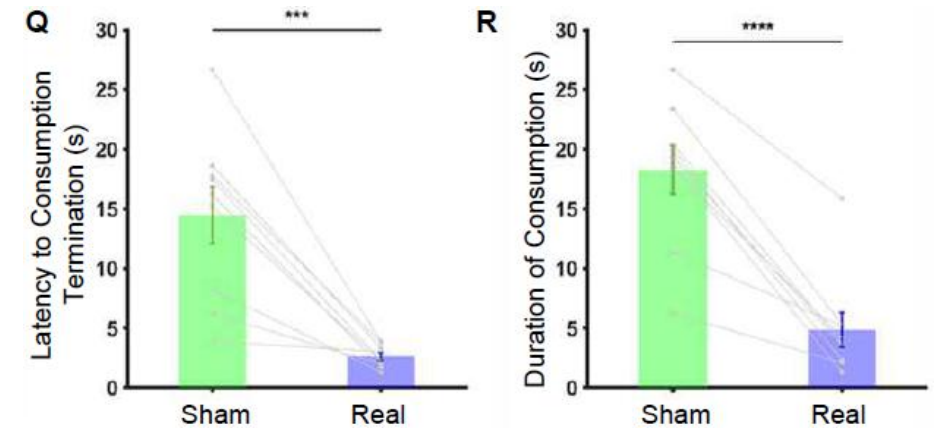
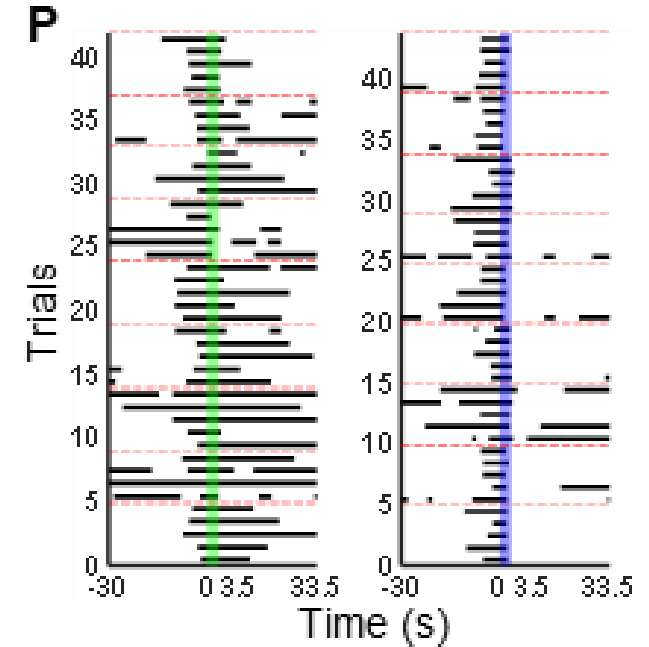
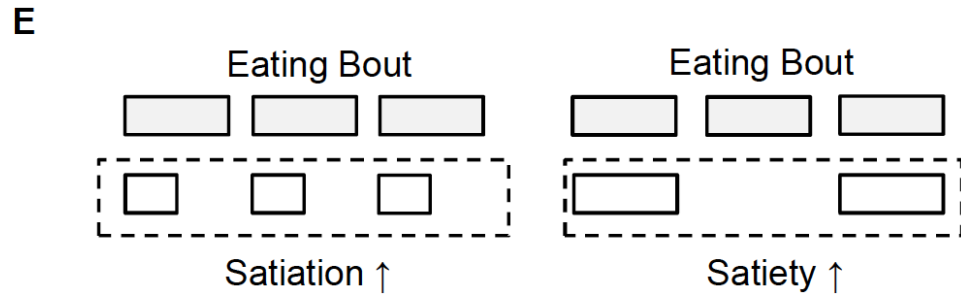


Inhibition of DMH^{GLP-1R} Neurons
Suppress Satiety



Eating Bout Duration ↑
Bout Frequency n.s. → Satiety ↓

Activation of DMH GLP-1R Neurons induce satiation



Activation of DMH^{GLP-1R} Neurons
Evoke Satiation

Result Summary

- GLP-1RAs can significantly increase cognitive satiation in humans.
- Notable distribution of GLP-1Rs in DMH is apparent in mice and humans
- **DMH GLP-1R neurons are necessary and sufficient for satiation**

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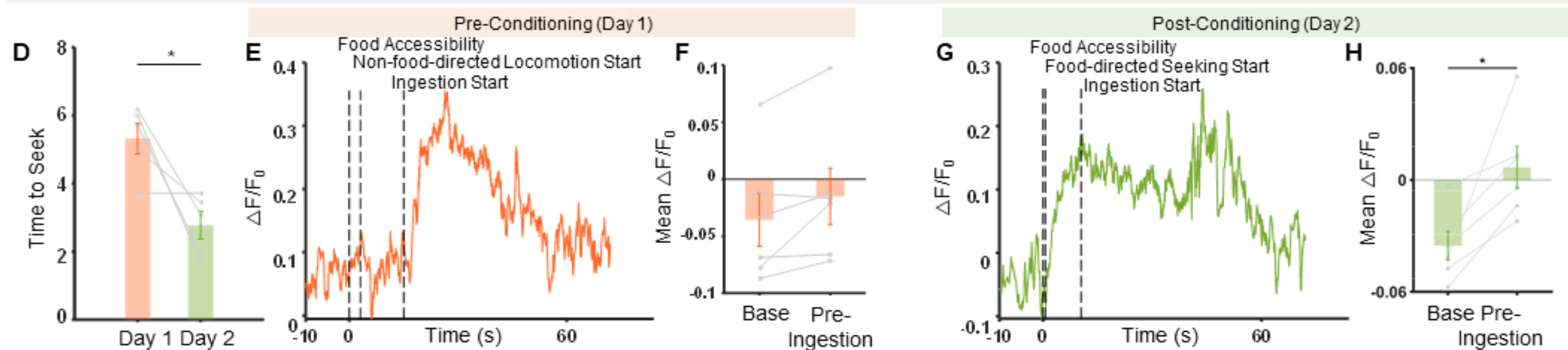
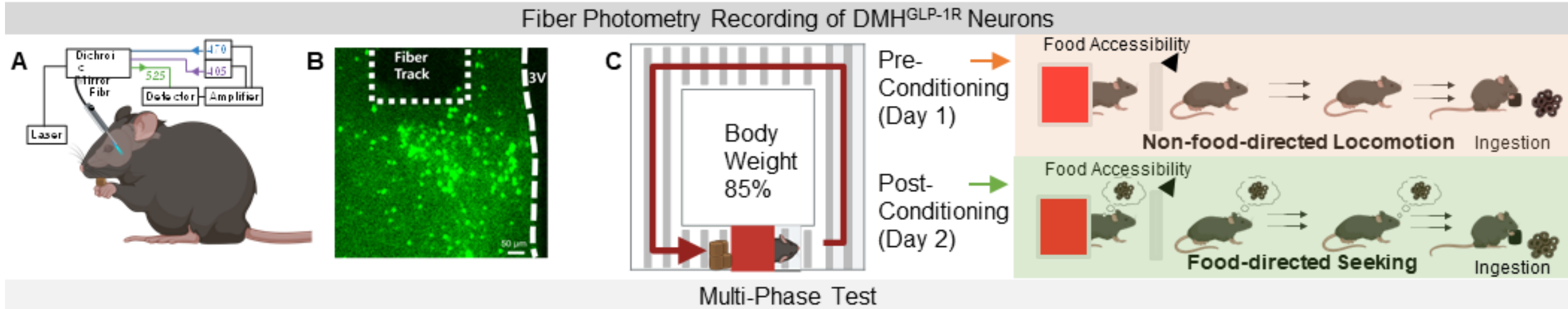
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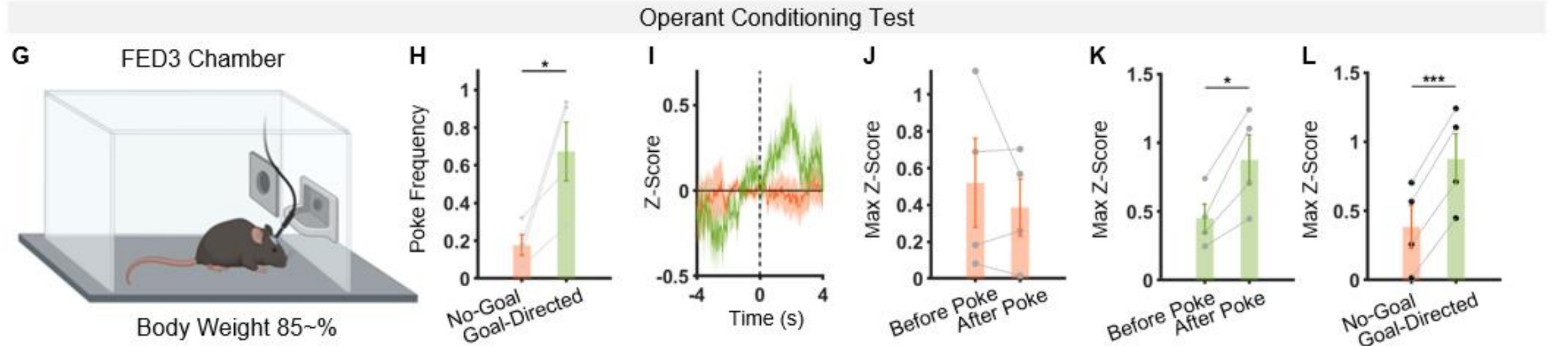
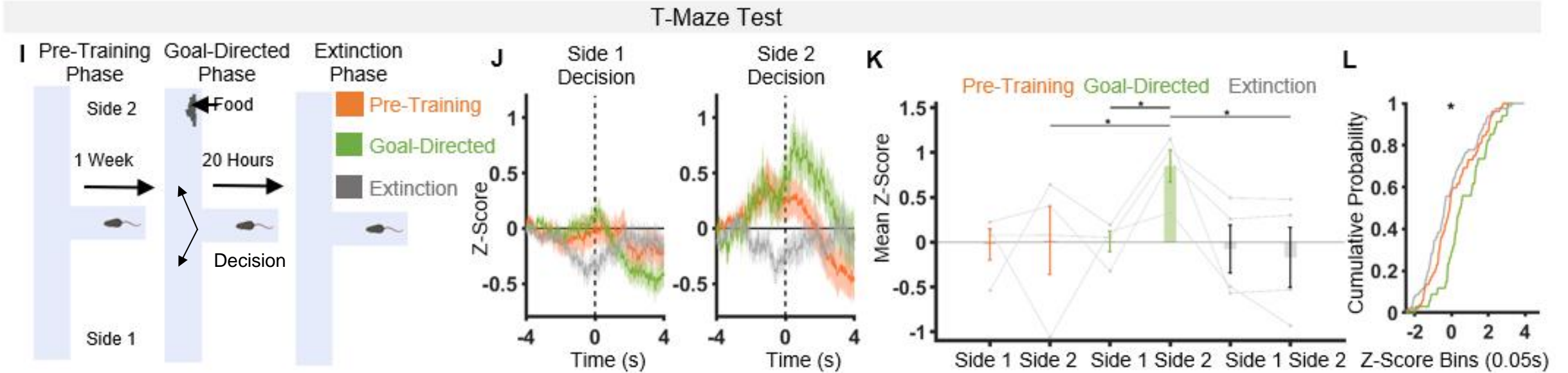
03. Photometry

Question: How do DMH GLP-1R neuron signals change according to eating behavior?

DMH GLP-1R neurons are activated at food cognition



DMH GLP-1R neurons are activated at food cognition



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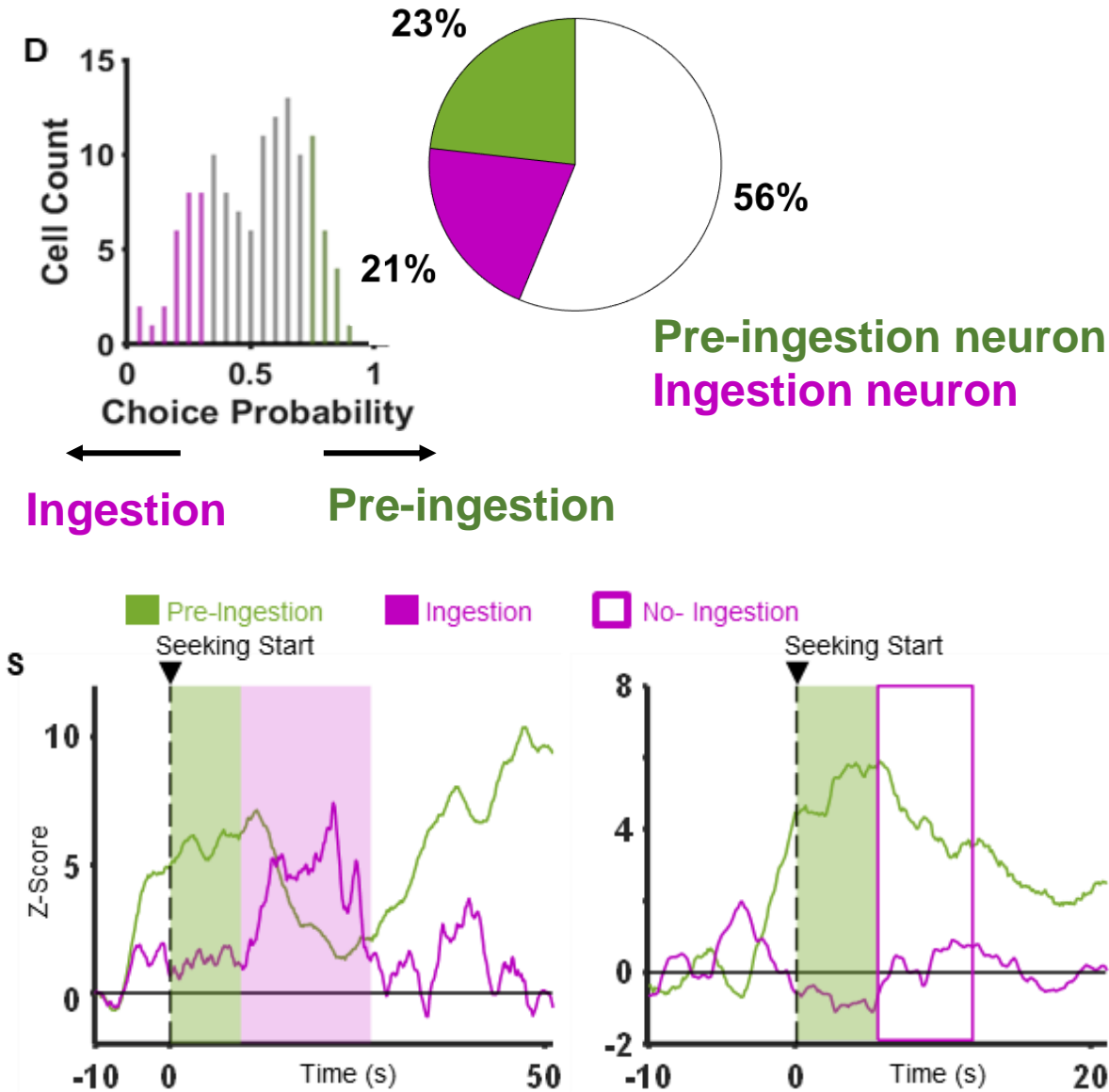


04. Miniscope

Question: How do individual DMH GLP-1R neuronal populations react regarding cognitive satiation?

Two distinct populations of DMH GLP-1R neurons respond to different eating phases

Two Distinct Population of DMH^{GLP-1R} Neurons Respond to Different Phases of Eating



Result Summary

- GLP-1RAs can significantly increase cognitive satiation in humans.
- Notable distribution of GLP-1Rs in DMH is apparent in mice and humans.
- DMH GLP-1R neurons are necessary and sufficient for satiation.
- DMH GLP-1R neurons encode cognitive satiation.
- **Distinct DMH GLP-1R Neuronal Populations Encode Different Stages of Cognitive Satiation: Pre-ingestion and Ingestion.**

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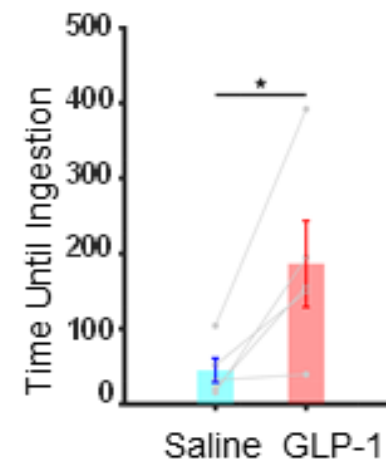
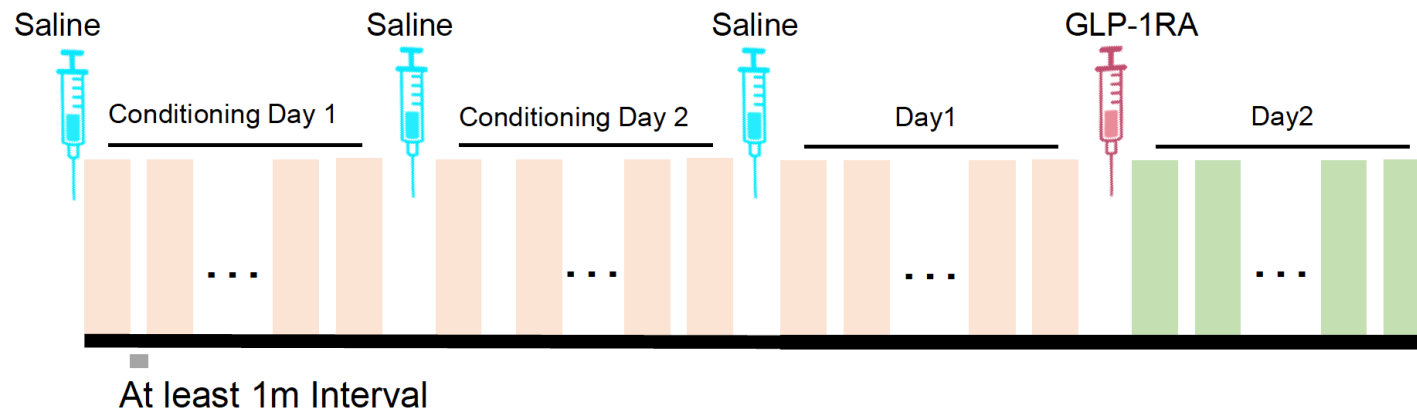
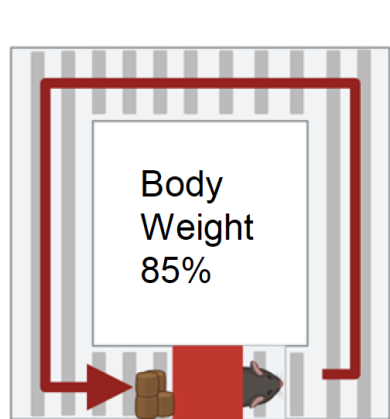


05. GLP-1 injection

Question: How will GLP-1 injection affect DMH GLP-1R neuronal response in mice?

GLP-1R Agonist Injection Potentiates DMH GLP-1R Neurons During Eating Behavior of mice

A



Pre-Ingestion phase

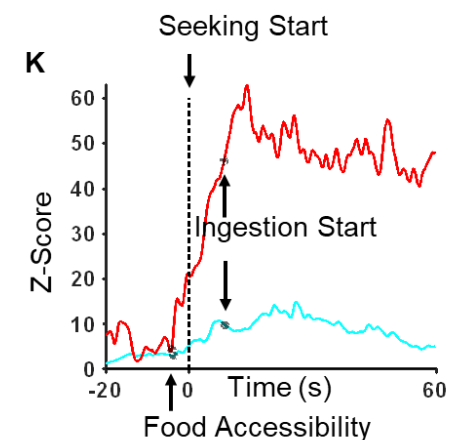
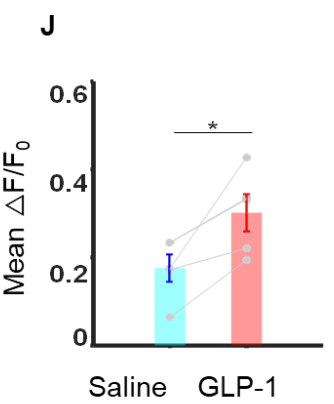
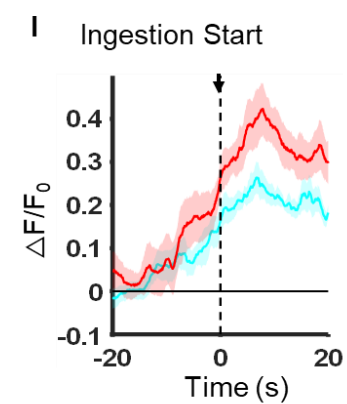
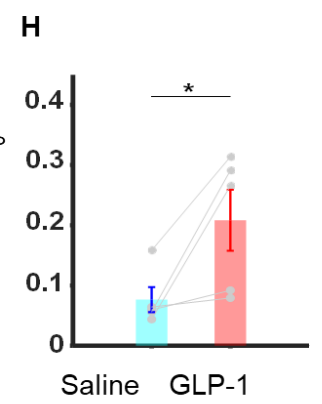
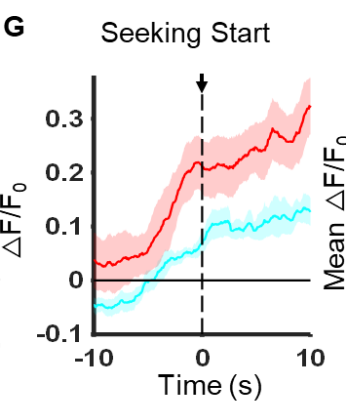
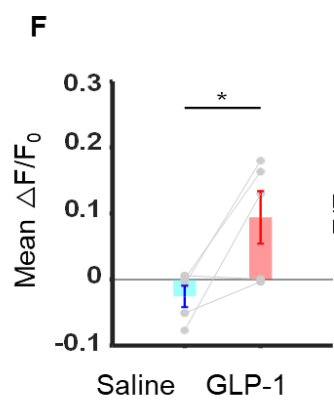
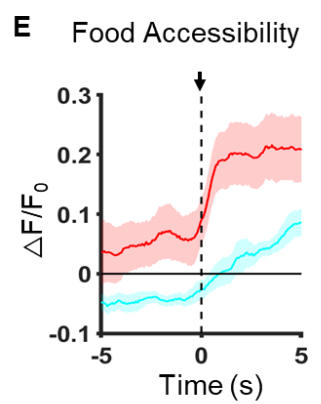
Ingestion phase

Rate of Change

Food Accessibility

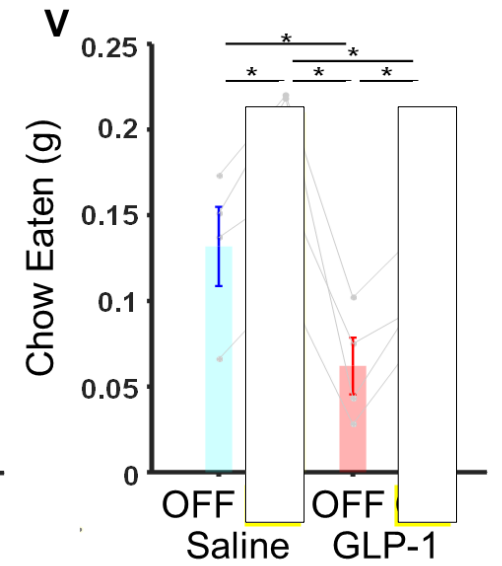
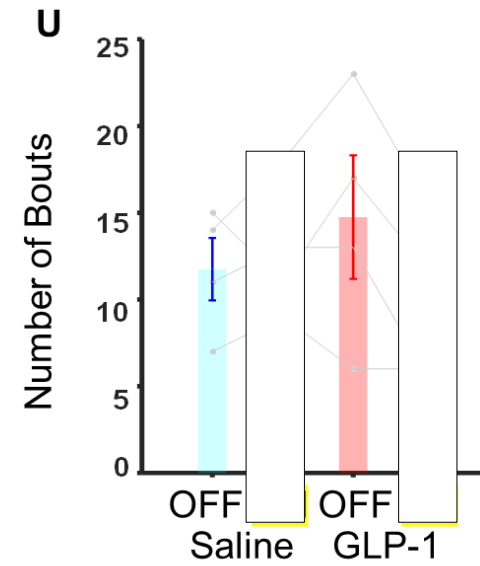
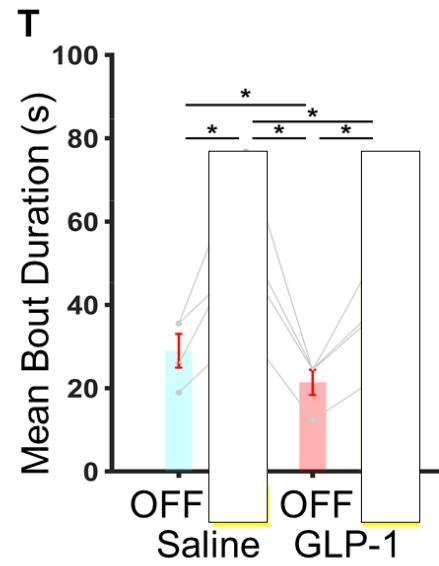
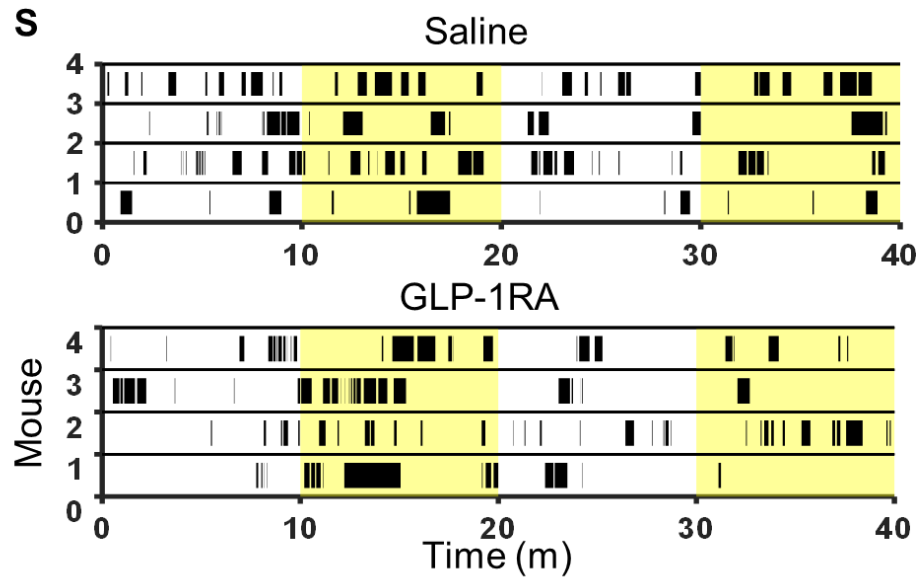
Seeking Start

Ingestion Start



Inhibition of DMH GLP-1R neurons can attenuate GLP-1RA effects on satiation

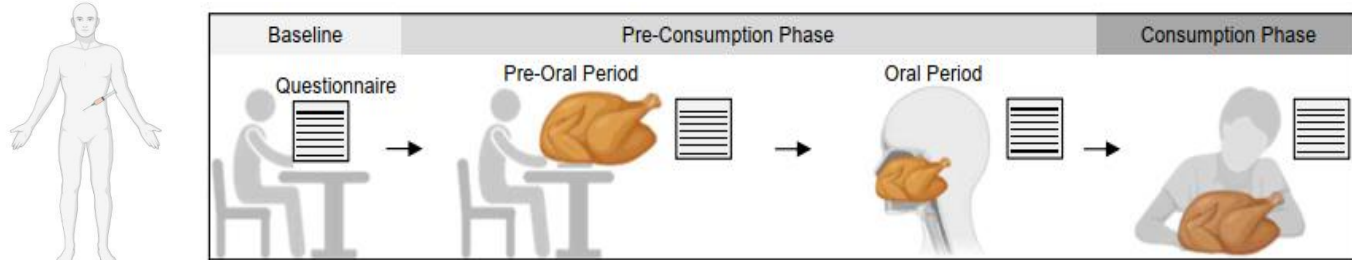
Optogenetic Inhibition of DMH^{GLP-1R} Neurons After GLP-1RA Injection



Result Summary

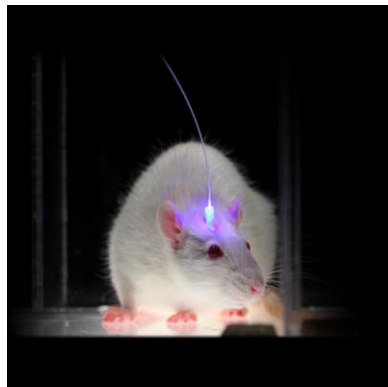
- GLP-1RAs can significantly increase cognitive satiation in humans.
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- DMH GLP-1R neurons encode cognitive satiation.
- Distinct DMH GLP-1R Neuronal Populations Encode Different Stages of Cognitive Satiation: Pre-consumption and Consumption.
- **GLP-1R Agonist Injection Activates DMH GLP-1R Neurons Only During Eating Behavior**

Conclusion



**Human:
GLP-1 injection -> Cognitive Satiety**

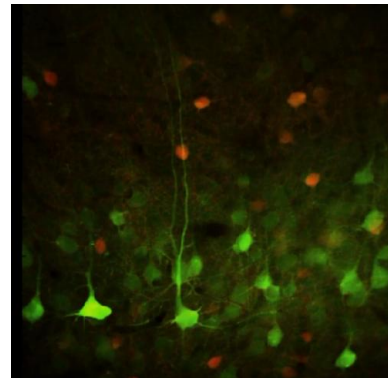
**Optogenetics
(Neuron->Behavior)**



Awake, Freely
behaving mice

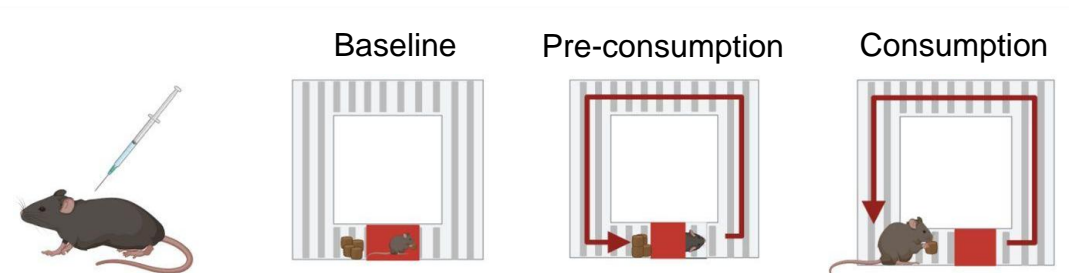
**DMH GLP-1R neurons
->Satiety**

**Fiber photometry,
Miniscope
(Behavior->Neuron)**



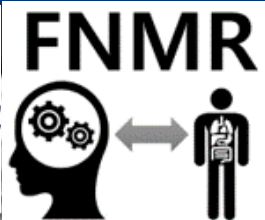
**Cognitive Satiety
->DMH GLP-1R neurons**

Mice: GLP-1 injection



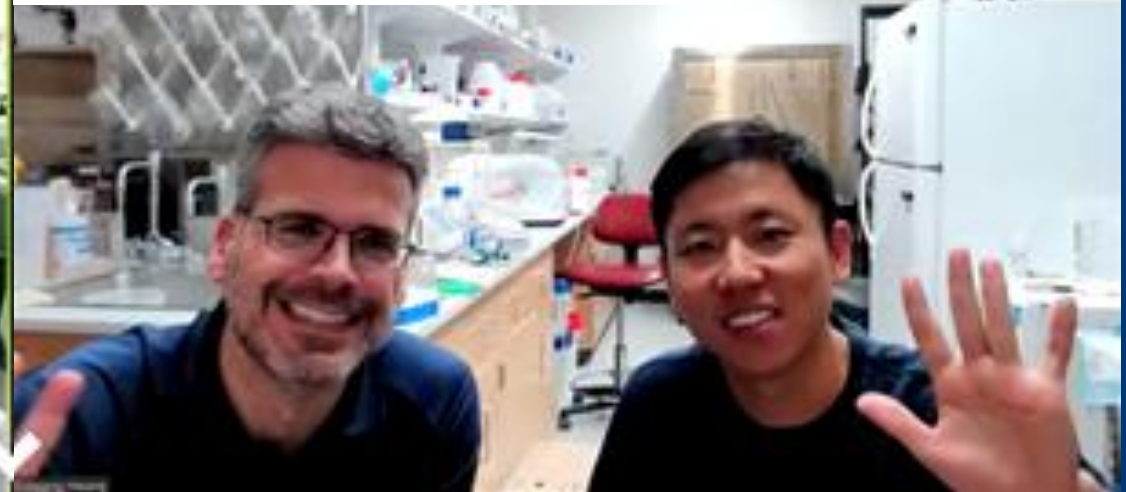
**GLP-1 injection -> DMH GLP-1R neurons
-> Cognitive Satiety**

GLP-1 Increases Cognitive Satiety via Hypothalamic Circuits in Mice and Humans



UT Southwestern
Medical Center®

Williams Lab



**Kyu Sik Kim*, Joon Seok Park*, Kyung-min Kim, Young Hee Lee,
Hwa Yoon- Shin, Sang-Ho Jung, Min-Jung Park, Hyung Jin Choi**

Eunsang Hwang*, Kevin Williams



Thank you for your attention!