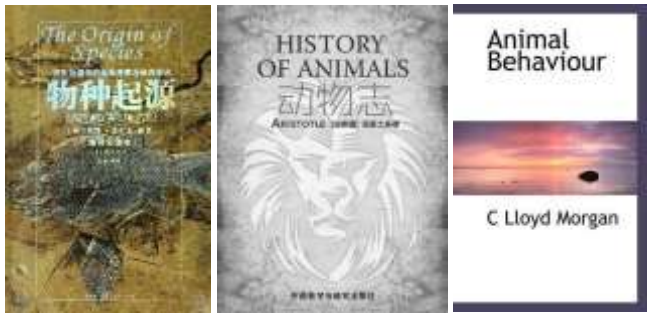
Three Complex Neural Mechanisms of Sequence Behaviors in Mice

MMZ JSM CDL

20240125

The Development of Animal Behavior Research

Paleolithic Age
Domesticated animals



17th to 20th centuries
Observing animal behavior

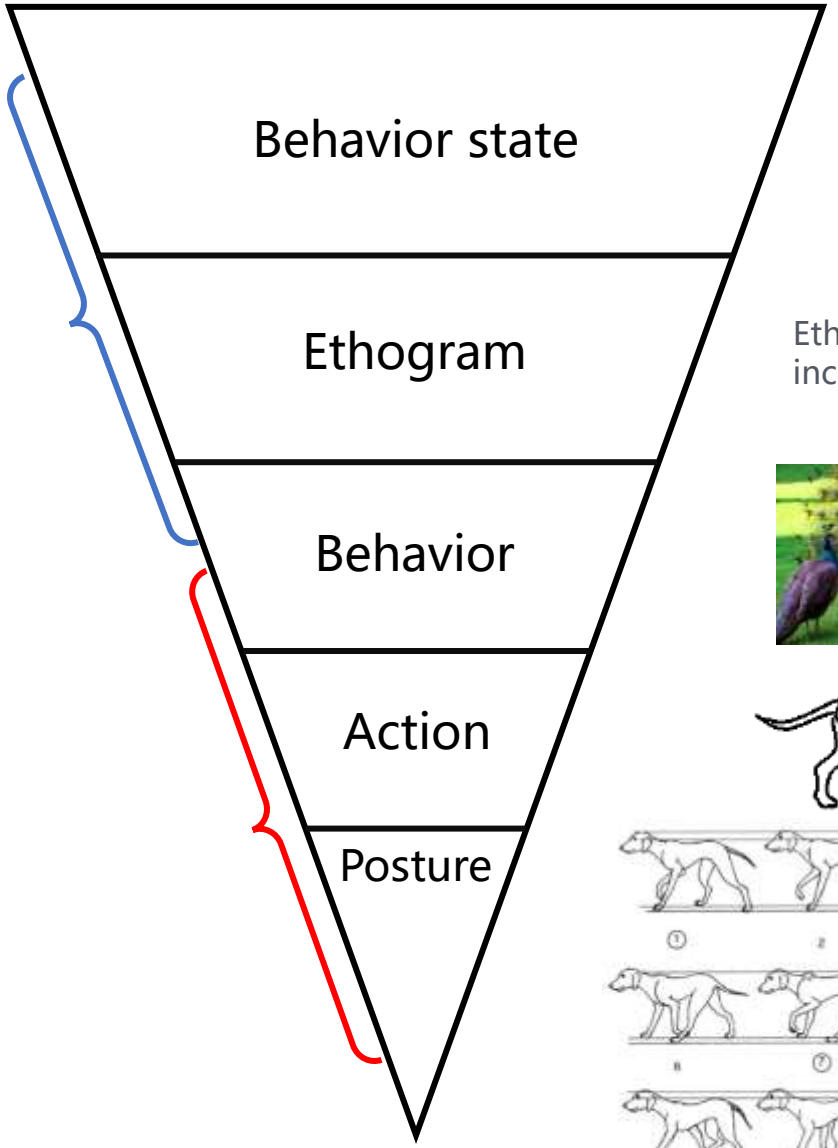
The modern times
Studying animal behavior in the laboratory

Why should we study animal behavior?

- Provide better animal welfare
- Understanding the evolution of species
- Revealing the functions of the brain

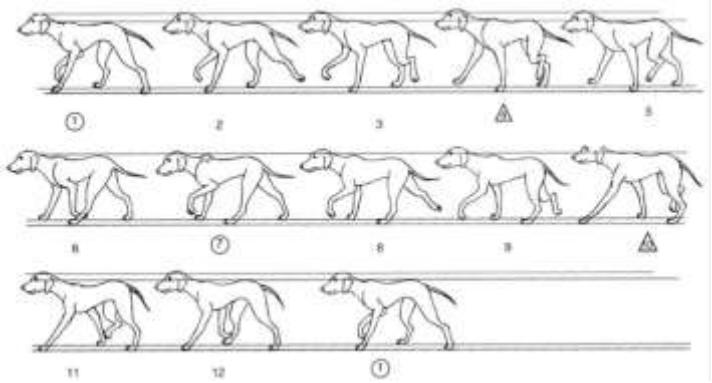
…

The level of behavioral research

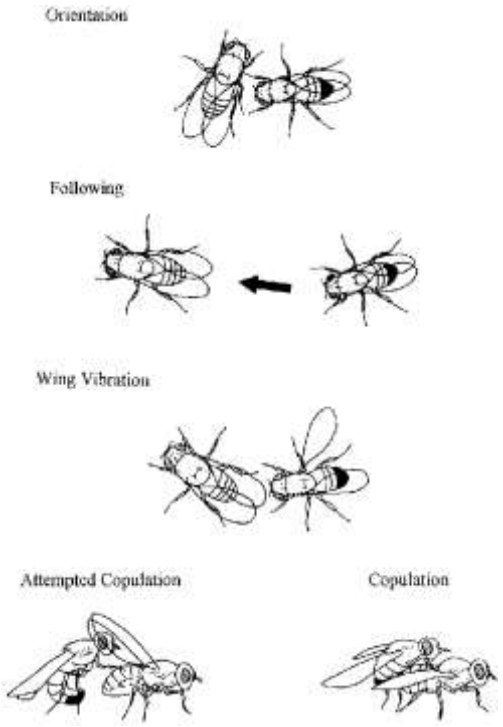


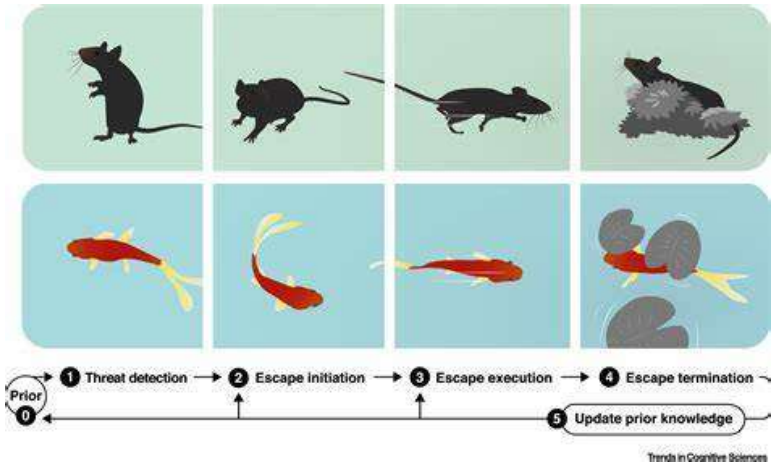
Animals are more likely to exhibit certain behaviors and less likely to exhibit other behaviors under the influence of the environment

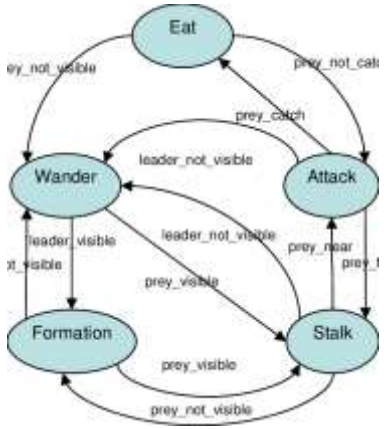
Ethogram is a list of typical behaviors performed by an animal, including how often and how long the animal does them

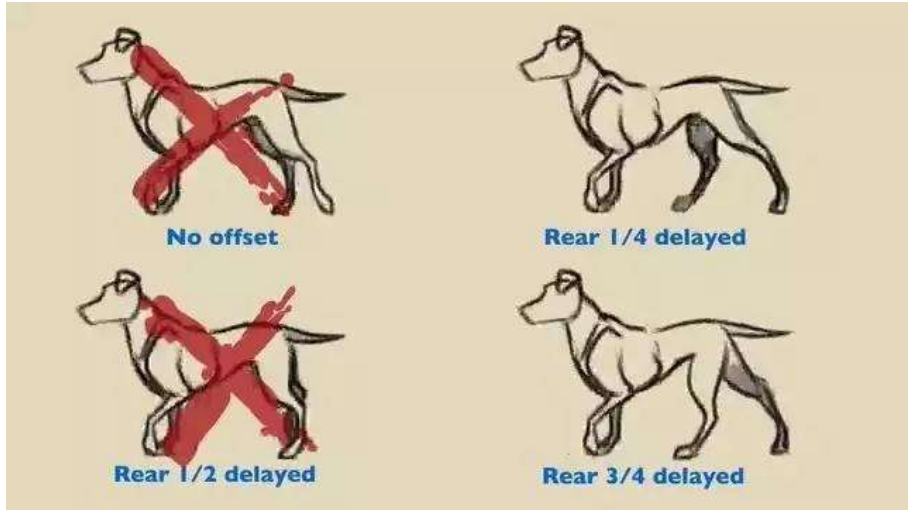


Behavior sequence: Within a certain period of time, behaviors are triggered in chronological order



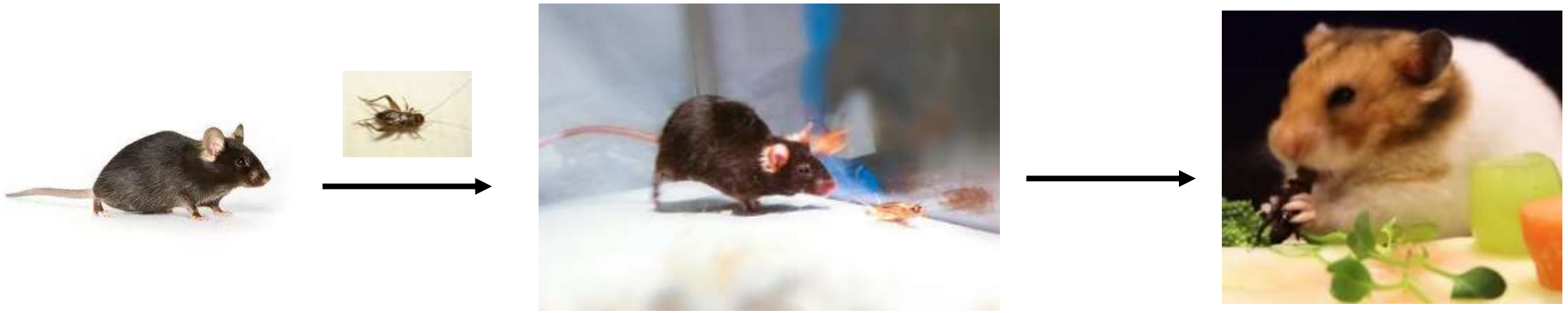






Questions

- What is the significance of behavioral sequences?
- How to maintain the sequence?
- Is there also a sequence between different behaviors?



- The temporally specific hunting behavior sequence —— 马铭泽
- Fragmentation of feeding behavior caused by environment and motivation —— 姜思梅
- The transition mechanism between planning and execution —— 陈东亮

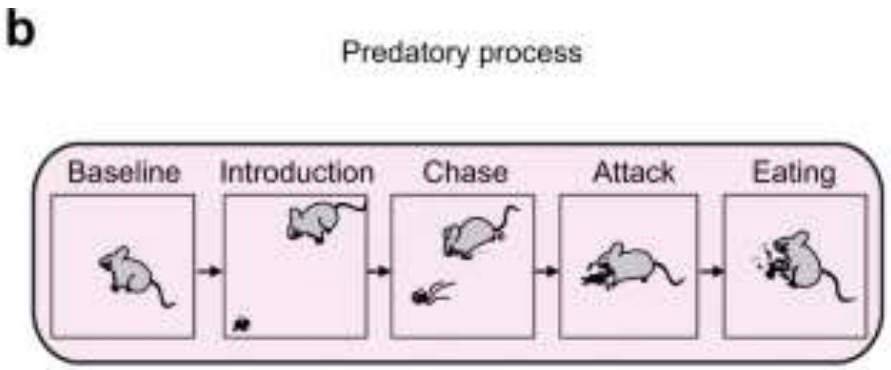
The temporally specific hunting behavior sequence

MMZ

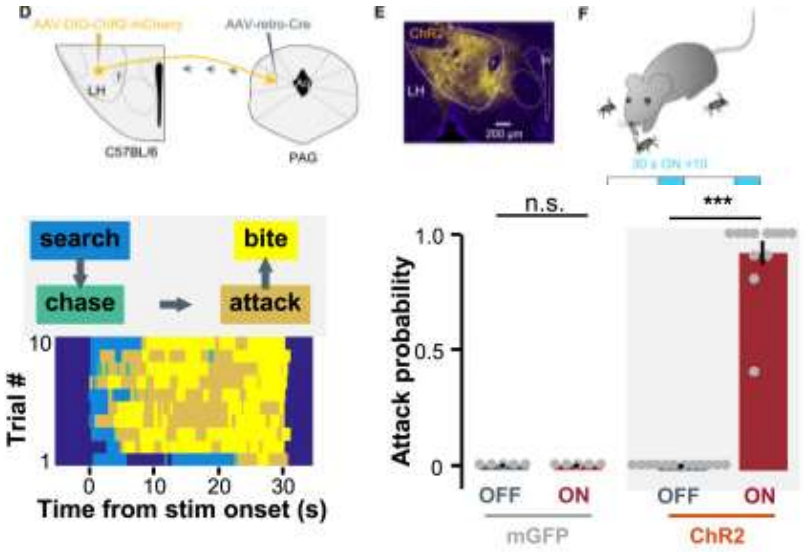
Hunting behavior

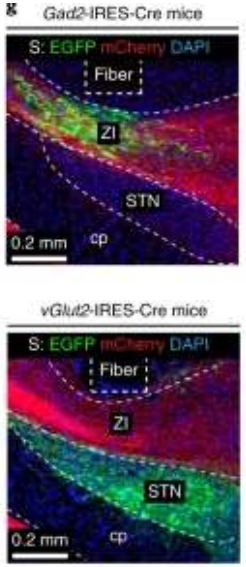
predatory hunting

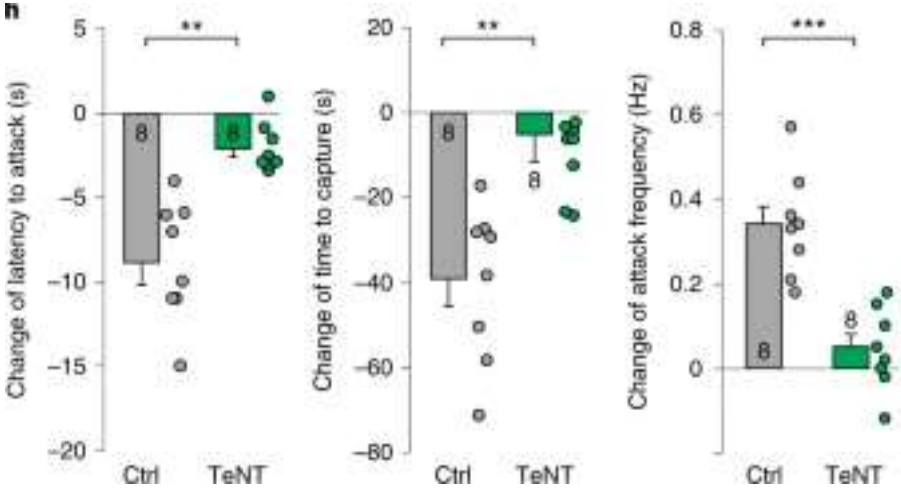
trophy hunting

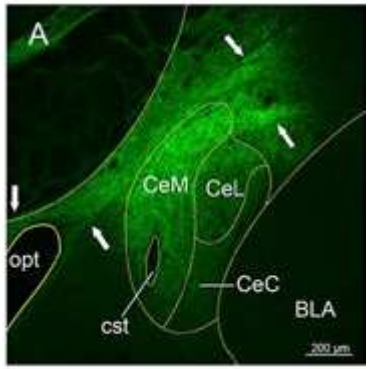


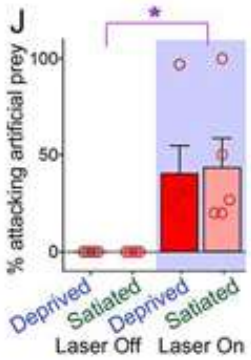
LH, ZI, CeA participate in hunting behavior through PAG

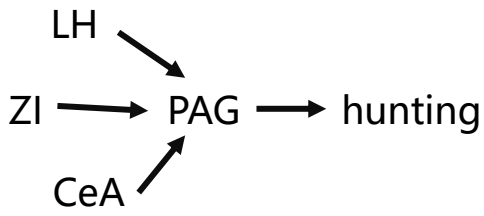


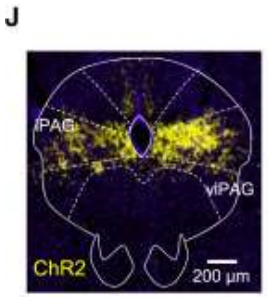


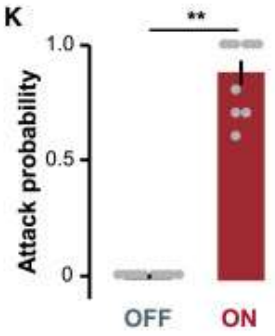










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Periaqueductal gray neurons encode the sequential motor program in hunting behavior of mice

Hong Yu, Xinkuan Xiang, Zongming Chen, Xu Wang, Jiaqi Dai, Xinxin Wang, Pengcheng Huang, Zhengdong Zhao, Wei L. Shen ✉ & Haohong Li ✉

Nature Communications 12, Article number: 6523 (2021) | Cite this article

6339 Accesses | 15 Citations | 1 Altmetric | Metrics

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- 睡眠稳态的生理和病理性调节机制

- 神经振荡异常和神经精神类疾病的关系

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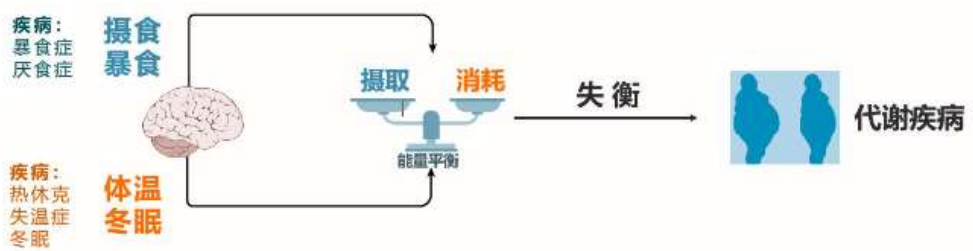
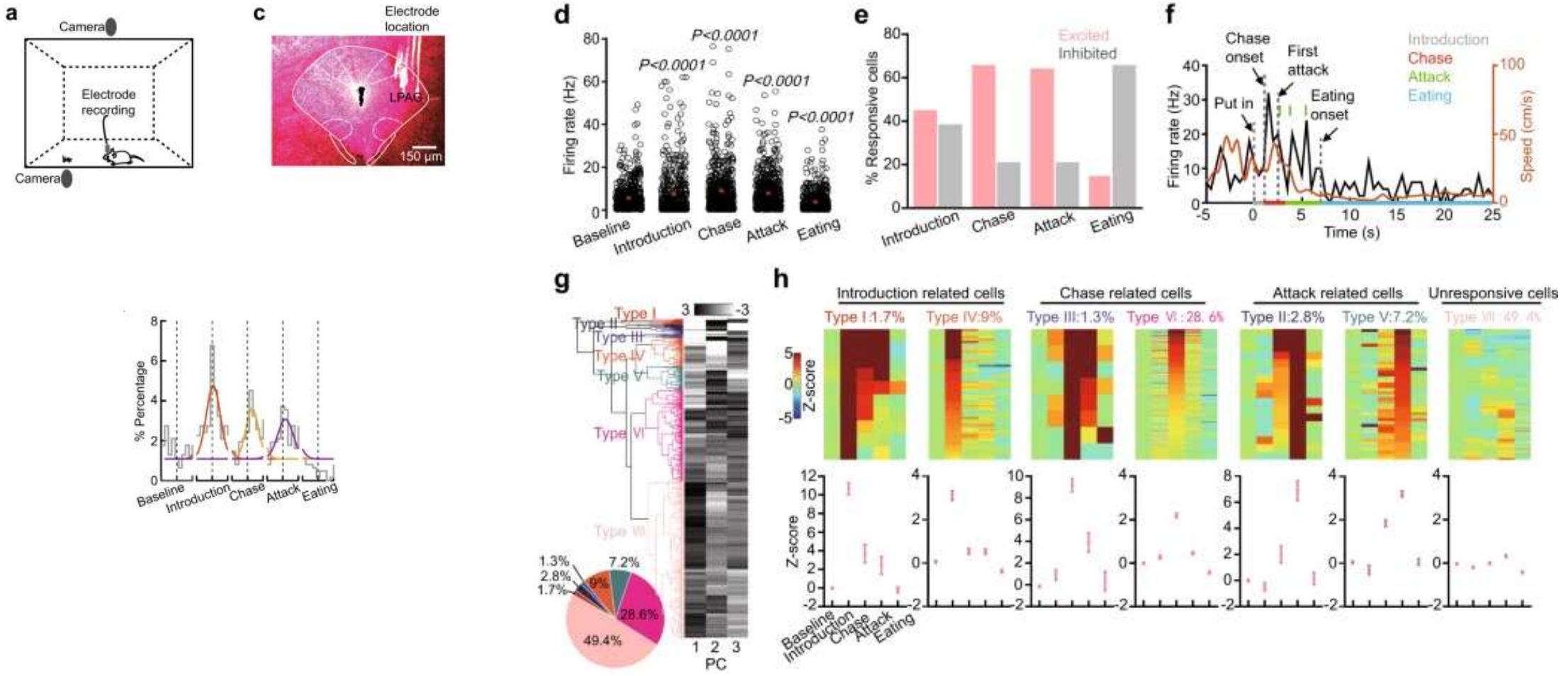
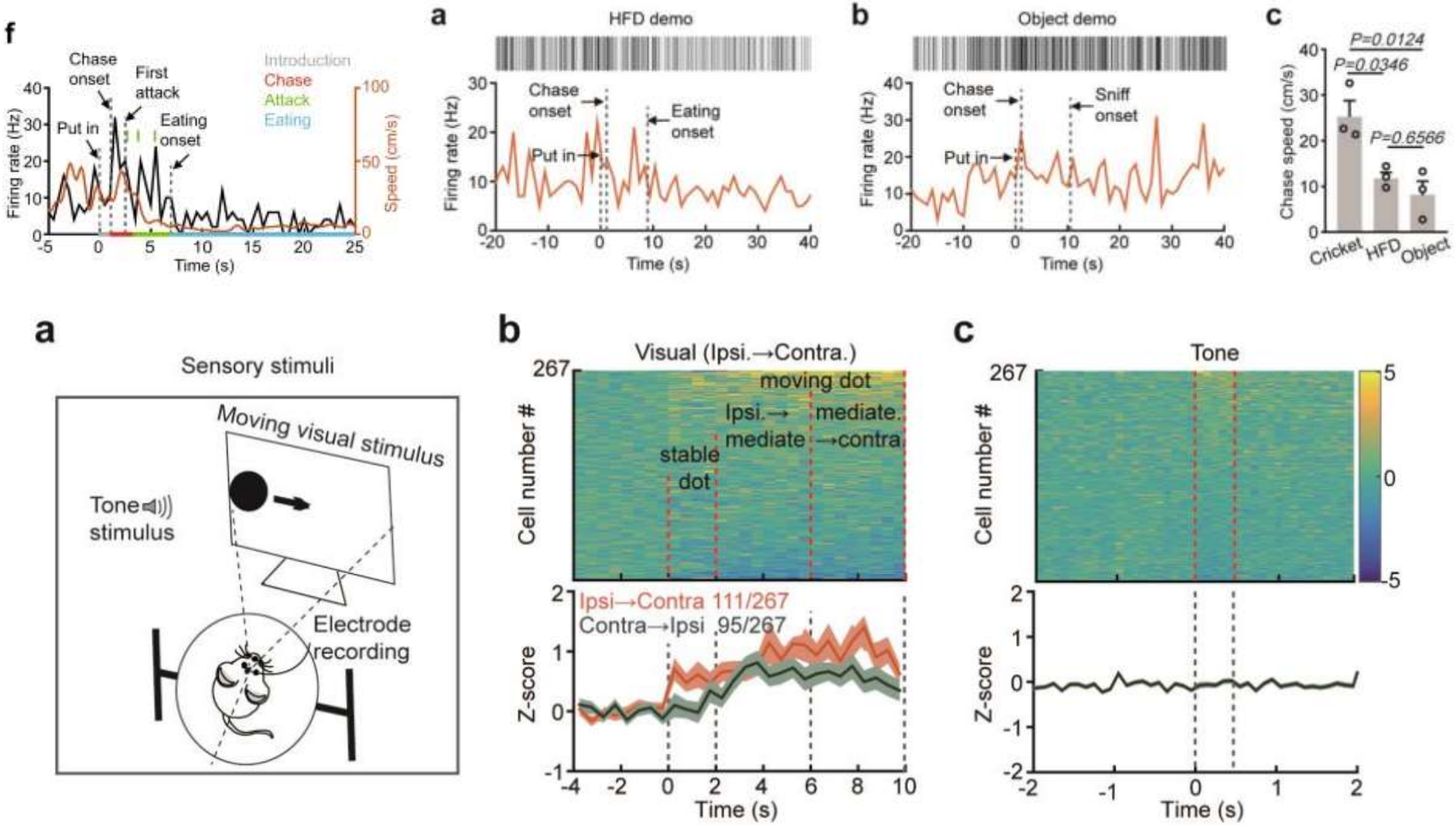


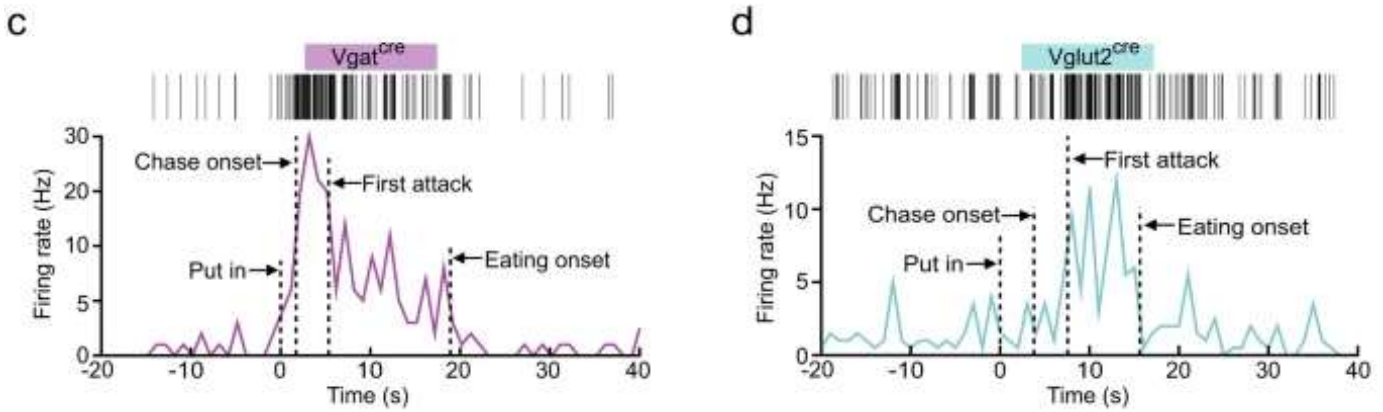
Distinct clusters of LPAG neurons are sequentially recruited in predatory hunting



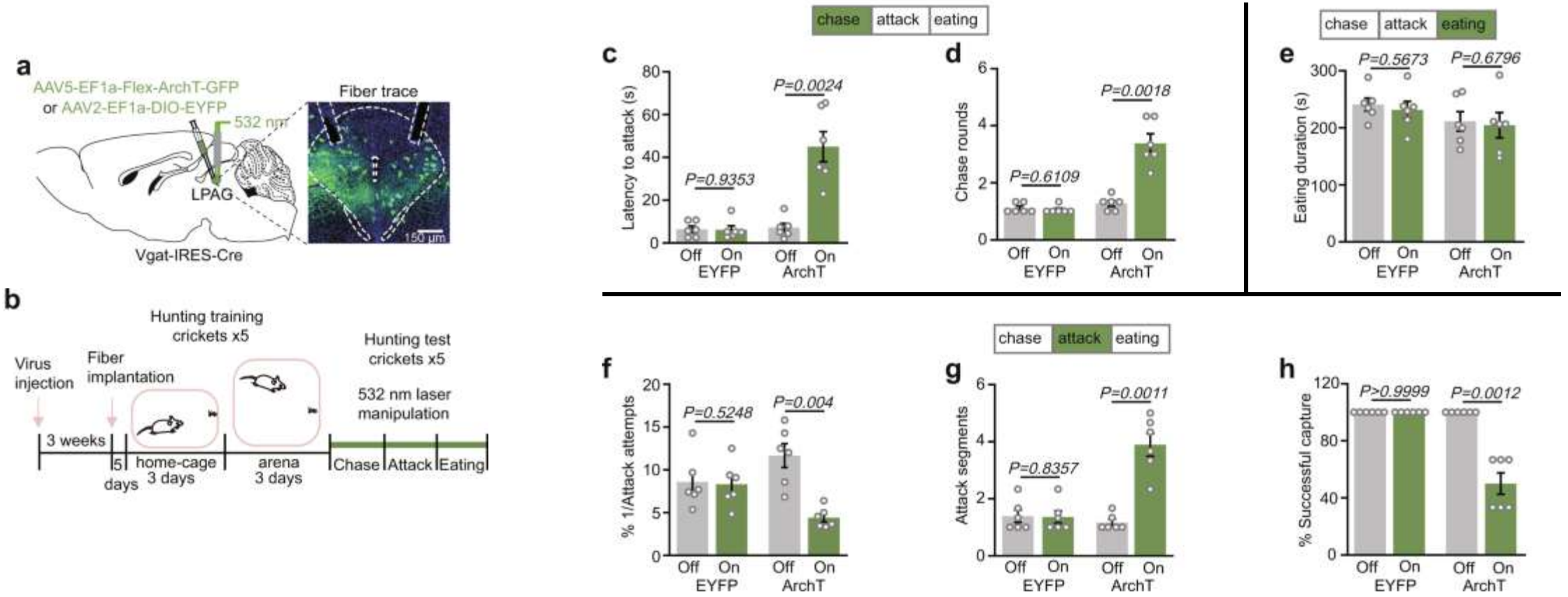
Mobile visual stimuli can cause strong responses from LPAG neurons



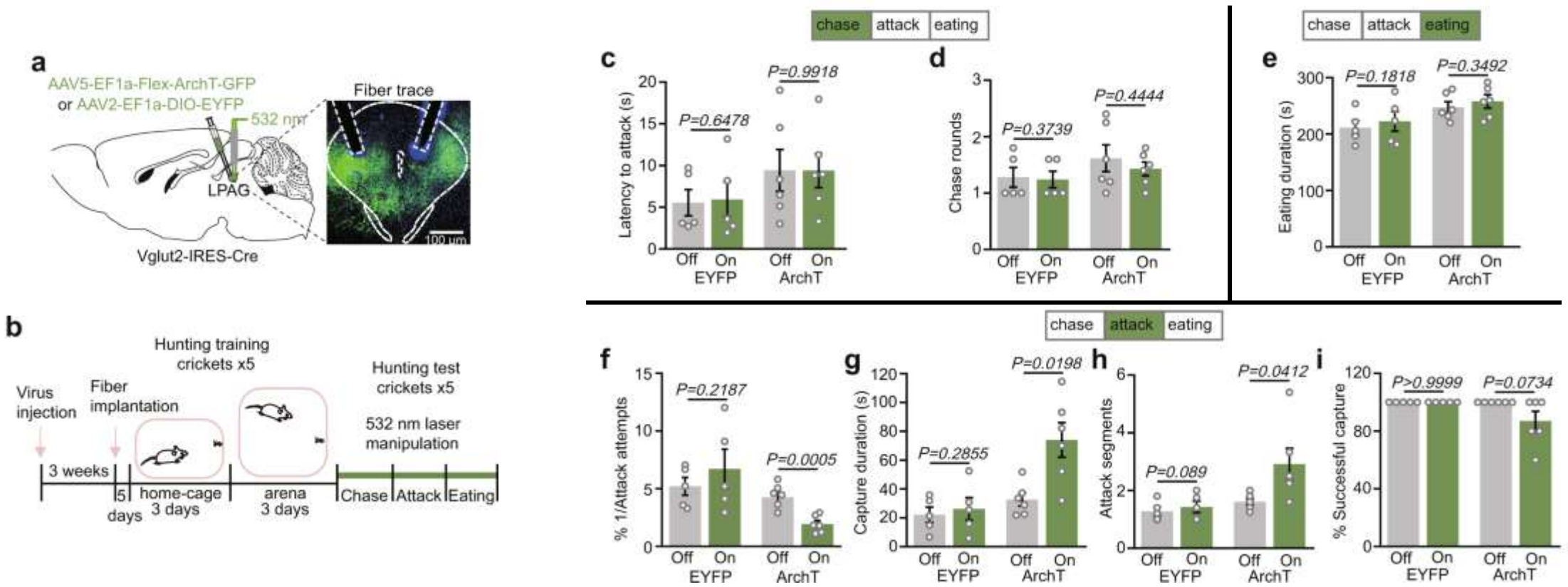
Two types of LPAG neurons are activated in different stages of hunting



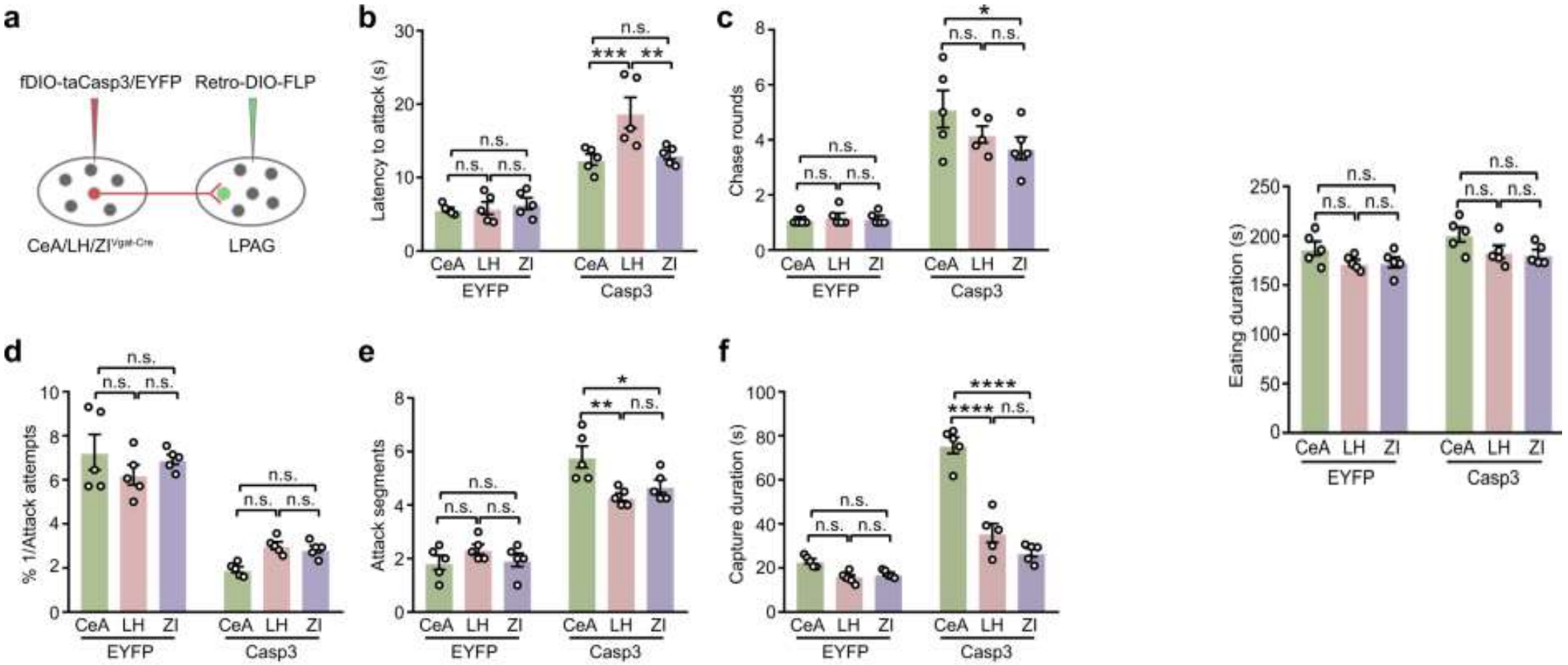
Inactivation of LPAG^{Vgat} neurons inhibits chasing and attacking



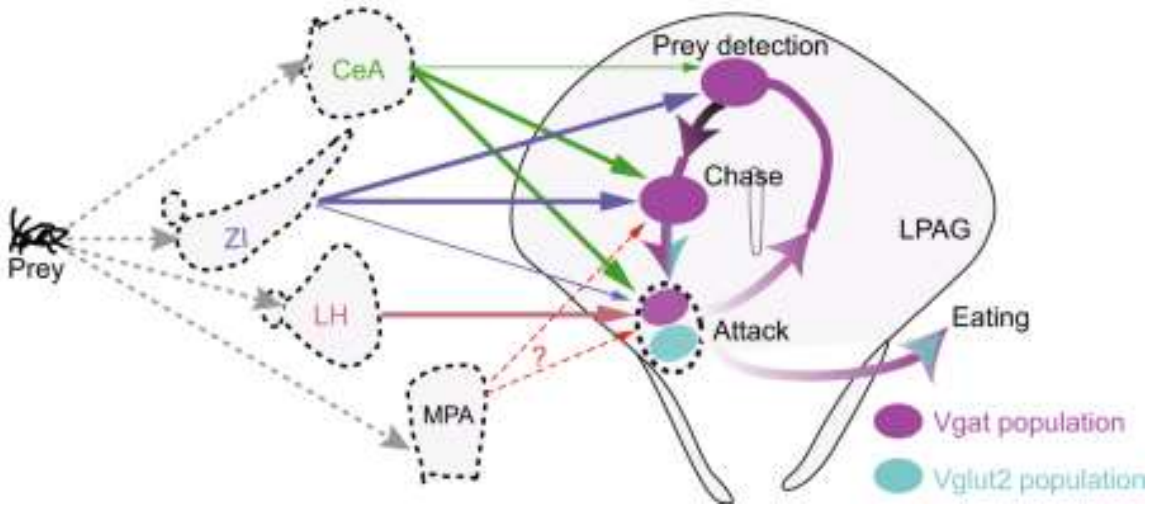
Inactivation of LPAG^{Vglut2} neurons specifically inhibiting attacks



The loss of any afferents will weaken hunting behavior



Summary



- The behavioral sequence is maintained by the sequential activation of neurons
- Afferents have impacts on the sequence behavior

Why do afferents affect the entire hunting process?

Current Biology

CellPress

Volume 30, Issue 1, 6 January 2020, Pages 54-69.e9

Article

Deconstructing Hunting Behavior Reveals a Tightly Coupled Stimulus-Response Loop

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Herwig Baier [1,4]

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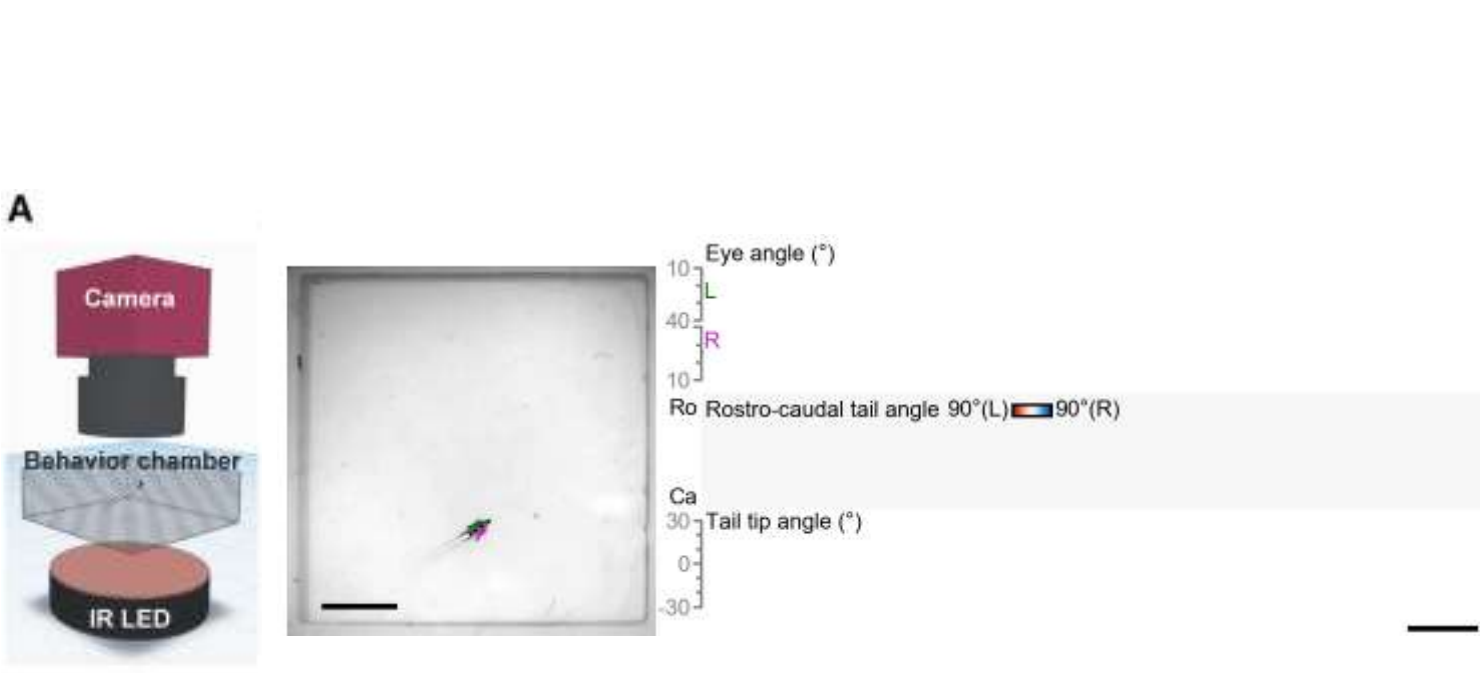
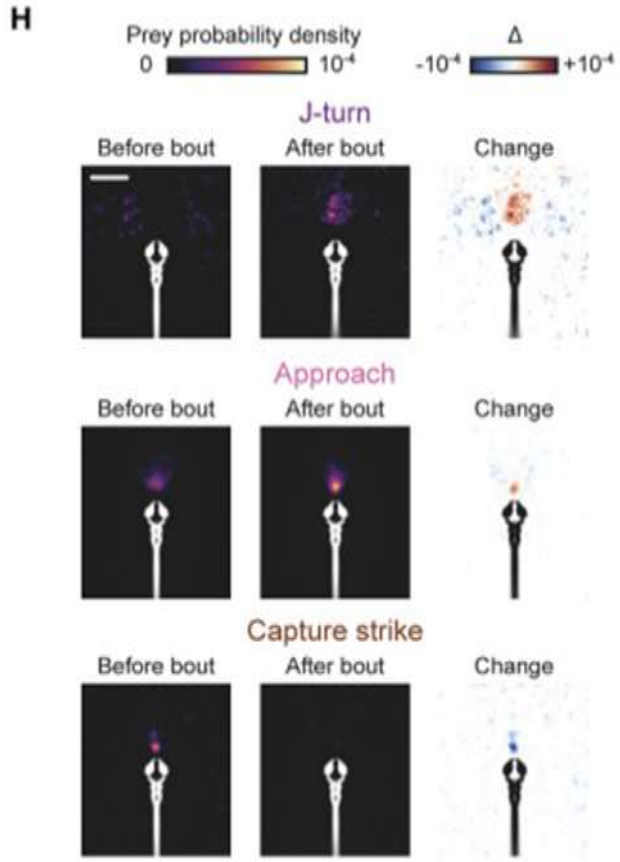
Research overview

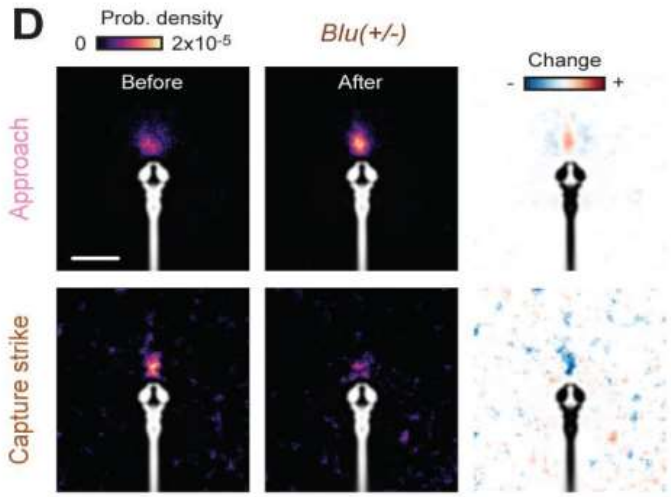
All sensory perception and every coordinated movement, as well as feelings, memories and motivation, arise from the bustling activity of many millions of interconnected cells in the brain. The ultimate function of this elaborate network is to generate behavior. We use zebrafish as our experimental model, employing a diverse array of molecular, genetic, optical, connectomic, behavioral and computational approaches. The goal of our research is to understand how neuronal circuits integrate sensory inputs and internal state and convert this information into behavioral responses.

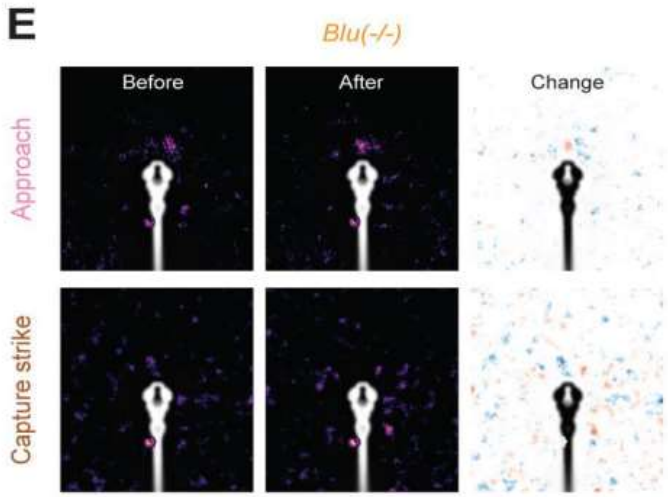
The hunting behavior of zebrafish



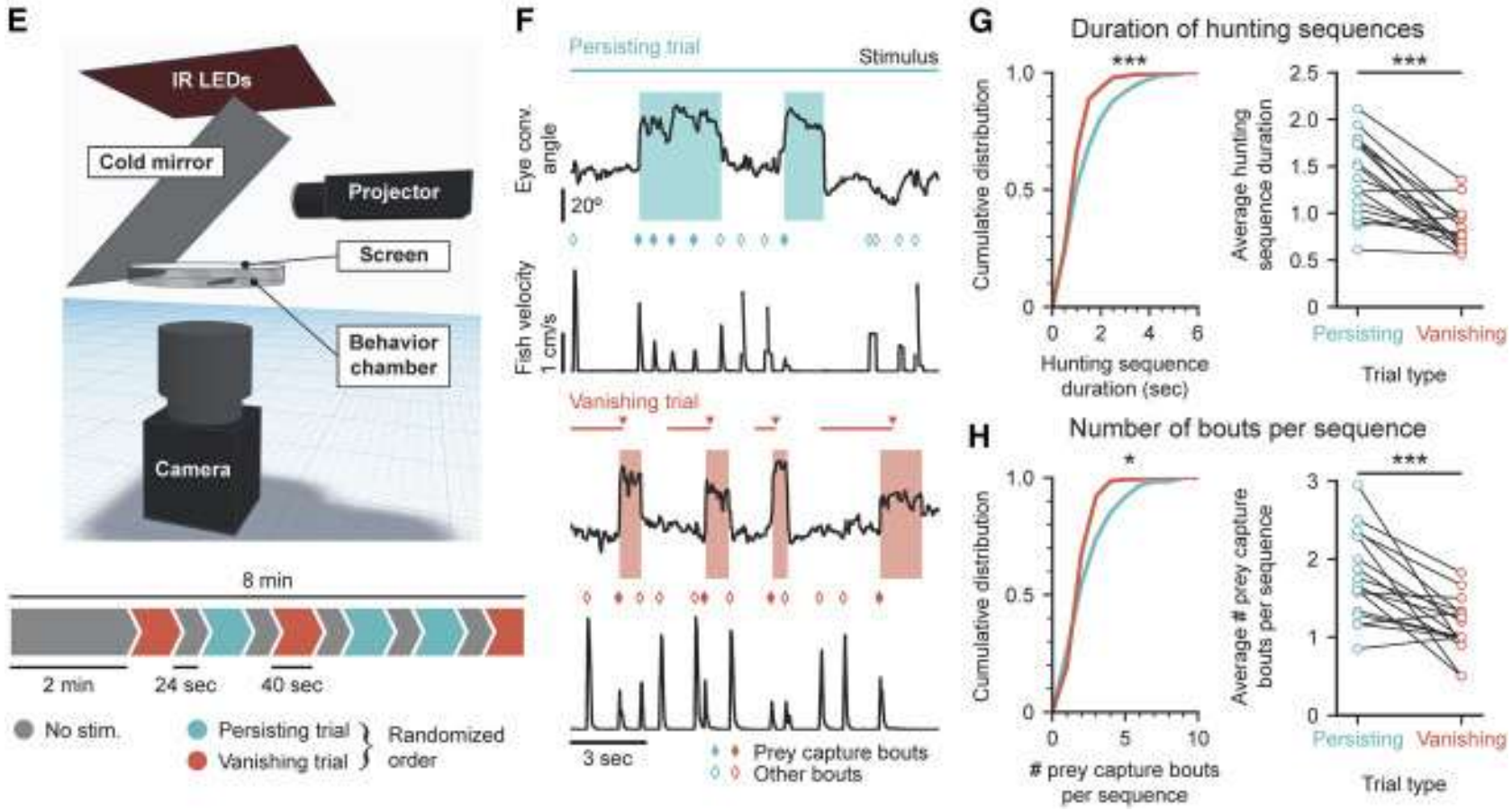


Visual information is crucial for initiating hunting

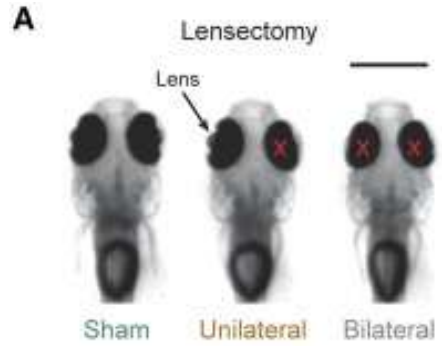


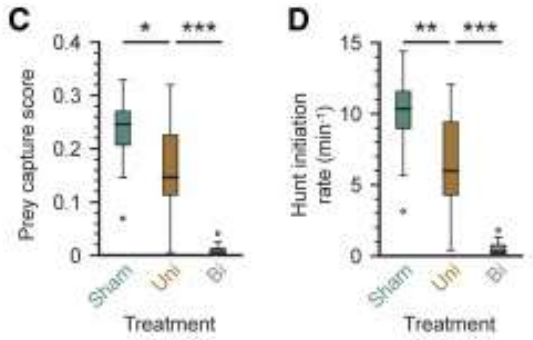


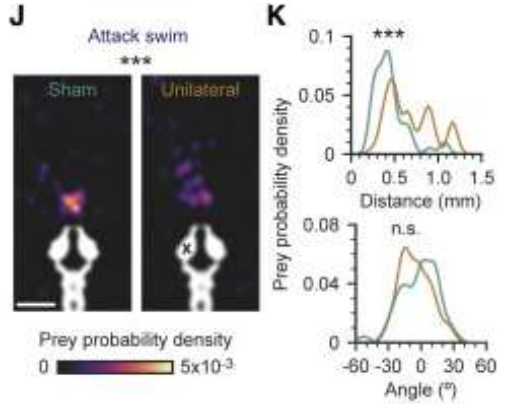
The disappearance of target can affect the normal progression of hunting behavior

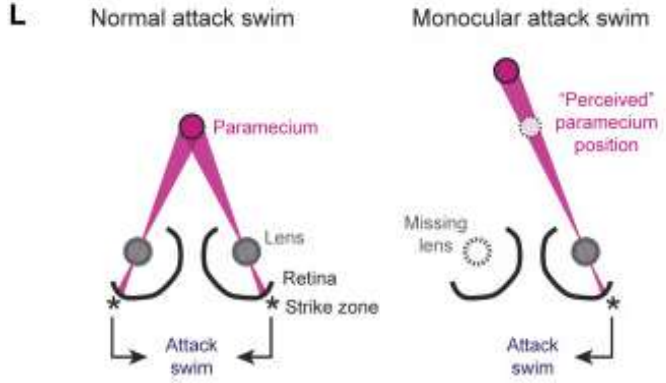


Monocular vision is responsible for the continuity of hunting, while binocular vision participates in the accurate subsequent process









Take home messages

- The ordered activation of neurons forms a stereotyped sequence of behavior
- The continuous input of sensory information ensures the accuracy of behavioral sequences

References

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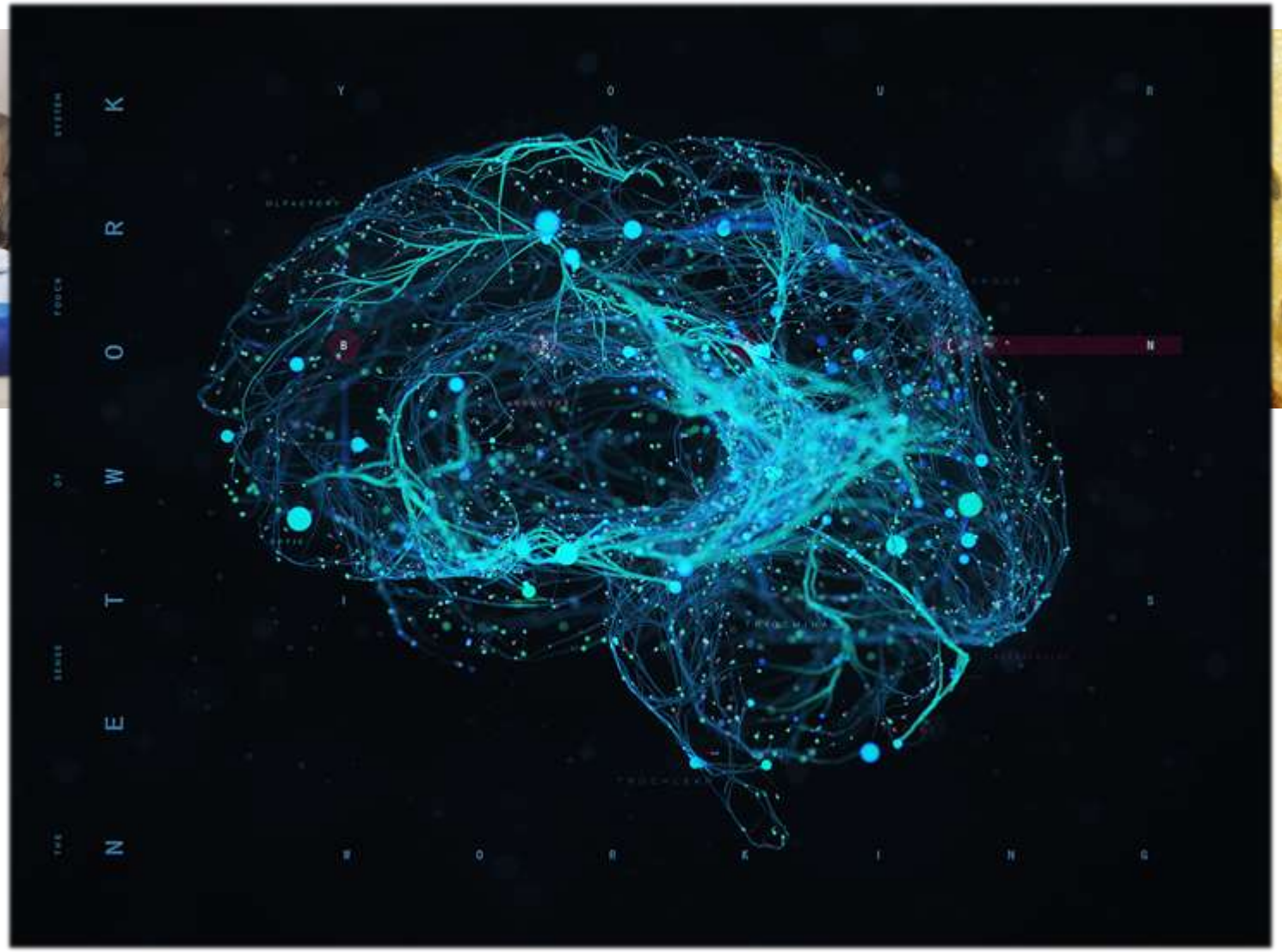
Thank you

Fragmentation of feeding behavior caused by environment and motivation

姜思梅

2024.01.25

Feeding is the first priority



Sustained disturbance of feeding-related behaviors lead to a variety of diseases

神经性贪食症

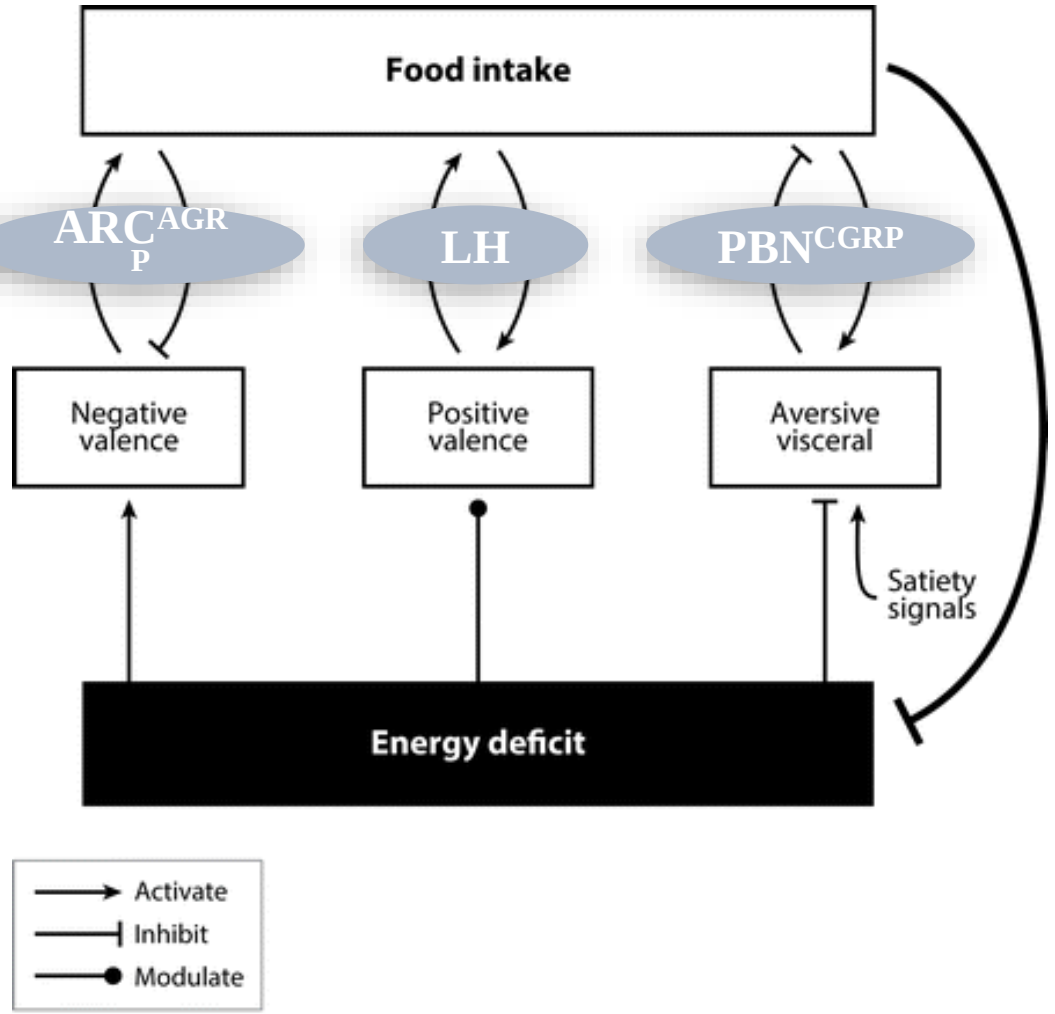
神经性厌食症

异食癖

反刍症

How is feeding behavior regulated?

Three pillars for the neural control of appetite

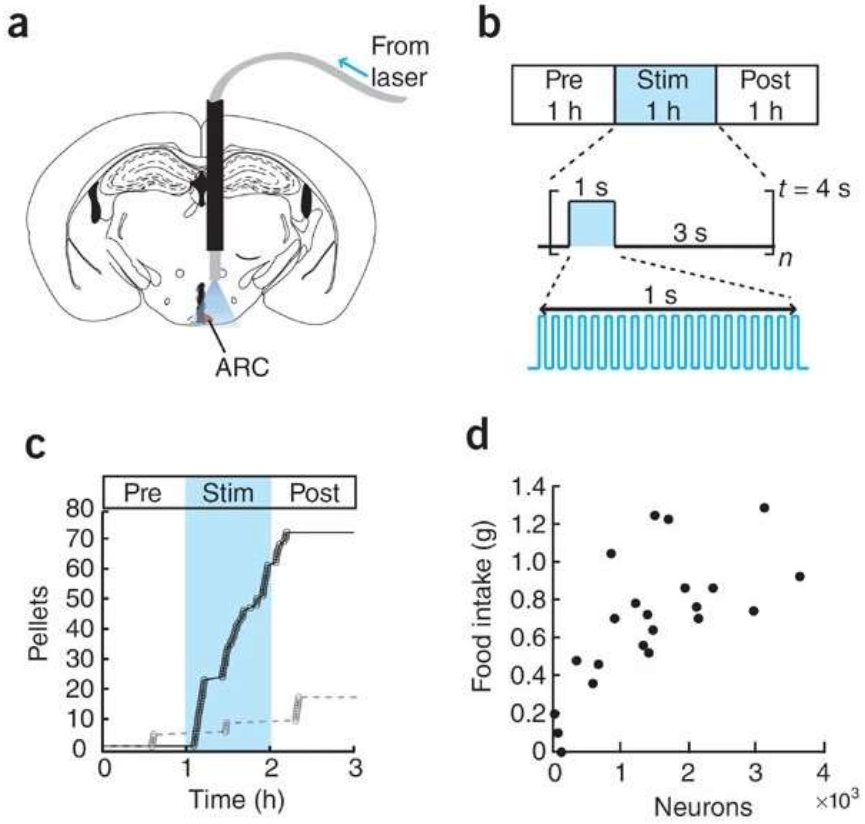


ARC：下丘脑弓状核
LH：外侧下丘脑
PBN：臂旁核

Sternson SM, et al. *Annu Rev Physiol*. 2017

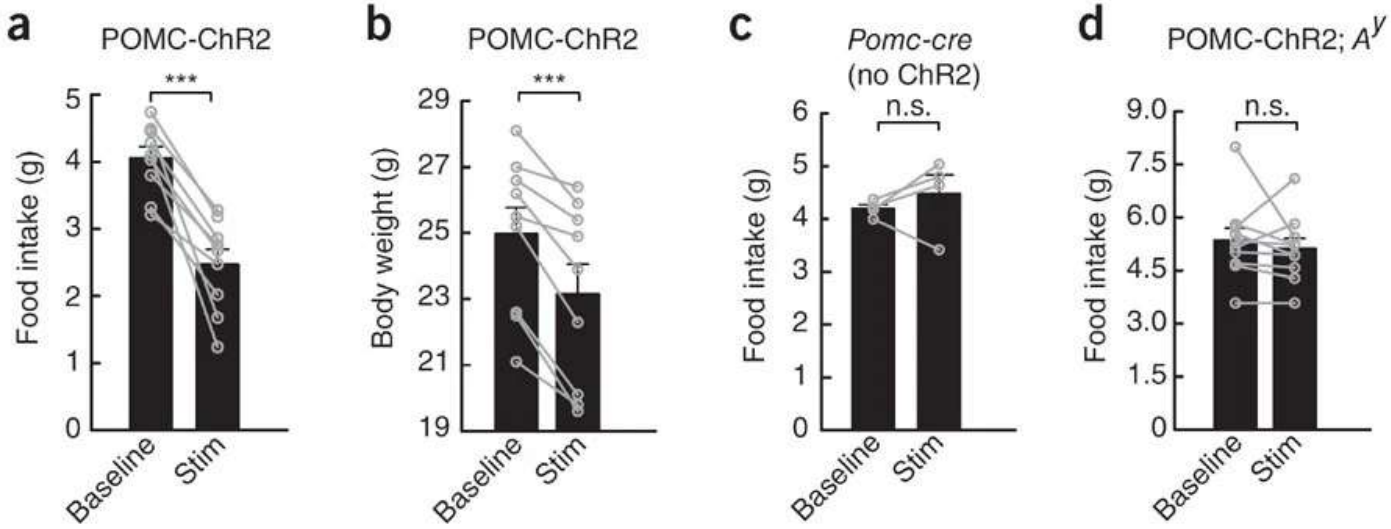
$ARC^{AGRP} \rightarrow ARC^{POMC}$

In the ARC, AGRP neurons inhibit POMC neurons.



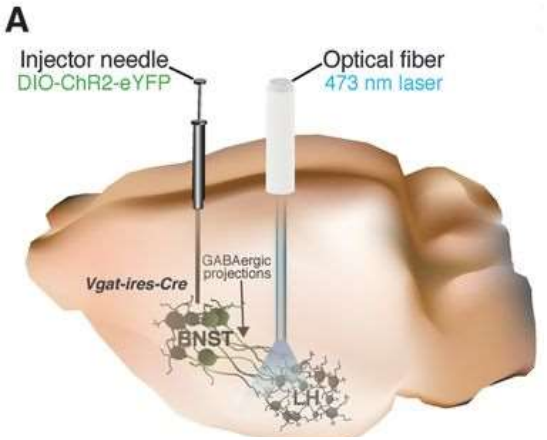
promote feeding

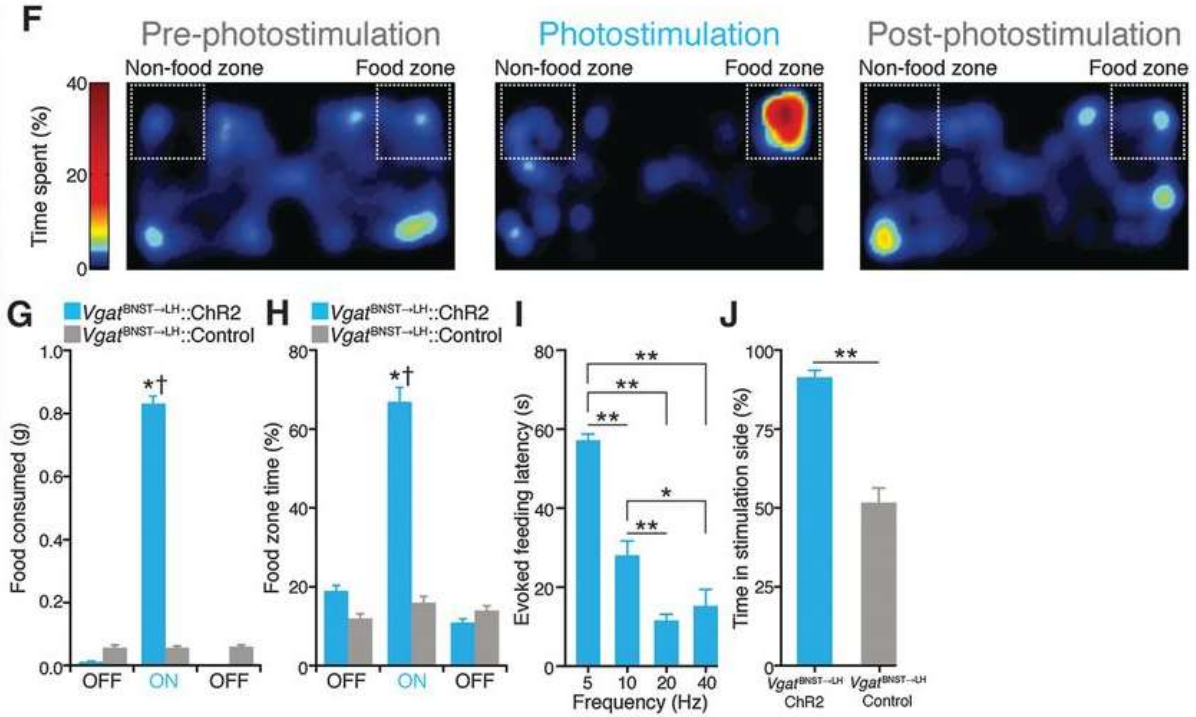
inhibit feeding

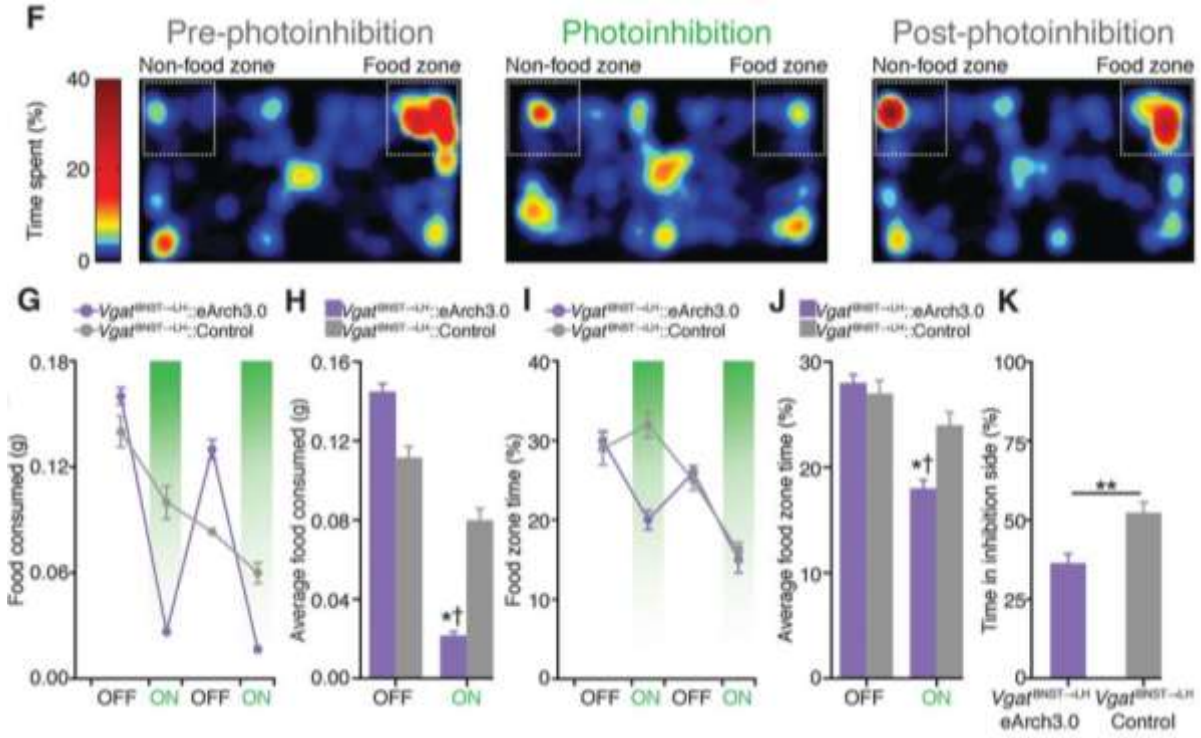


Aponte Y, et al. *Nat Neurosci*. 2011

$Vgat^{BNST} \rightarrow Vglut2^{LH}$

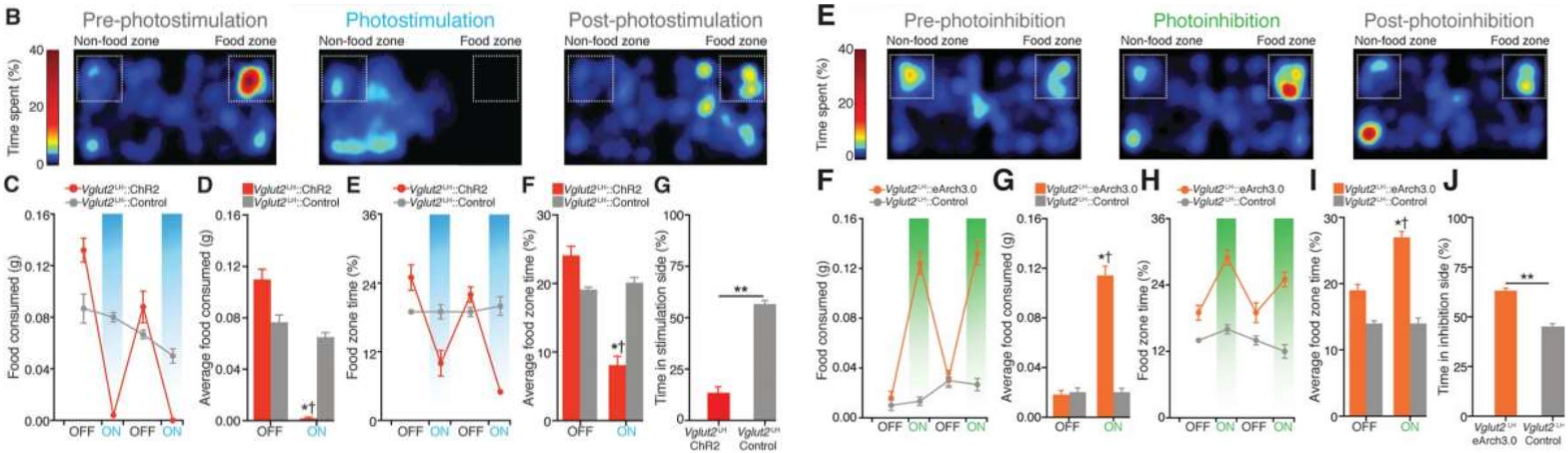






BNST：终纹床核

Jennings JH, et al. *Science*. 2013

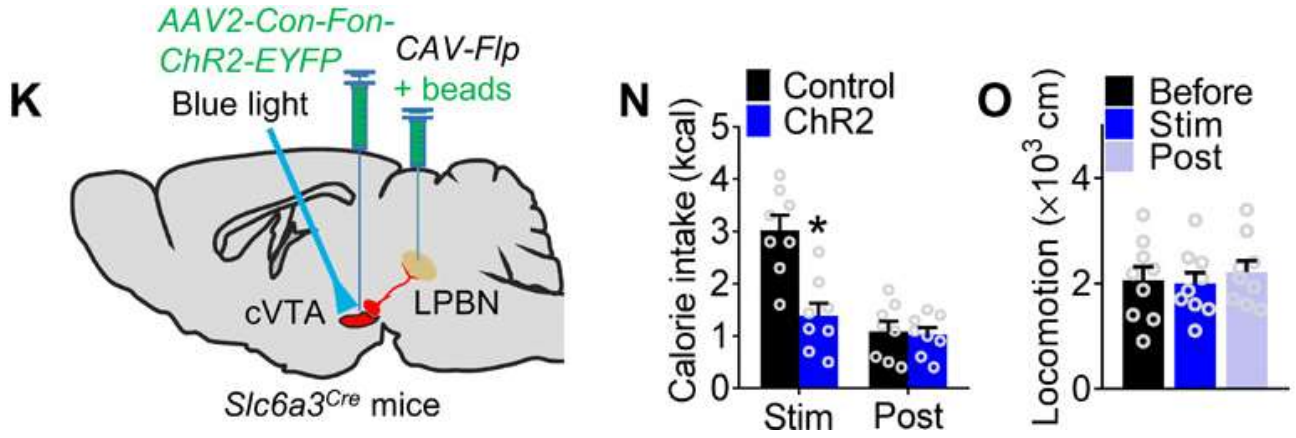


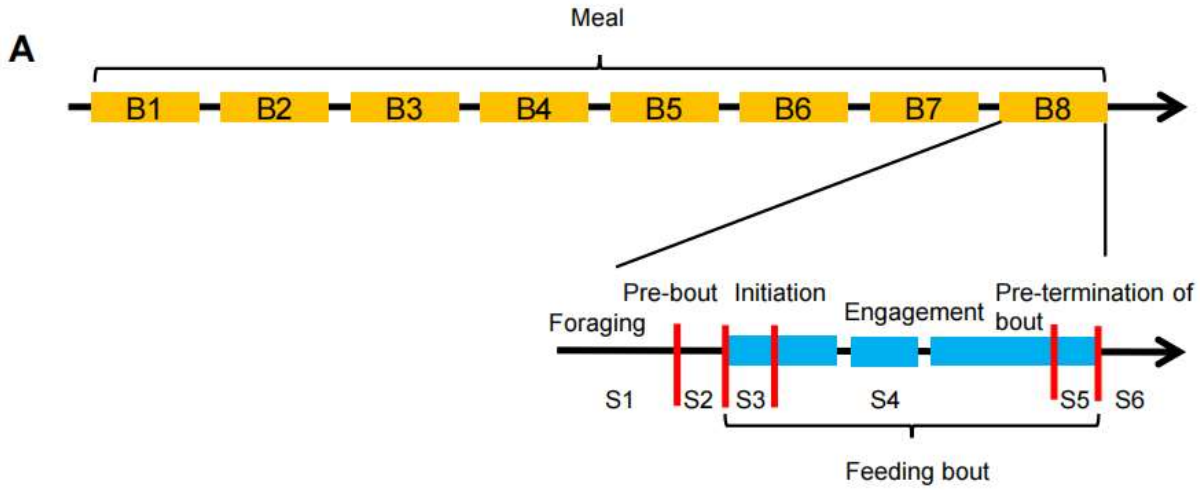
Jennings JH, et al. *Science*. 2013

What factors influence feeding behavior?

- ✓ Hunger or satiety signal（Intrinsic drive）
- ✓ Environmental factor（Extrinsic motivation）
  -
  -
  -

$DA^{cVTA} \rightarrow DRD1^{LPBN}$

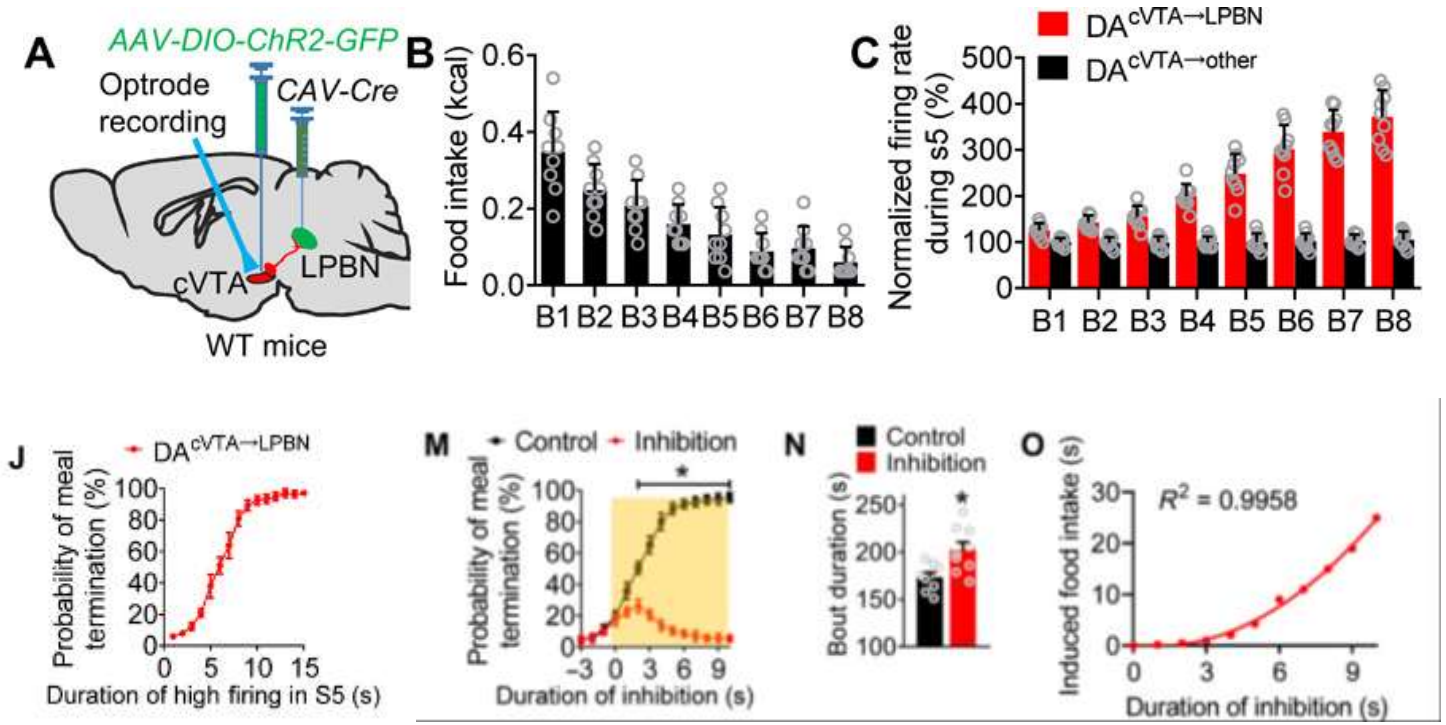




A typical meal consists of ~8 bouts (B1-B8).

Each feeding bout can be divided into 6 stages: foraging stage (S1); pre-meal stage (S2), 10 s before eating; initiation stage (S3), 10 s after eating; engagement stage (S4); pre-termination stage (S5), 10 s before bout cessation; inter-bout stage (S6).

Han Y, et al. *Sci Adv*. 2021



Han Y, et al. *Sci Adv*. 2021

Feeding behavior ≠ Food intake
Duration of feeding

For the first time, the team elucidated the sequential neuroregulatory mechanism of the whole process of feeding.

王立平

中国科学院深圳先进技术研究院脑认知与脑疾病研究所所长、中国科学院脑科学卓越中心骨干成员，博士生导师。主要致力于精神疾病病理生理机制的研究，着重于本能恐惧情绪神经环路生理机制的跨物种解析，以及精神疾病发生的神经环路病理机制和干预策略。已发表包括Nature，Nature Neuroscience，Neuron，Nature Communications，PNAS等在内的SCI论文68篇（其中第一作者/通讯作者Nature及其子刊论文7篇）。

主要研究方向及内容

1、非习得性恐惧的神经环路基础

以啮齿类和非人灵长类动物模型为研究对象，来解析非习得性恐惧，尤其是基于视觉刺激的非习得性恐惧的皮层下神经环路基础及其调控机制。基于此，还将进一步探索非习得性恐惧神经环路与习得性恐惧以及其他生存环路，如代谢等的相互调控机制。

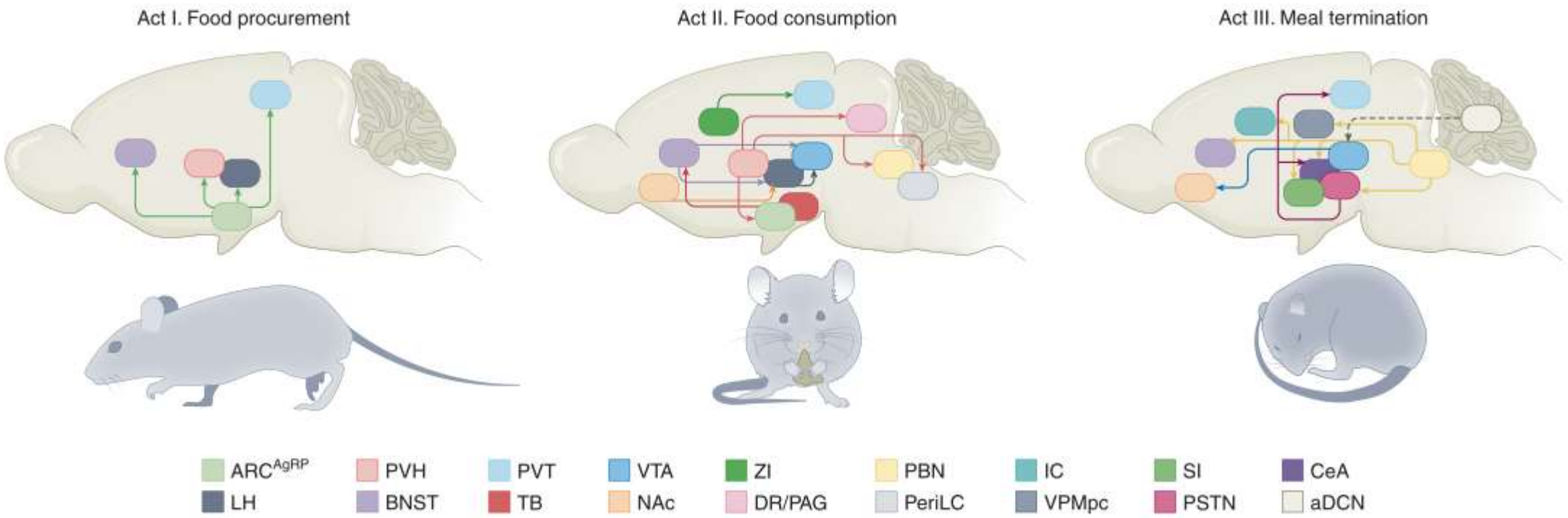
2、精神疾病神经环路层面的发生机制

研究导致精神分裂症、自闭症、多动症、抑郁症和双向情感障碍等精神疾病可能共有的症候，如情绪调控异常等的神经环路基础及其调控机制，进而为精神疾病的“病因”诊断提供实验依据。

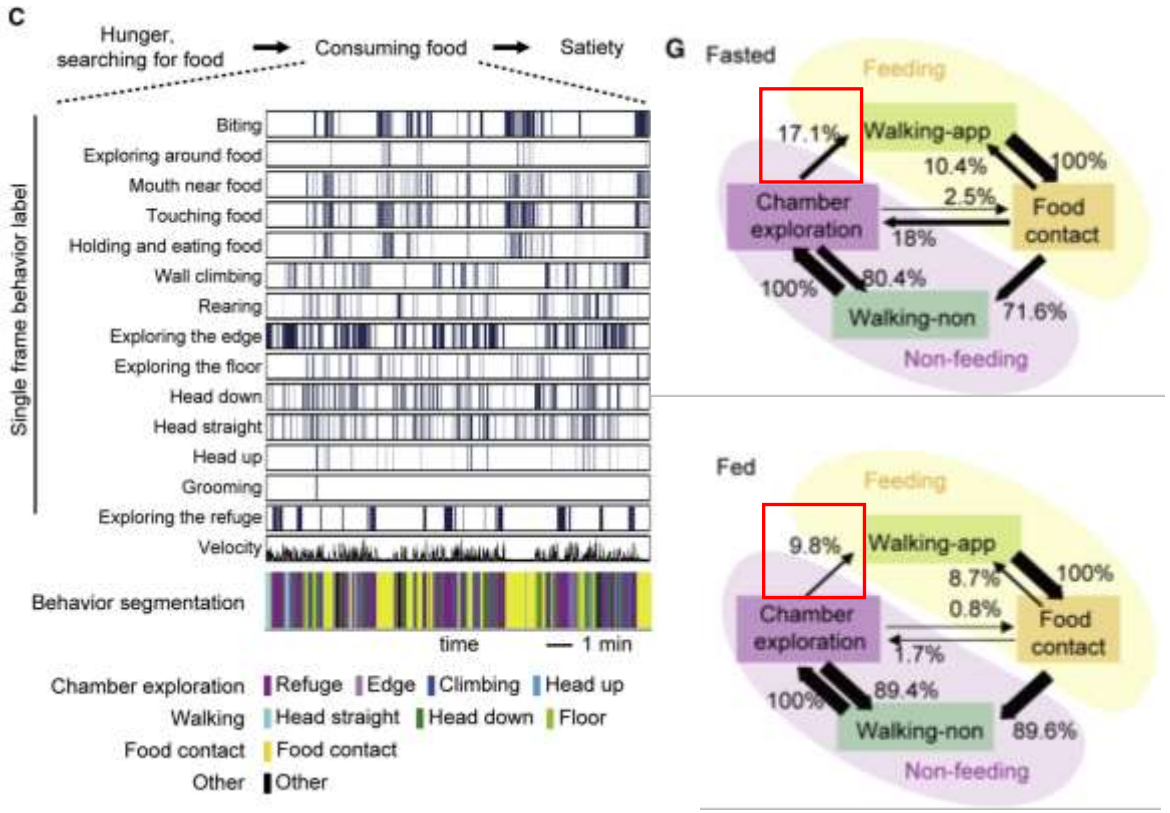
3、光遗传神经调控技术的研发

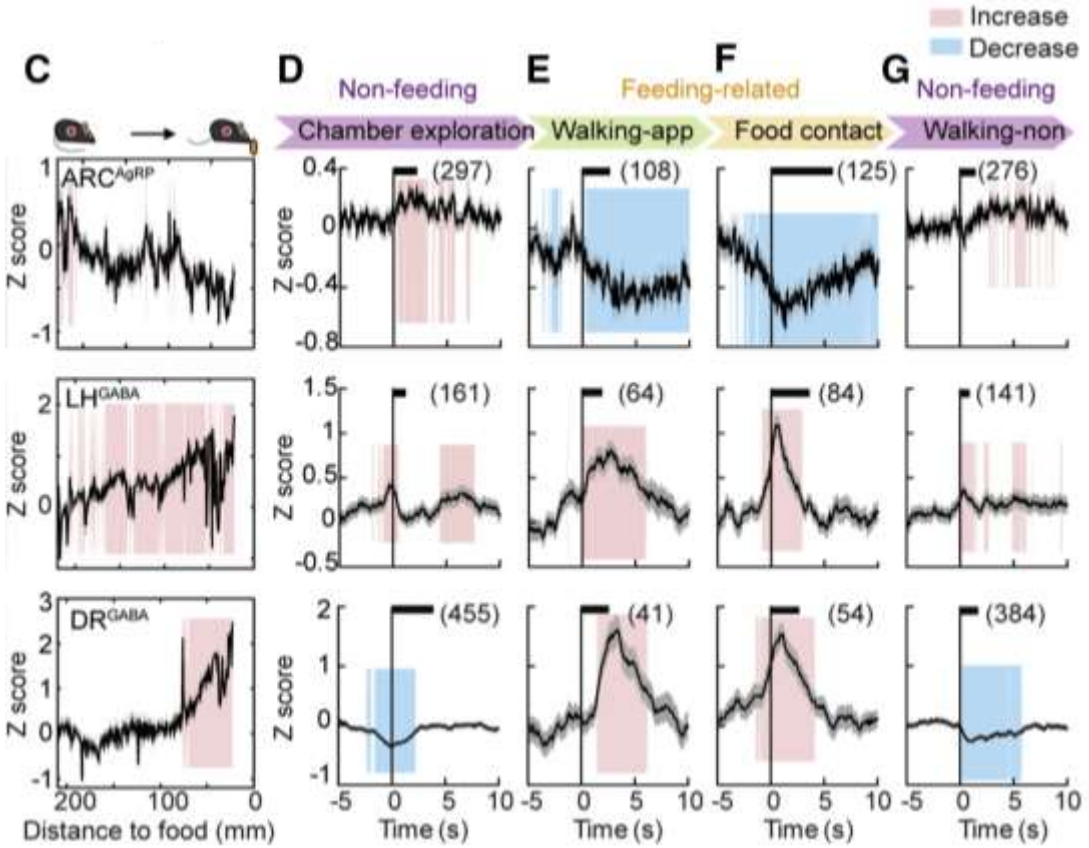
基于已经建立的光遗传神经调控技术研发，应用与资源共享平台，通过多个实验室合作，结合电生理、光学成像和磁共振技术来研究神经信号，包括神经节律震荡信号，磁共振信号的细胞起源。

The neural circuits underlying the phasic complexity and sequential nature of feeding



Alcantara IC, et al. *Nat Metab*. 2022

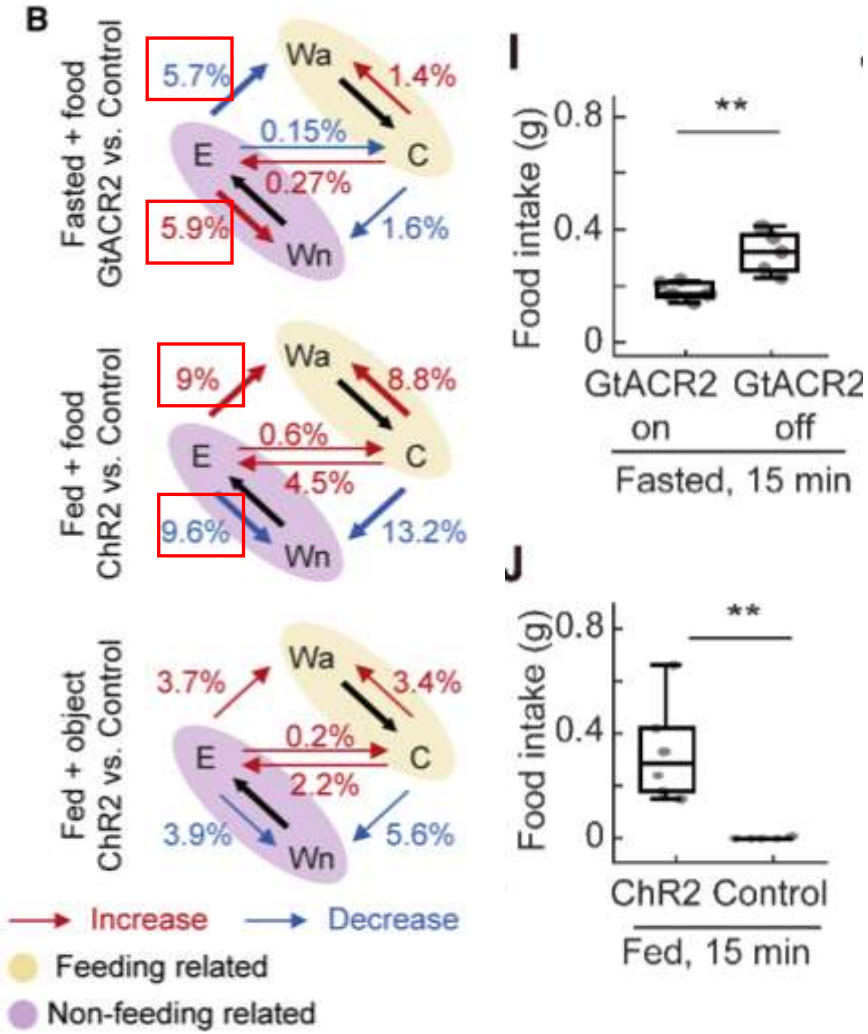




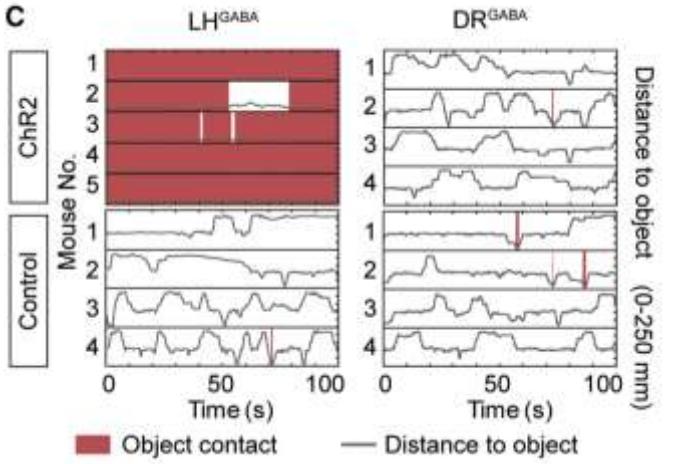
Food consumption can be thought of as not simply fulfilling appetite, but a dynamic competition between appetite and other conflicting motivations.

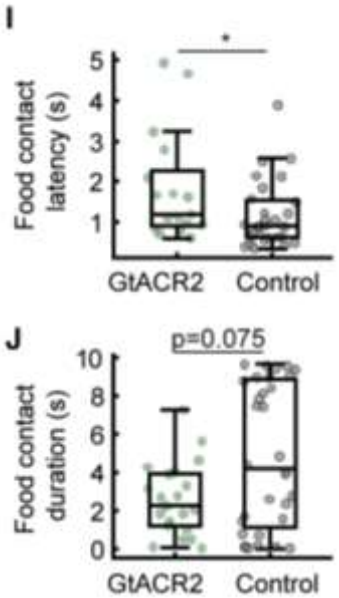
Liu QQ, et al. *Neuron*. 2023

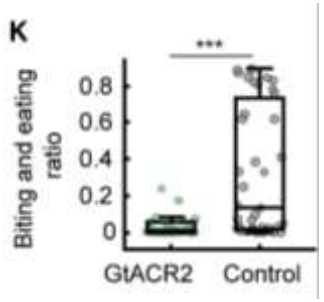
ARC^{AgRP} neurons



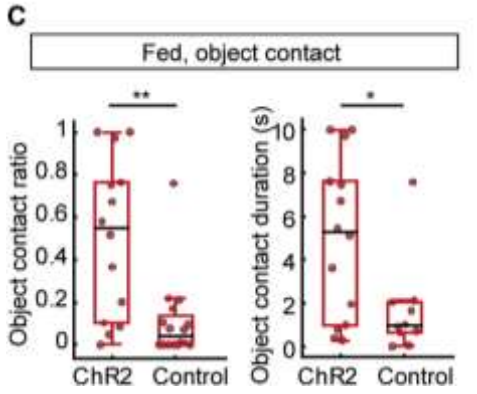
LH^{GABA} neurons

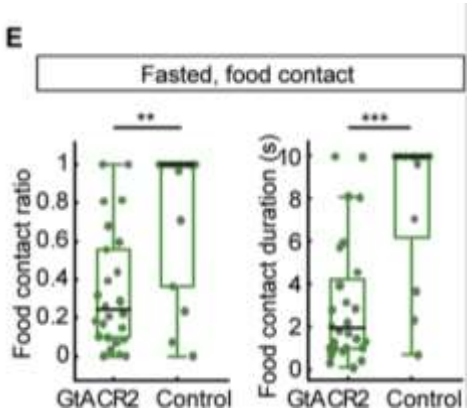




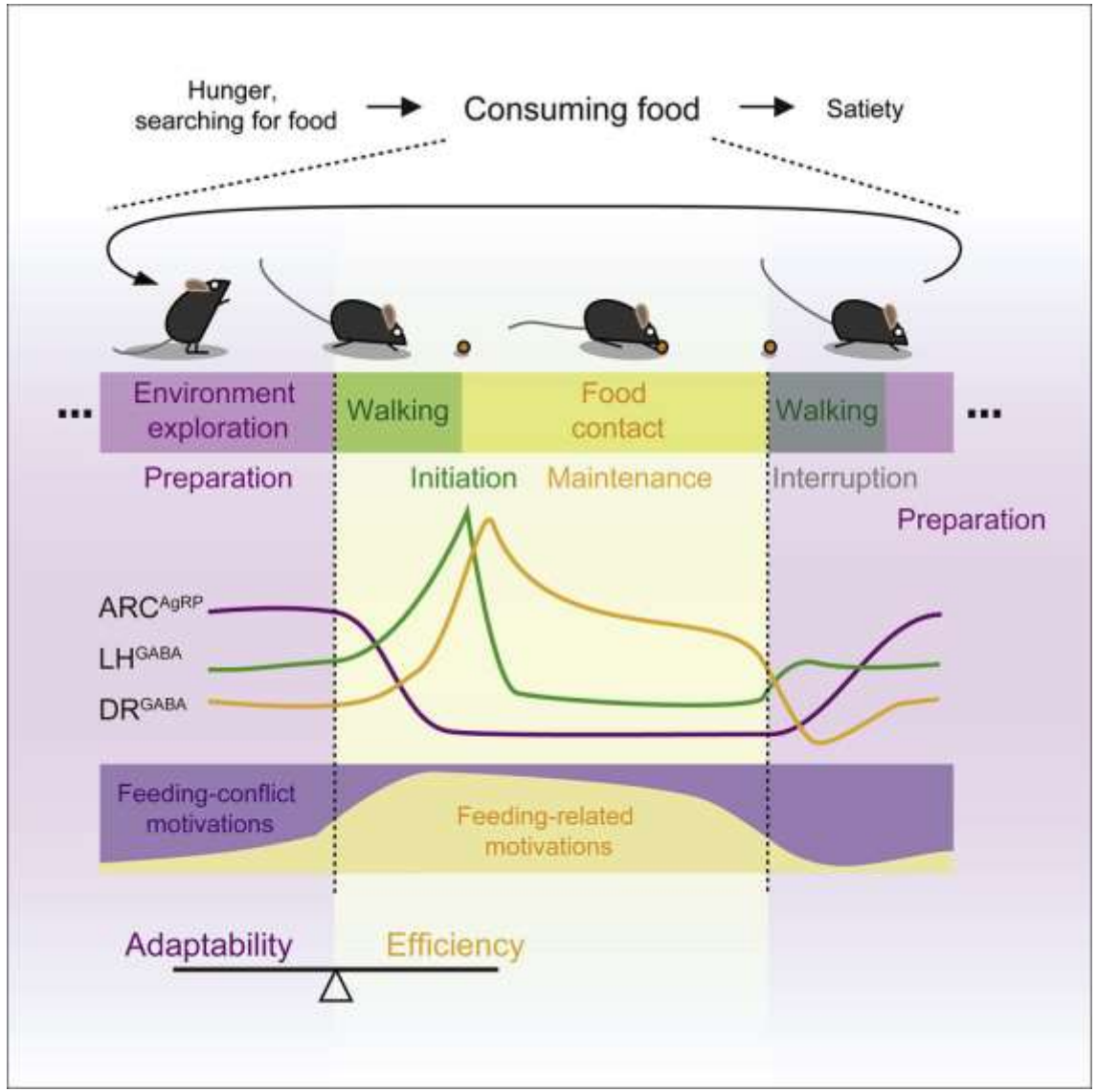


DR^{GABA} neurons





Liu QQ, et al. *Neuron*. 2023



"ARC^{AgRP}, LH^{GABA} and DR^{GABA} neurons function successively to regulate the preparation, initiation and maintenance of segmented feeding behaviors, respectively".

Summary

- Feeding behavior can be regulated by multiple brain regions and neurons, which form complex neural circuits.

  For example, ARC^{AGRP}, LH, PBN^{CGRP} neurons.

- Feeding behavior can be simplified into three stages: food procurement, food consumption, and meal termination.

- ARC^{AgRP}, LH^{GABA} and DR^{GABA} neurons mediate the sequential regulation of feeding behavior.

Thank you

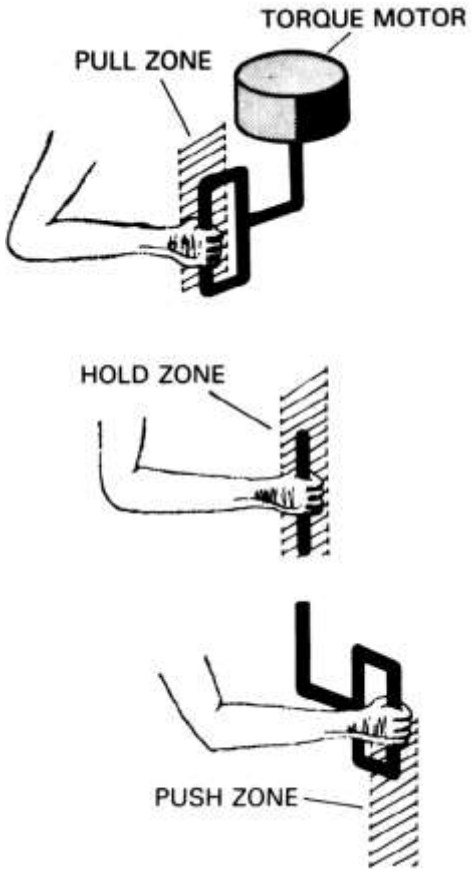
The transition mechanism between planning and execution

2024/1/25

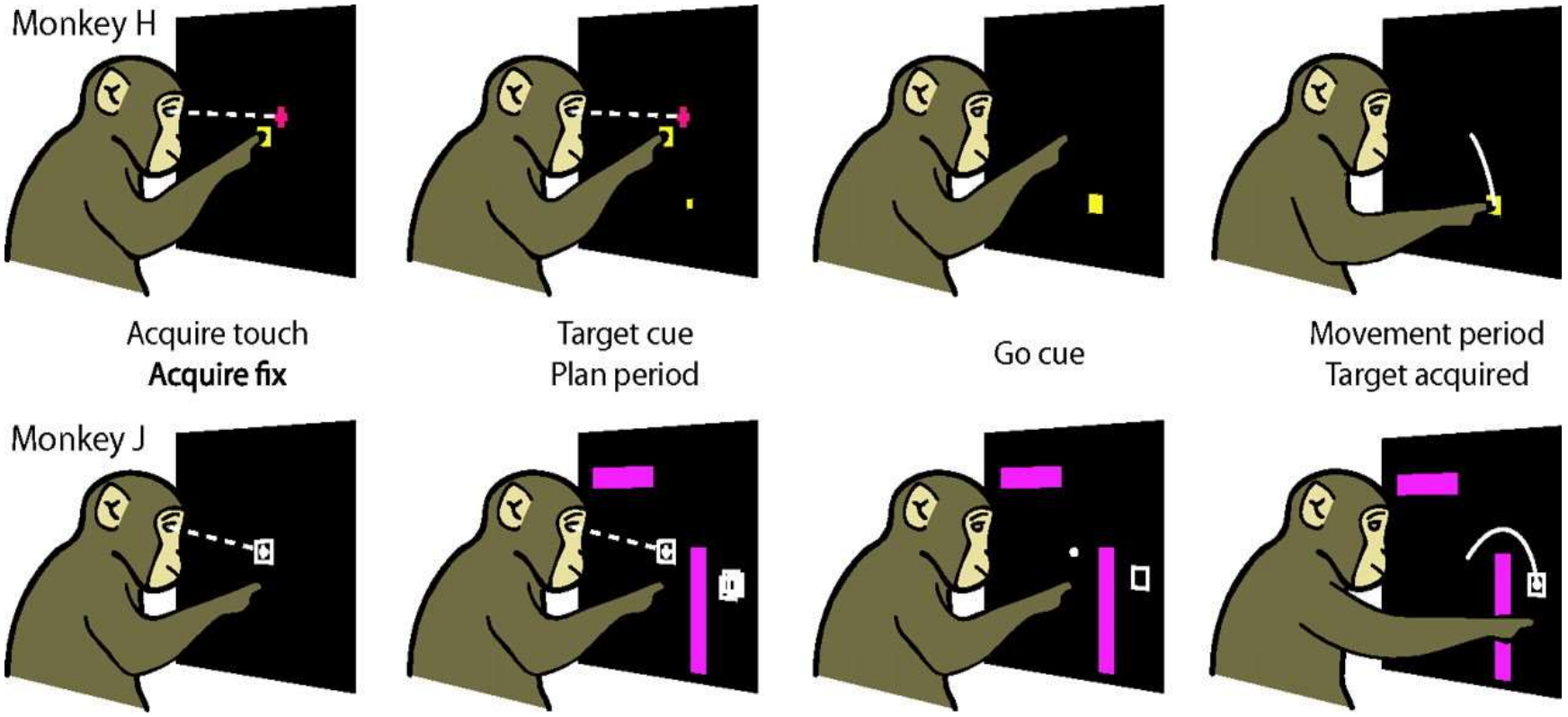
--CDL

The importance of planning and execution for human and animals?

How to study this behavior in the laboratory?

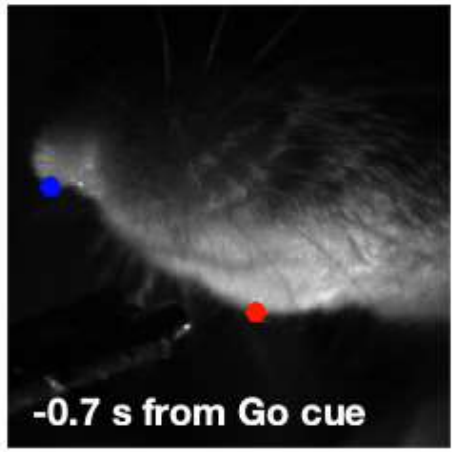


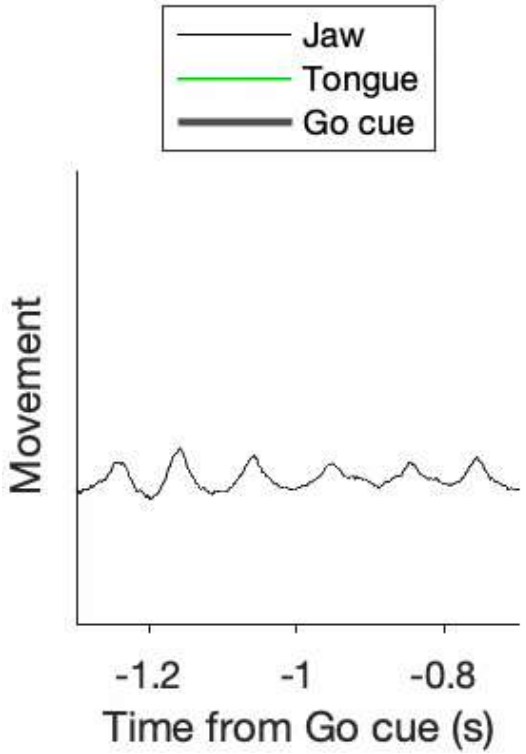
Funahashi, S.et al.*Neurophysiol*.1991.

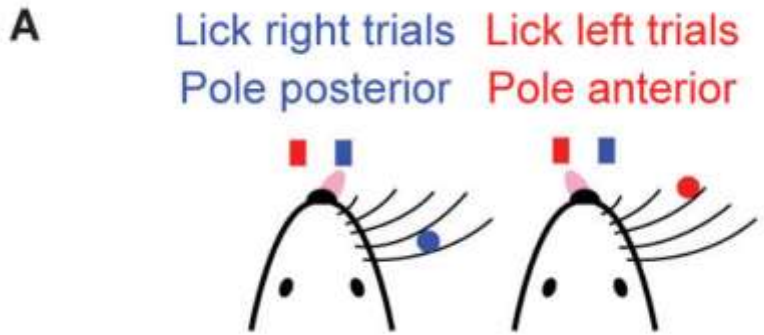


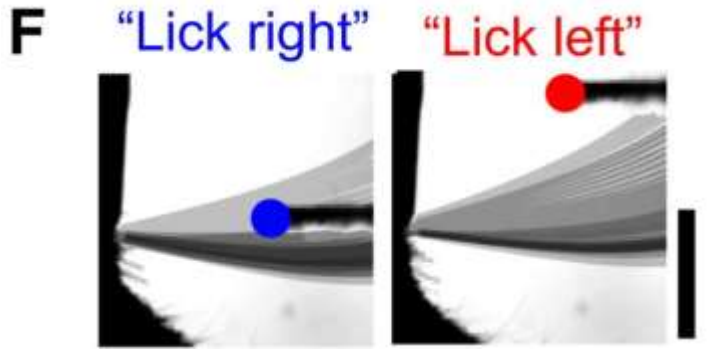
Kaufman, Matthew T et al. *Journal of neurophysiology*.2010.

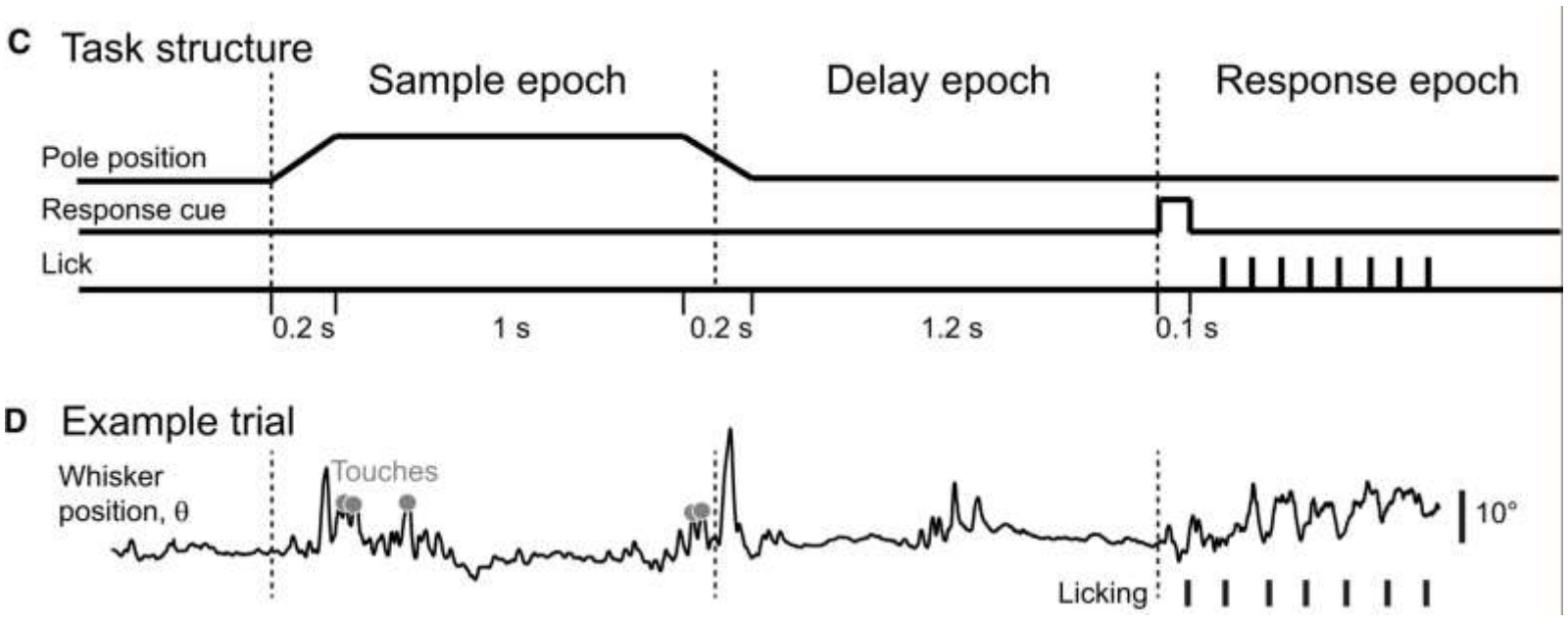
A paradigm for studying this behavior in mice.





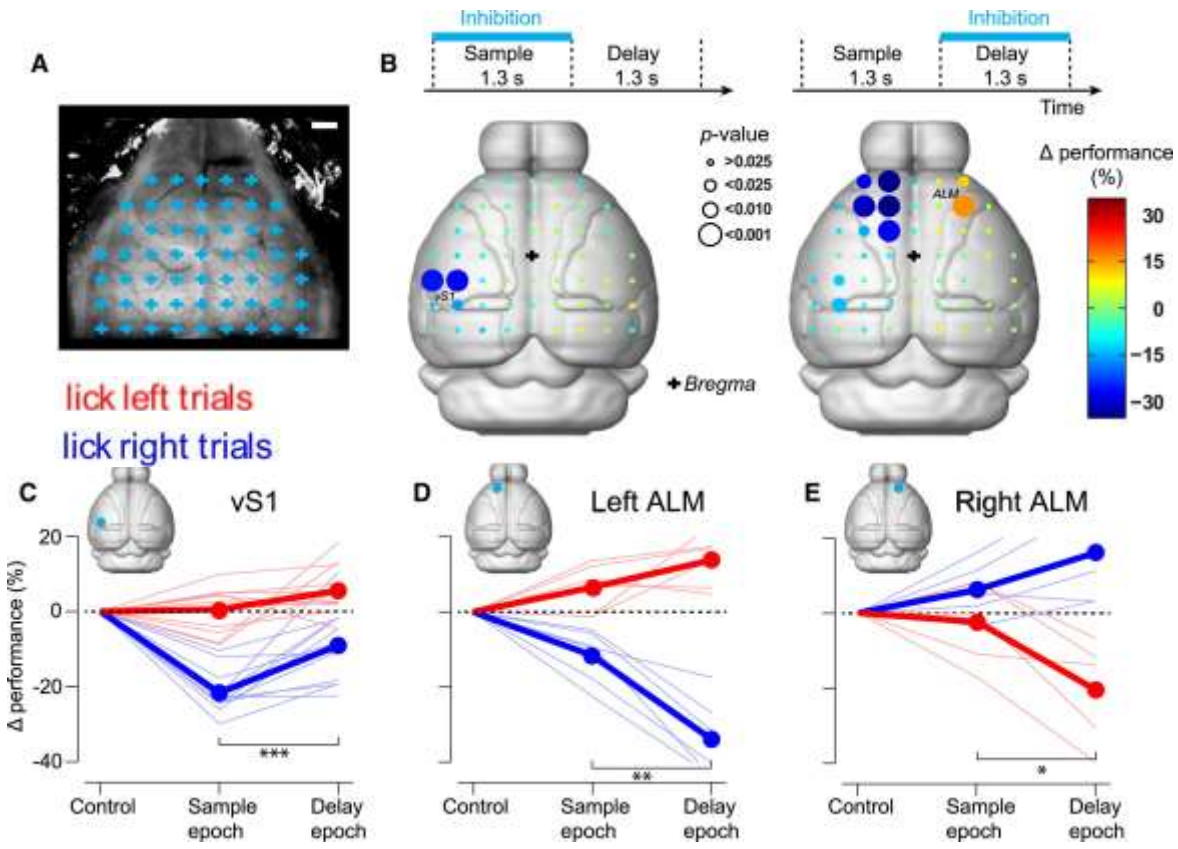


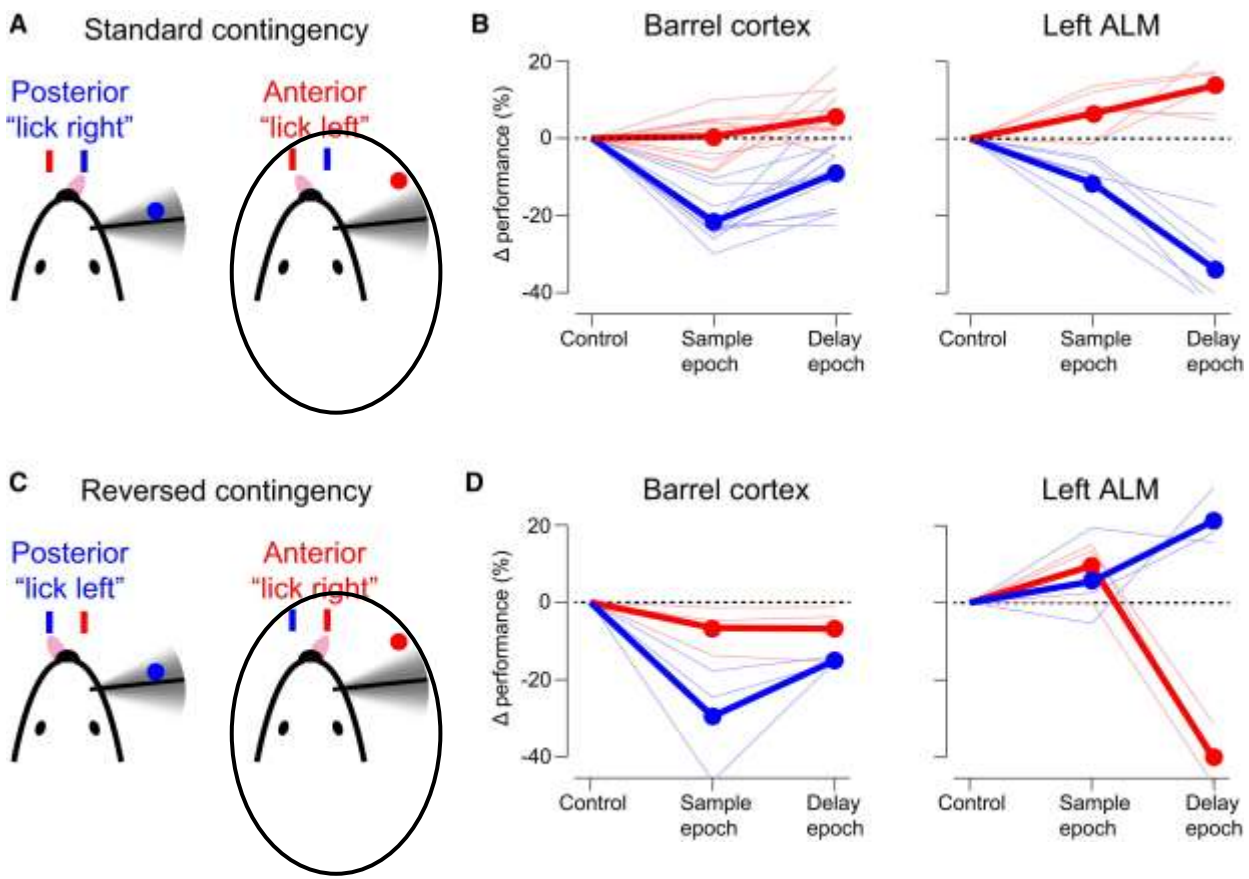




Inagaki, H. K. et al. *Cell*. 2022.

ALM involved in motor preparation

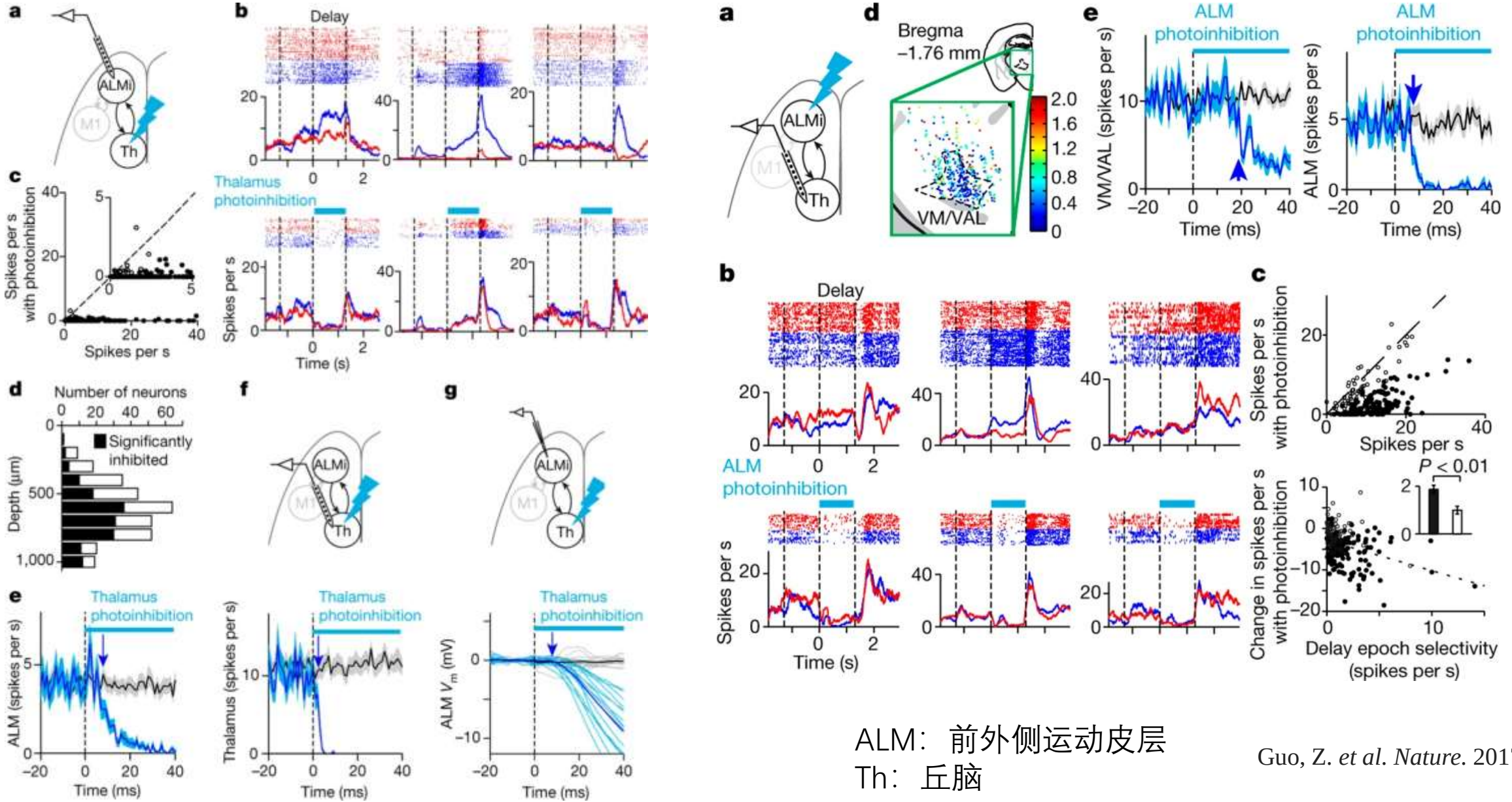




ALM：前外侧运动皮层

Guo Z V. et al. Neuron, 2014

Mutual drive of ALM and thalamus during the preparation phase



ALM：前外侧运动皮层
Th：丘脑

Guo, Z. *et al. Nature.* 2017.

What is the transition mechanism between planning and execution?

What is the transition mechanism between planning and execution?

- Subthreshold theory
- Gating theory
  - Brainstem oculomotor system
- A new theory

A midbrain-thalamus-cortex circuit reorganizes cortical dynamics to initiate movement

Hidehiko K. Inagaki[1,2,10,11,*], Susu Chen[1,3,10], Margreet C. Ridder[4], Pankaj Sah[4,5], Nuo Li[6], Zidan Yang[2], Hana Hasanbegovic[7], Zhenyu Gao[7], Charles R. Gerfen[8], Karel Svoboda[1,9,*]

Published as: *Cell.* 2022 March 17; 185(6): 1065–1081.e23.

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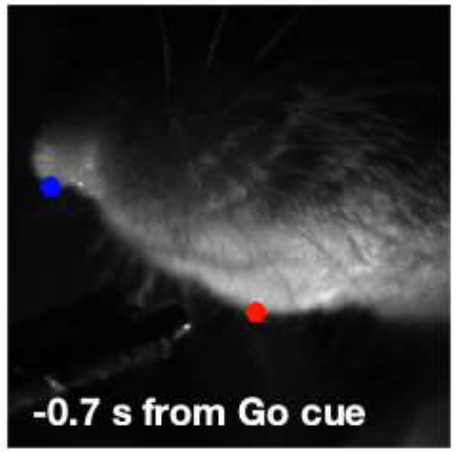
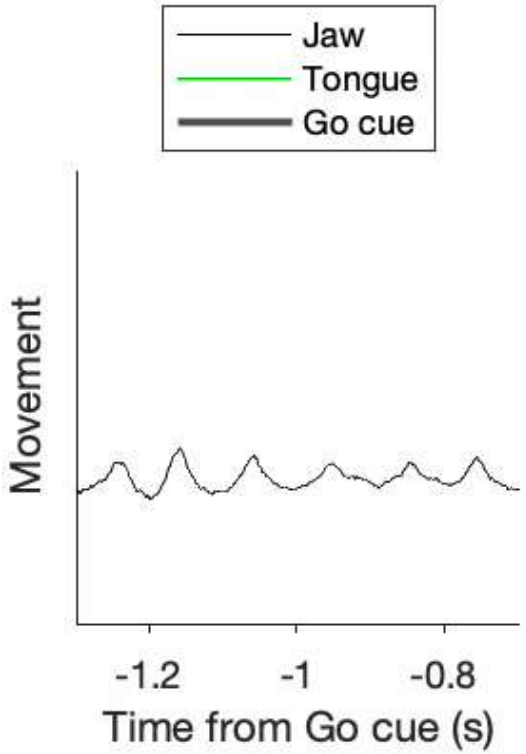
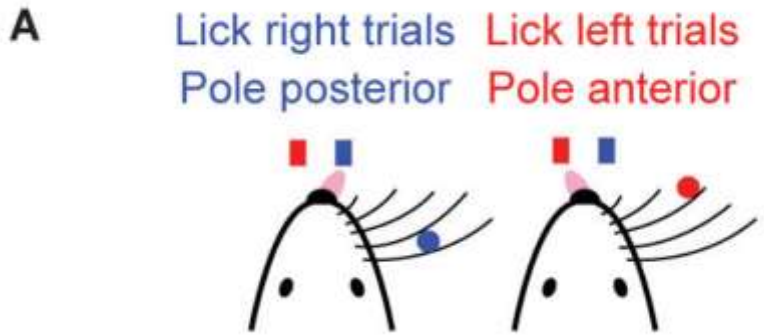
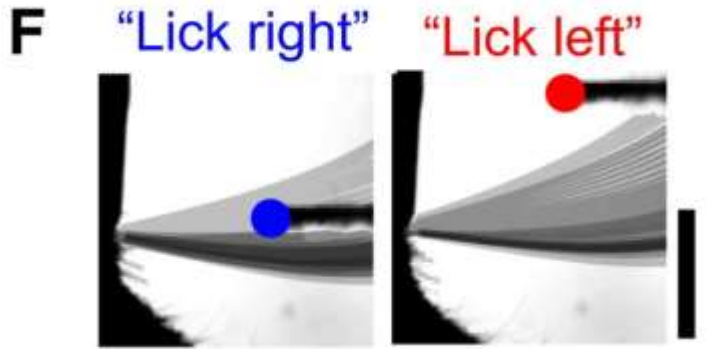
神经动力学，即神经元群体的动作电位模式，调节我们对世界的感知并驱动我们的行为。实验室的最终目标是了解神经动力学如何支持不同的认知和运动功能。目前，我们专注于运动启动和时机来研究神经元动力学如何在整个大脑中快速重新配置以控制行为。

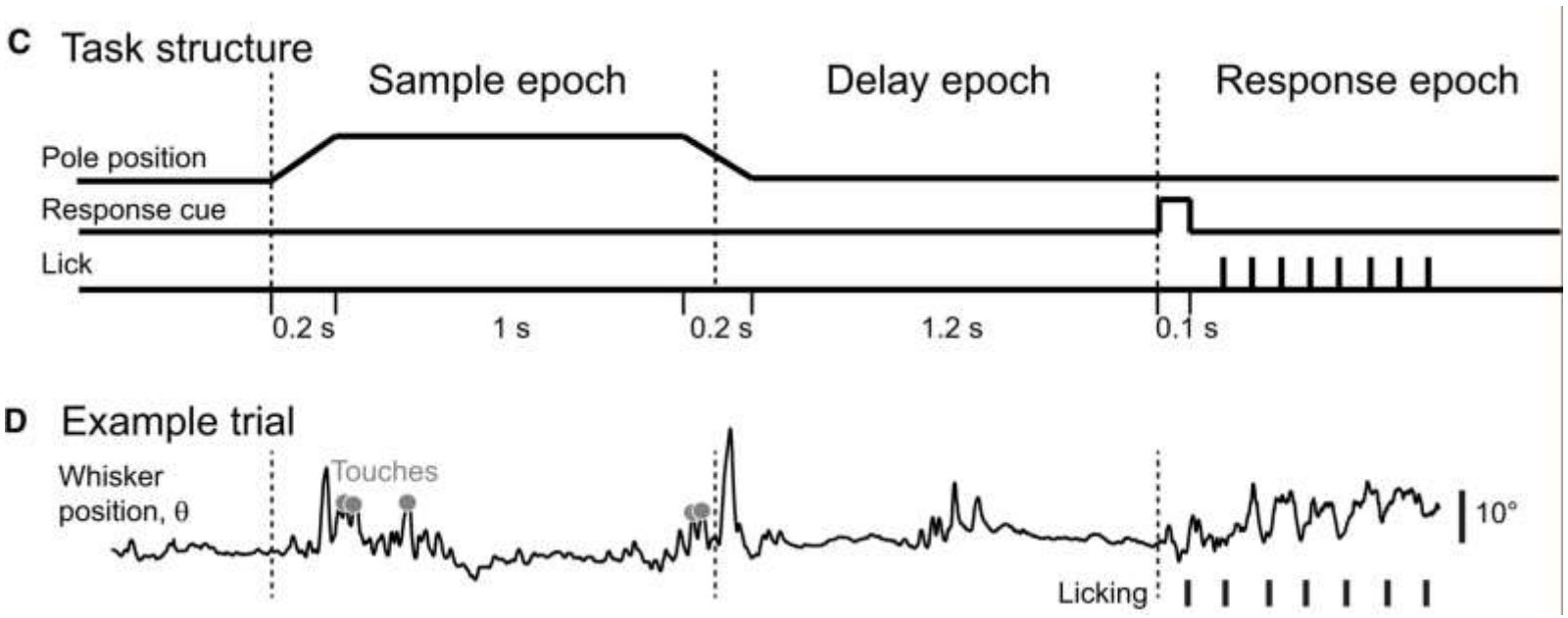
A paradigm for studying this behavior in mice.





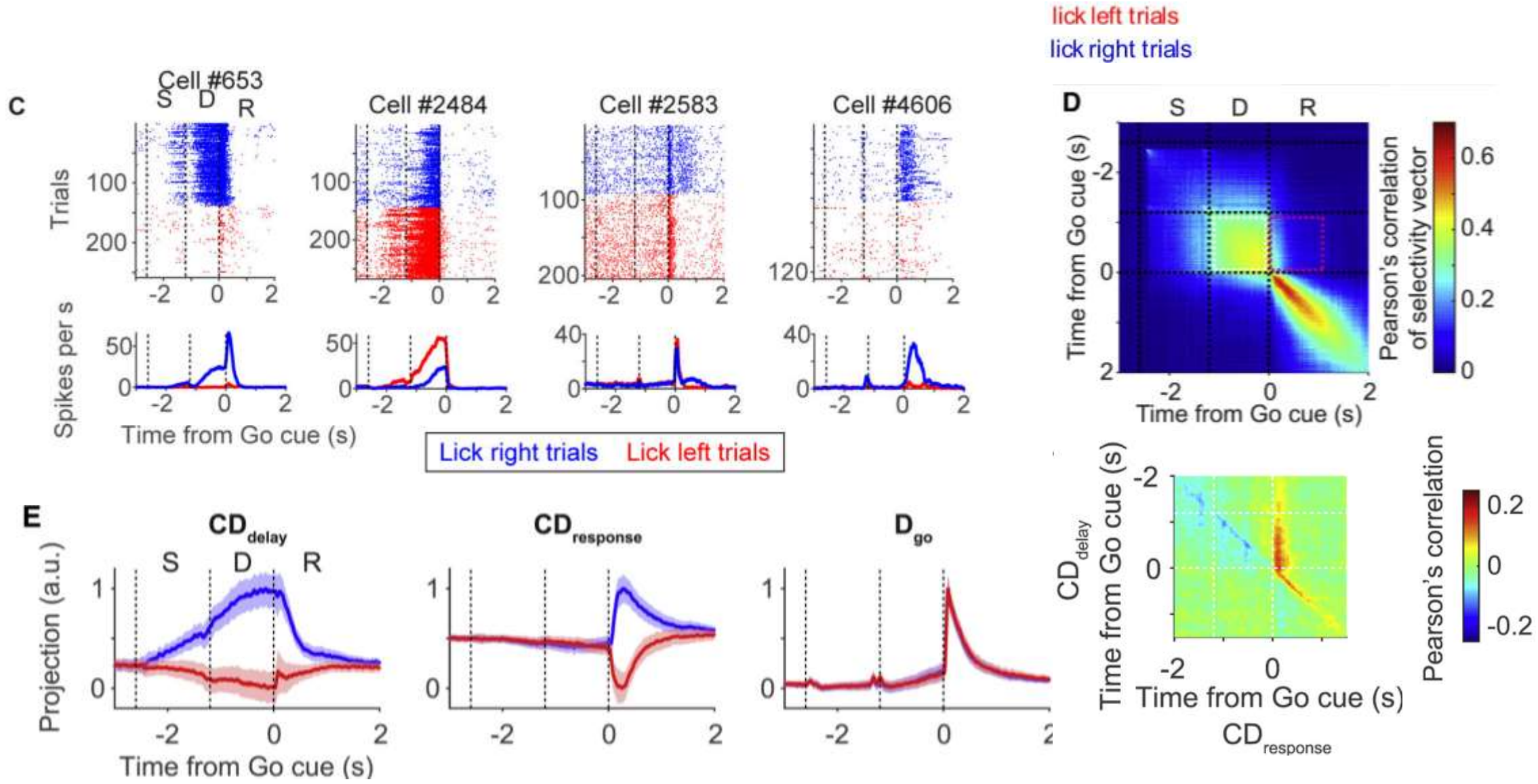




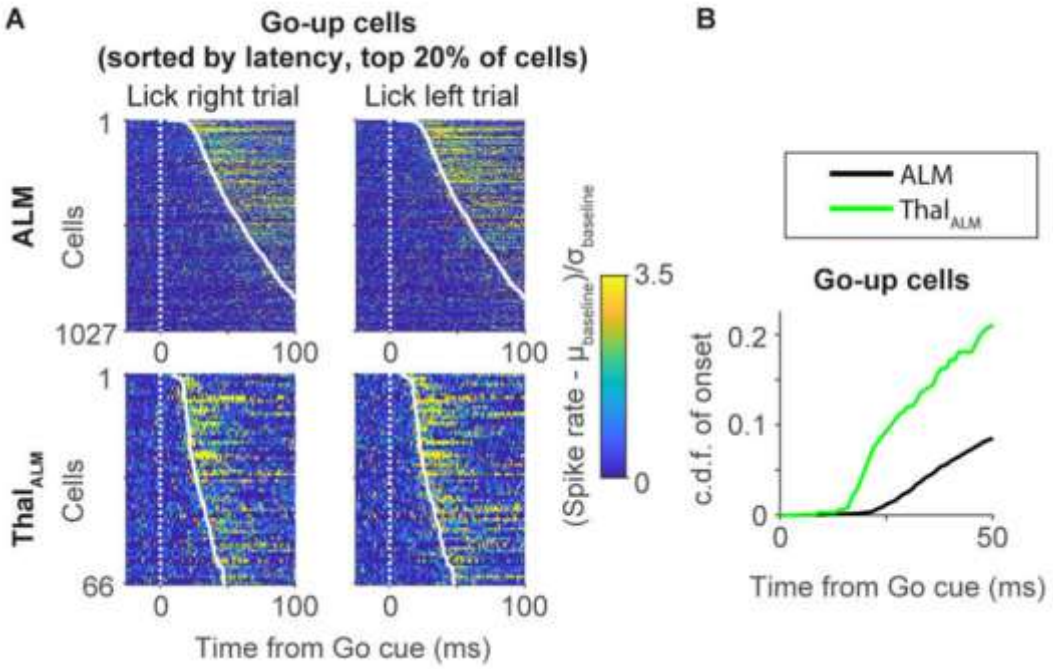


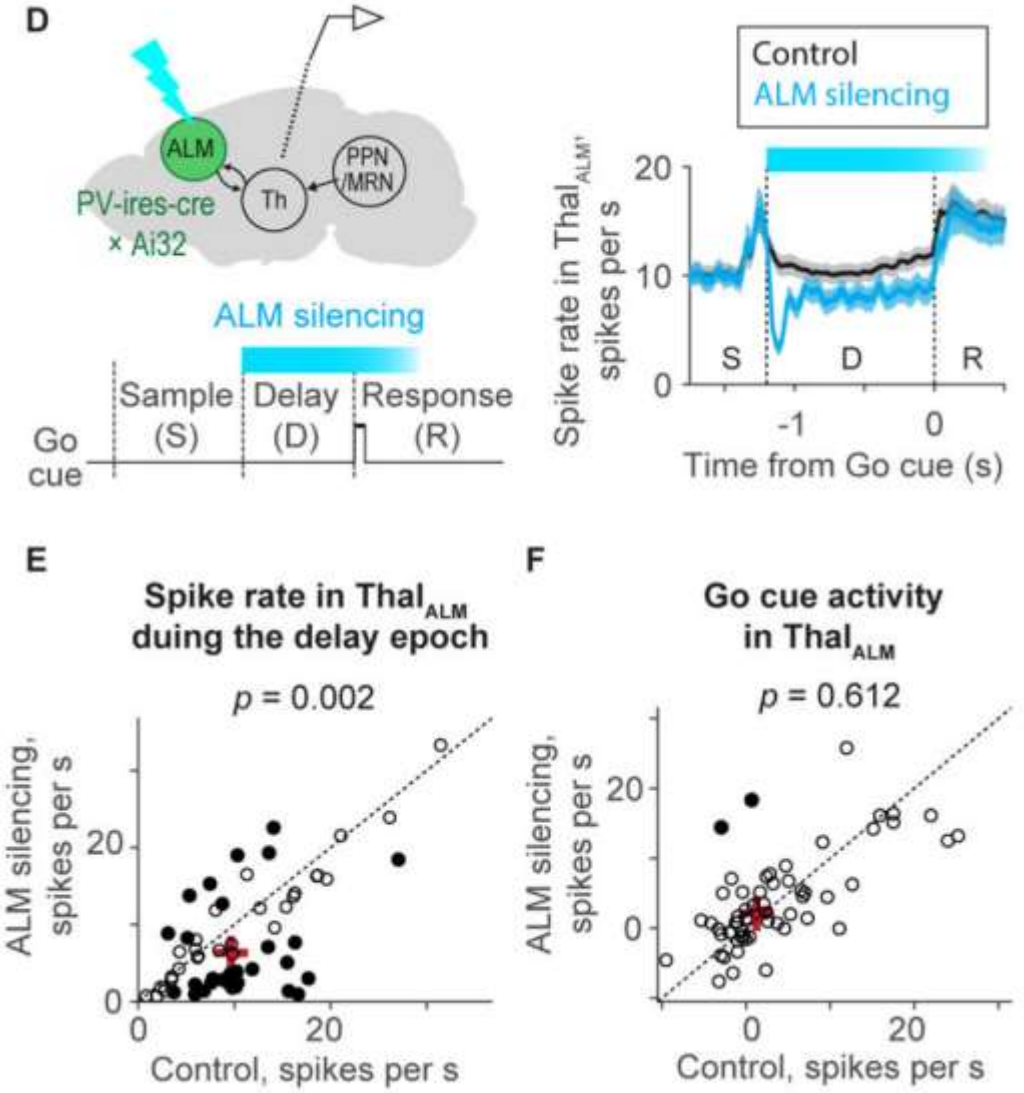
Inagaki, H. K. et al. *Cell*. 2022.

A mode switch before movement initiation



Thalamus conveys the Go cue signal to ALM

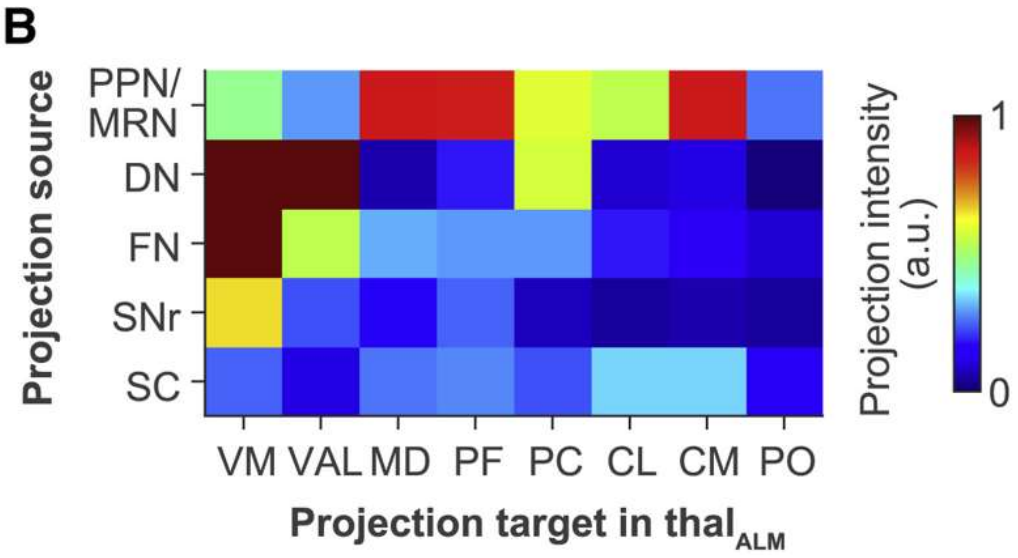


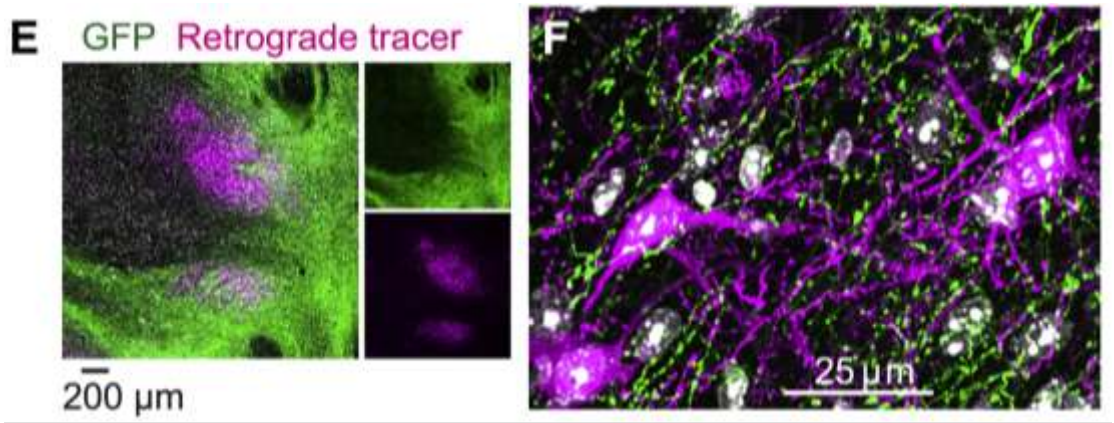


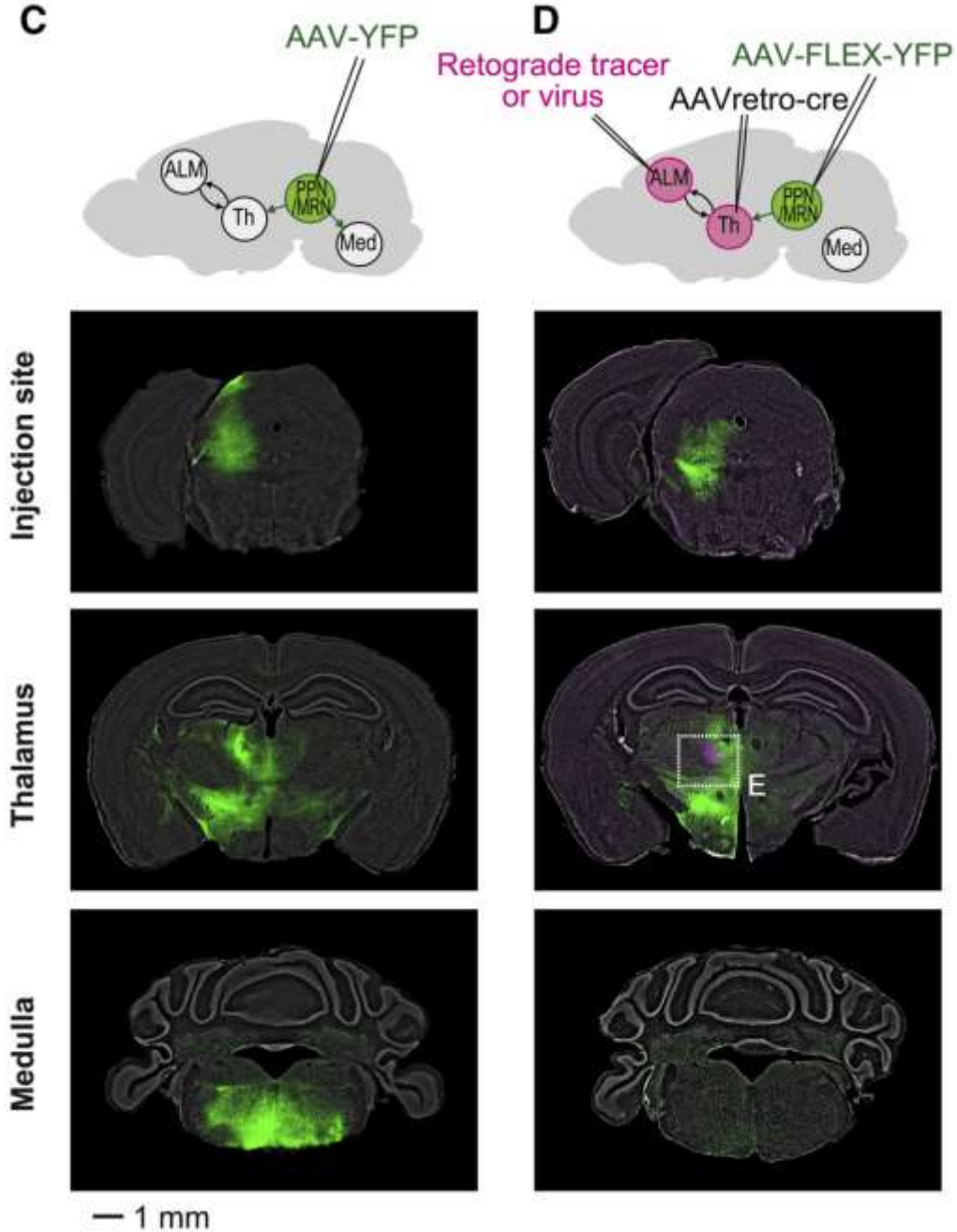
ALM：前外侧运动皮层

Thal$_{ALM}$：投射到ALM的丘脑神经元

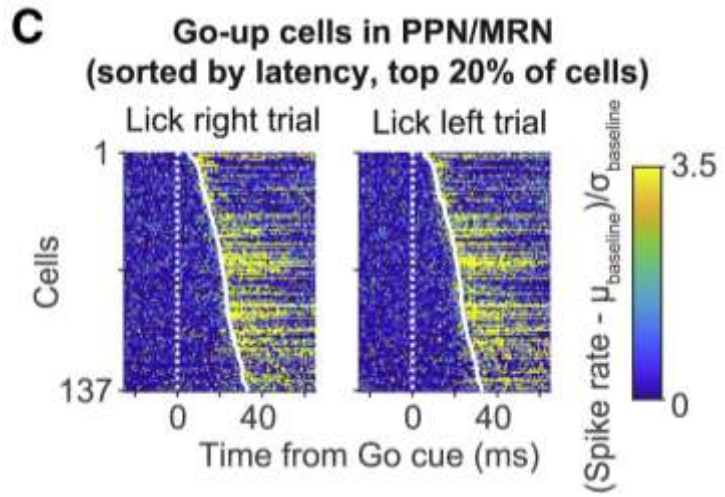
PPN/MRN projects to ALM-projecting thalamus

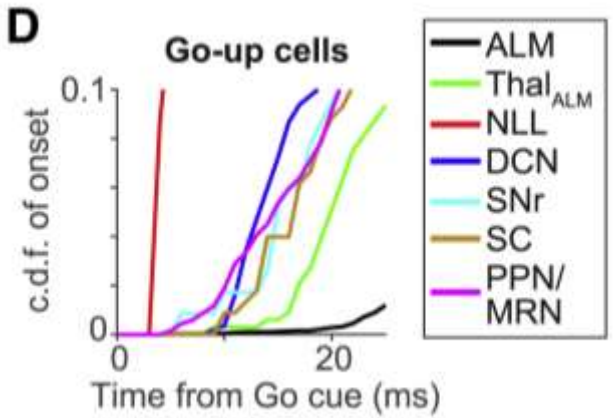


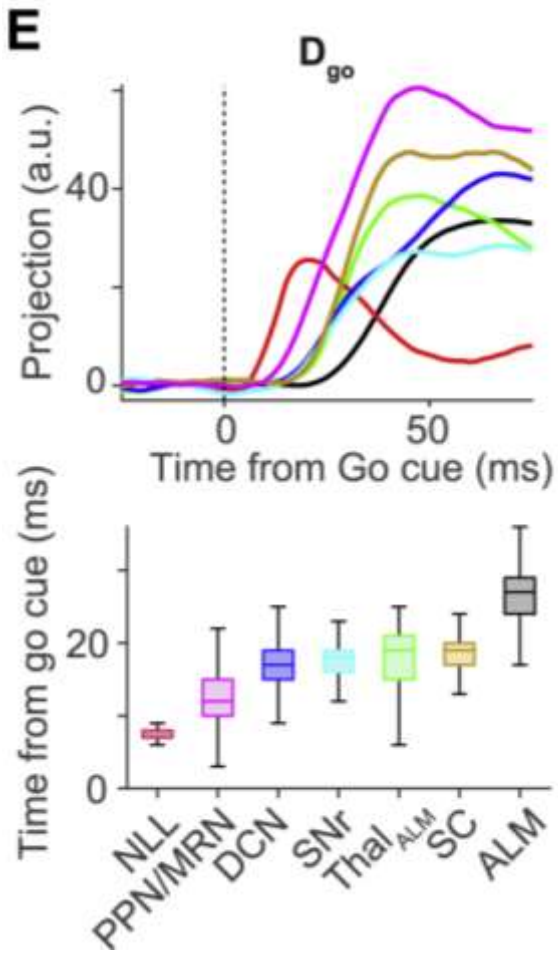




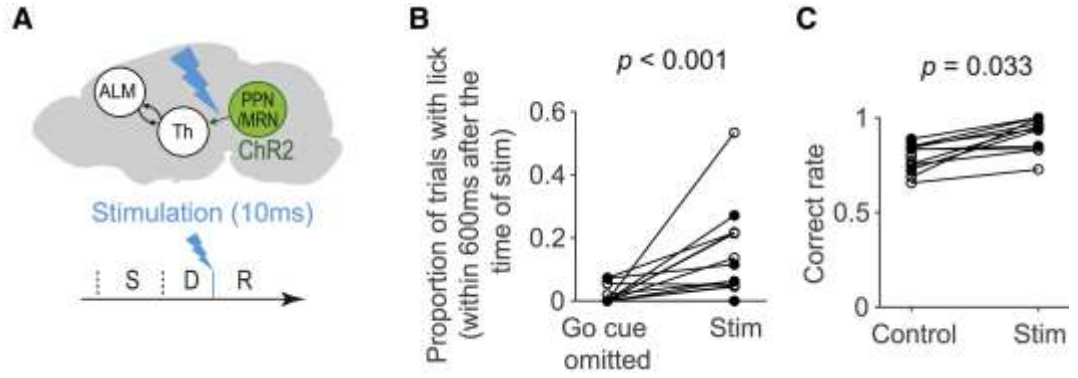
Latency after the Go cue in thalamus-projecting brain areas

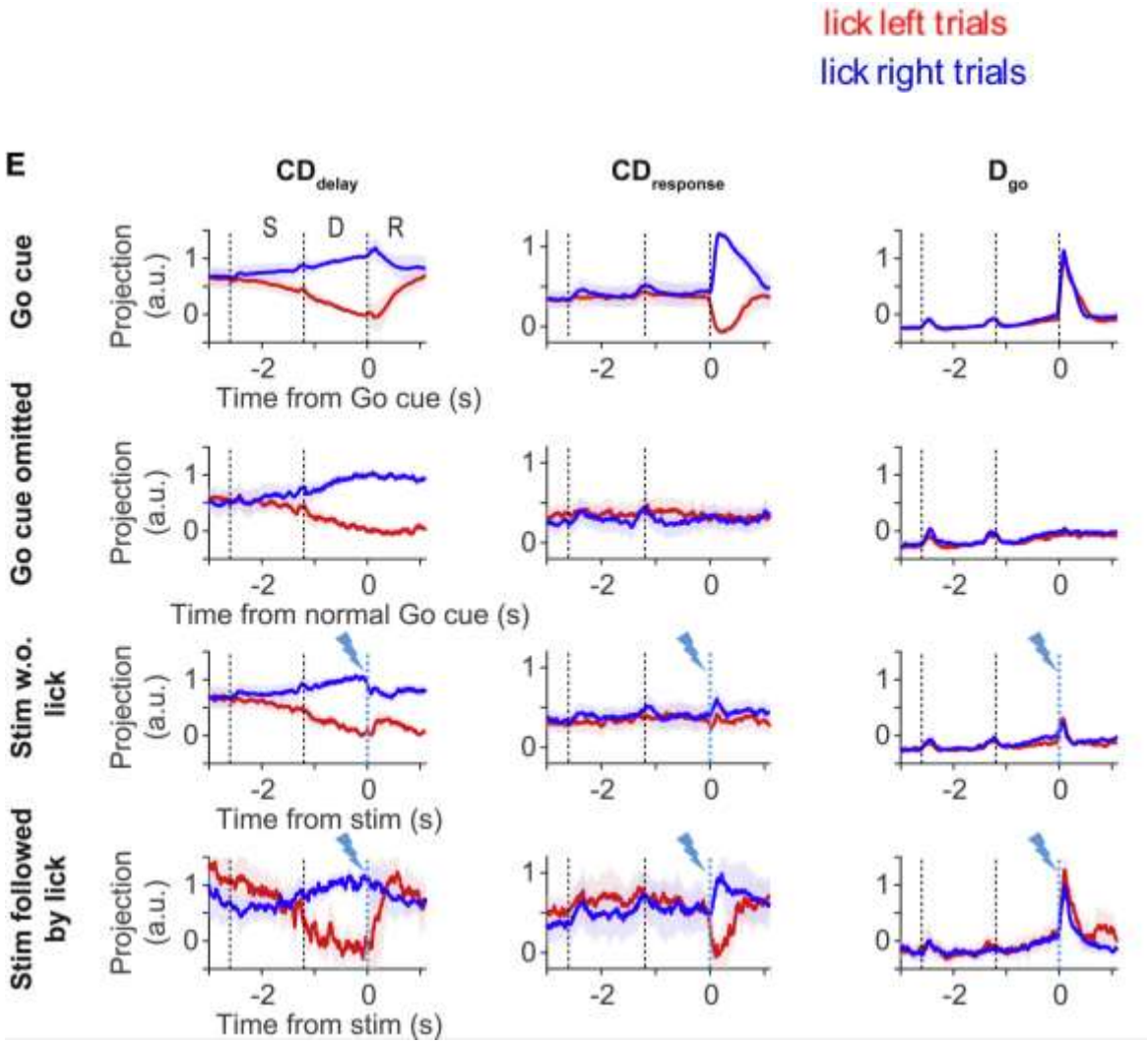




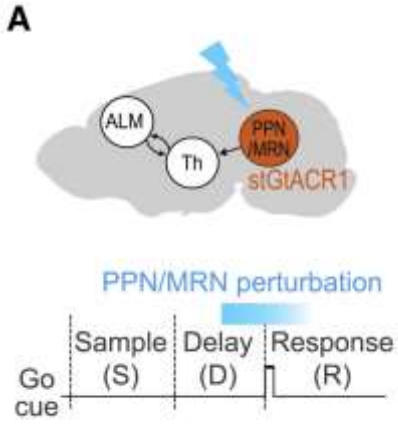


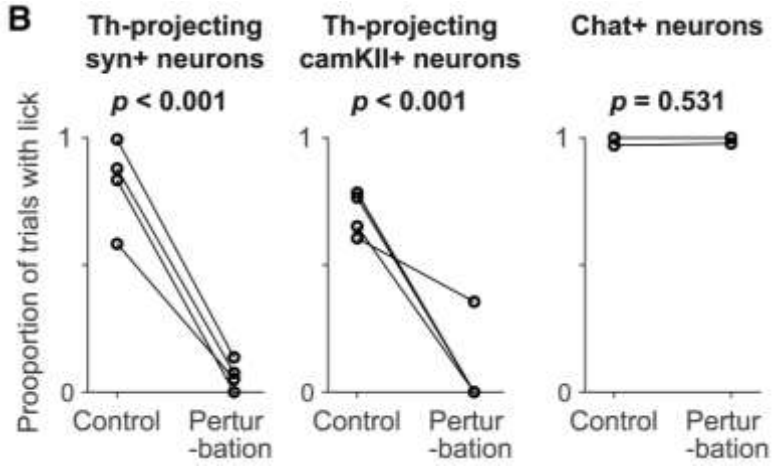
Phasic stimulation of thalamus-projecting PPN/MRN neurons mimics the Go cue

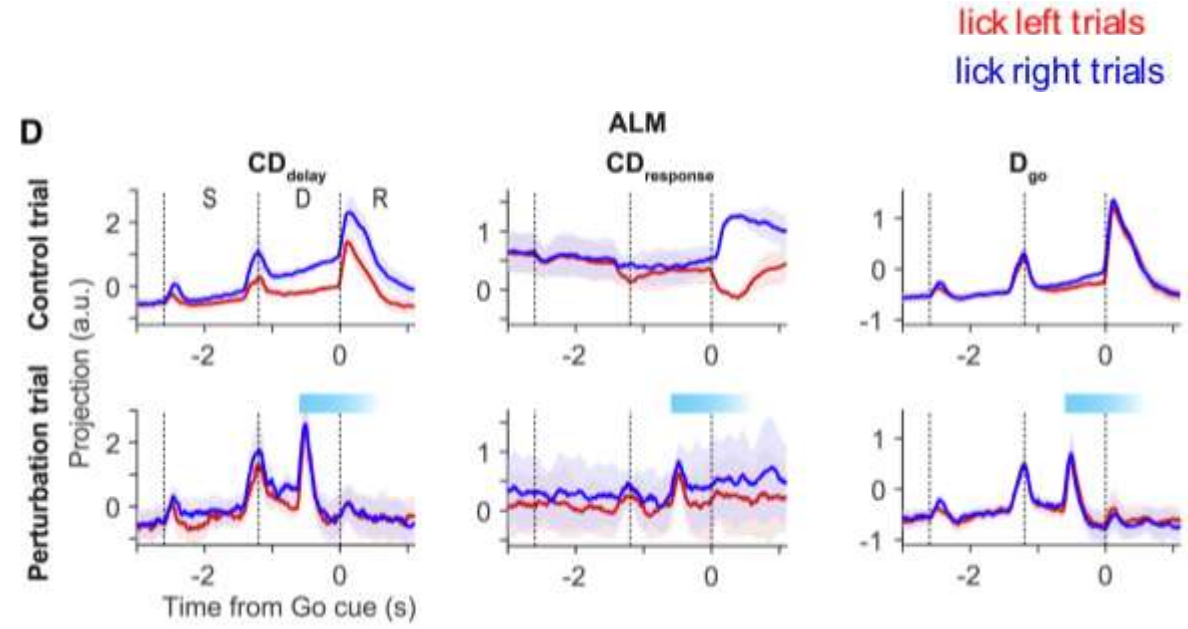


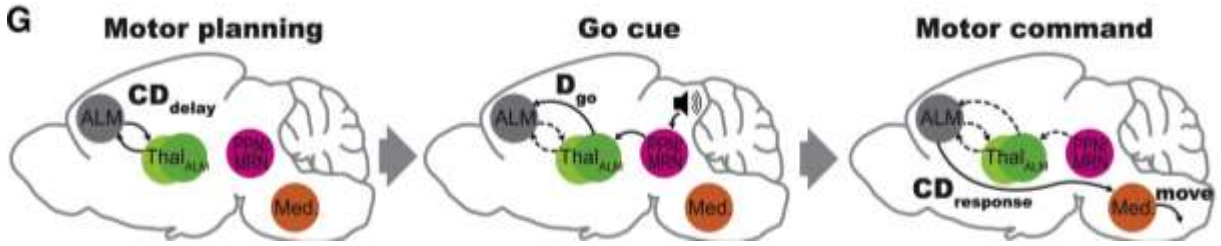


Perturbation of thalamus-projecting PPN/MRN neurons blocks movement initiation



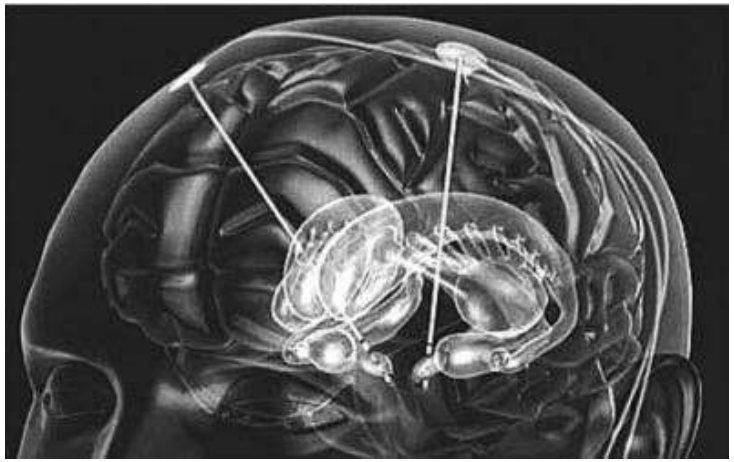






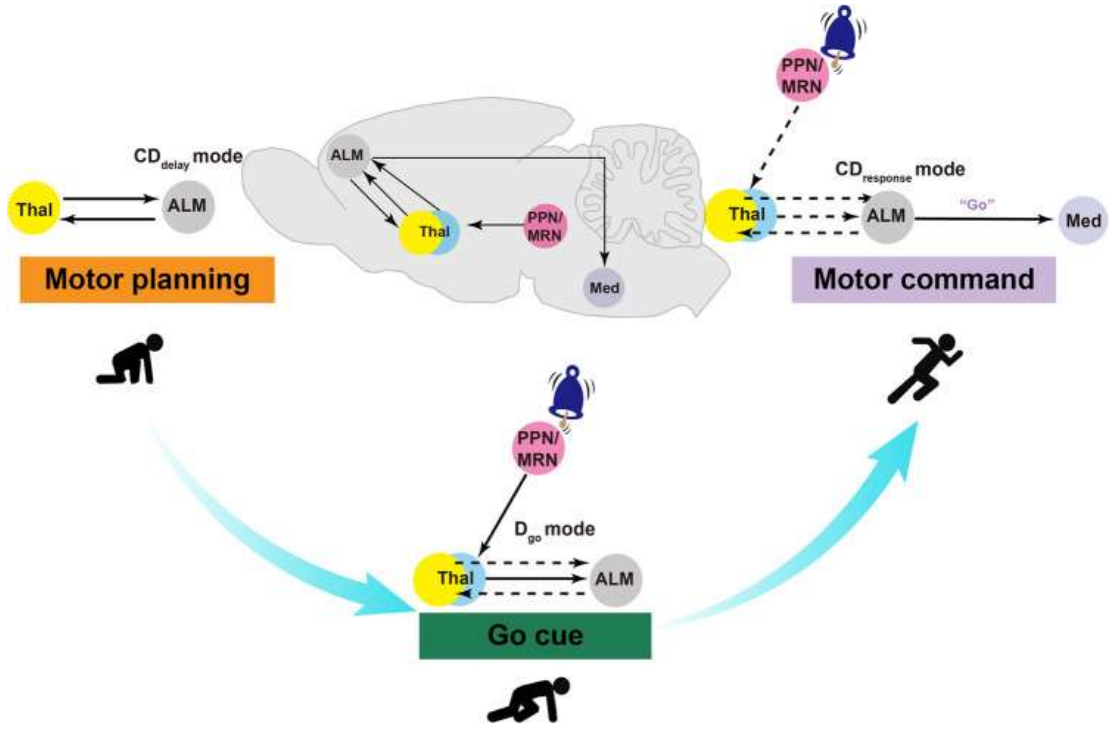
Meaning of this research

- 有助于完善帕金森病等运动障碍的治疗
- PPN 的电刺激已被用于治疗帕金森病患者
- 目前的研究表明，在这种深部脑刺激过程中选择性激活 PPN 丘脑投射可能会提高治疗效果，并防止因刺激脑干 PPN 投射而引起的潜在副作用。
- Inagaki和同事的研究结果还表明，只有引起活动模式重组的转换才能触发有计划的运动。如果可以在深部脑刺激过程中记录患者运动皮层的神经元，那么就有可能利用神经元群活动的读数来微调标准治疗失败的个体的刺激方案。



Take home message

- The interesting paradigm for studying planning and execution in mice
- ALM involved in motor preparation
- The mutual drive between ALM and thalamus makes ALM sustainably excited during the preparation phase
- The transition mechanism between planning and execution in delayed-response task



Thanks!