本能行为的神经基础

Neural Basis of Innate Behaviors

许晓鸿

How the brain encodes behaviors?

"Nothing in neuroscience makes sense except in the light of behavior"

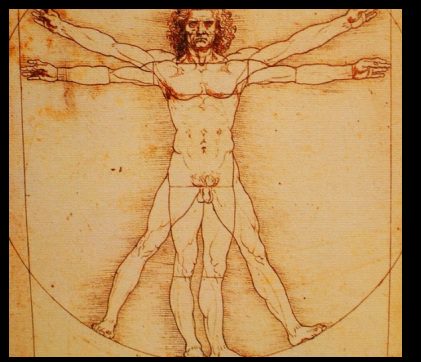
--- NIH BRAIN interim report

External stimuli →

→ **Behavioral outputs**

本能行为对比习得性行为

Innate behavior	Learned behavior
Fast	*Laborious*
Reliable	*Variable*
Fixed	*Malleable*
Genetically wired	*Experience-dependent*



本能行为

1. 不需任何训练
2. 行为种族特定
3. 行为模式化

鹅的滚蛋行为

控制本能行为的神经环路是在发育过程中由基因决定的

本能行为的神经基础

交配行为

攻击行为

母性行为

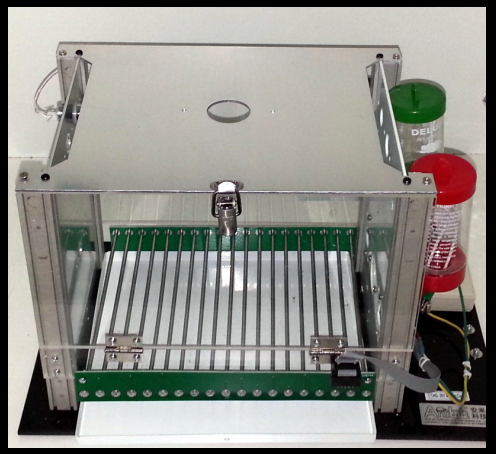
摄食行为

研究手段

基因突变

细胞特异性 *Cre*

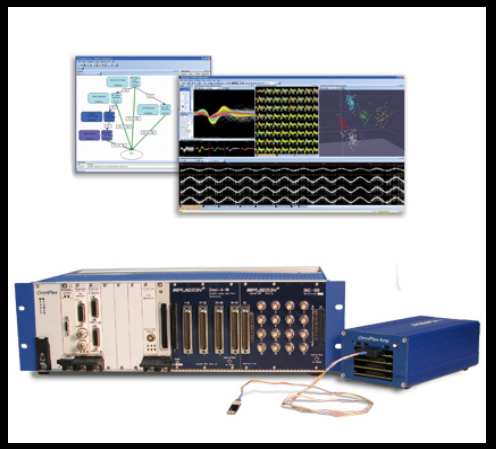
条件性敲除



AAV-CMV-CreGFP

AAV-DIO-EF1a-CHR2

AAV-CMV-GOI



讲座提纲

1. 行为的神经环路基础:

   摄食和饮水

   社会行为（攻击, 求偶, 防御, 母性行为）

2. 情感的神经环路基础: *恐惧, 愉悦*

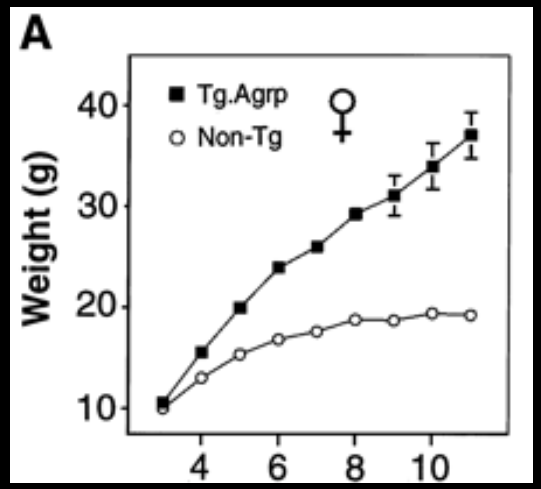
3. 研究手段思路等

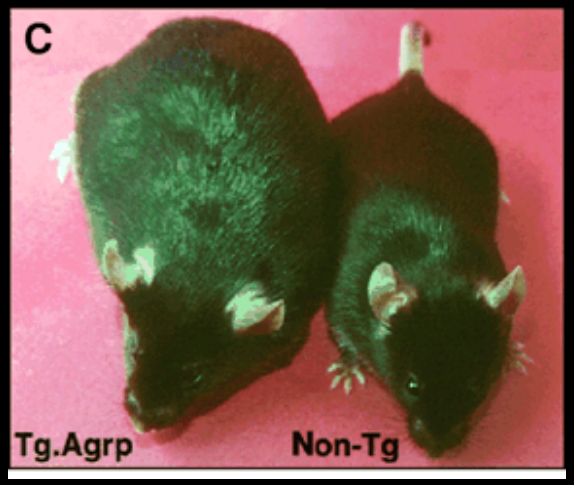
一个神奇的神经多肽的发现

1. 不同的小鼠品系颜色各异

2. “致命黄色”小鼠 (*lethal yellow allele*)

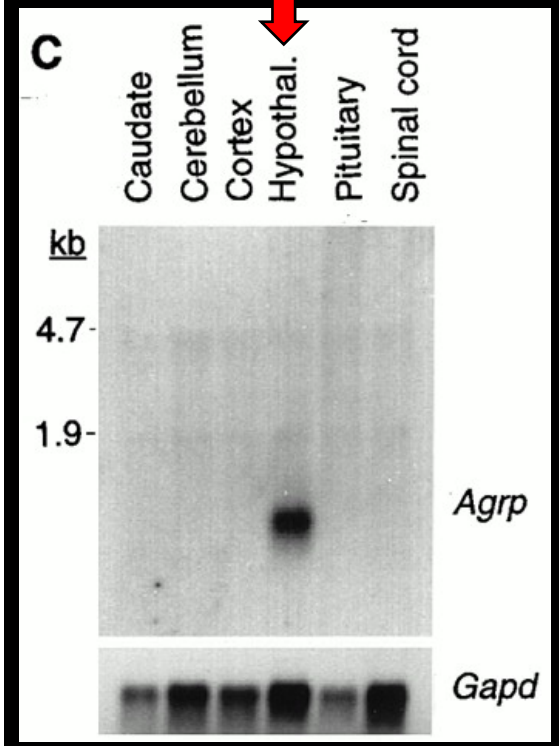
3. 克隆 Agouti 基因 以及 Agouti-related peptide (Agrp)



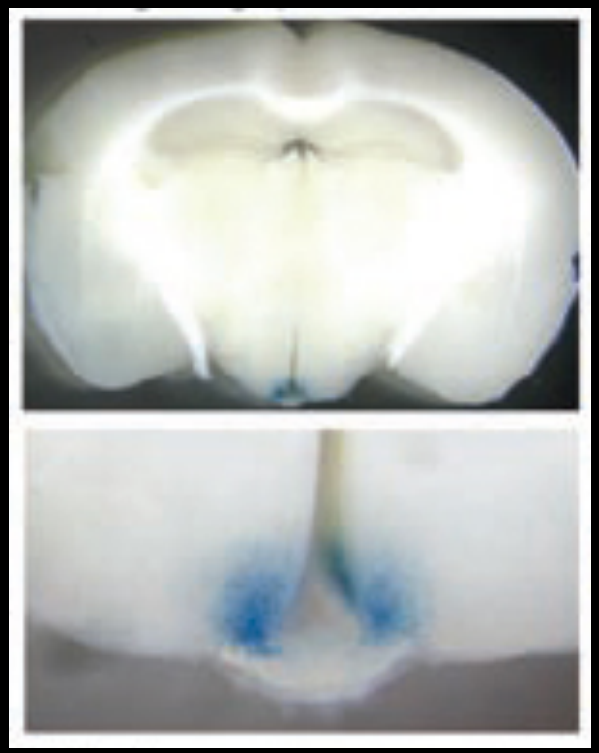


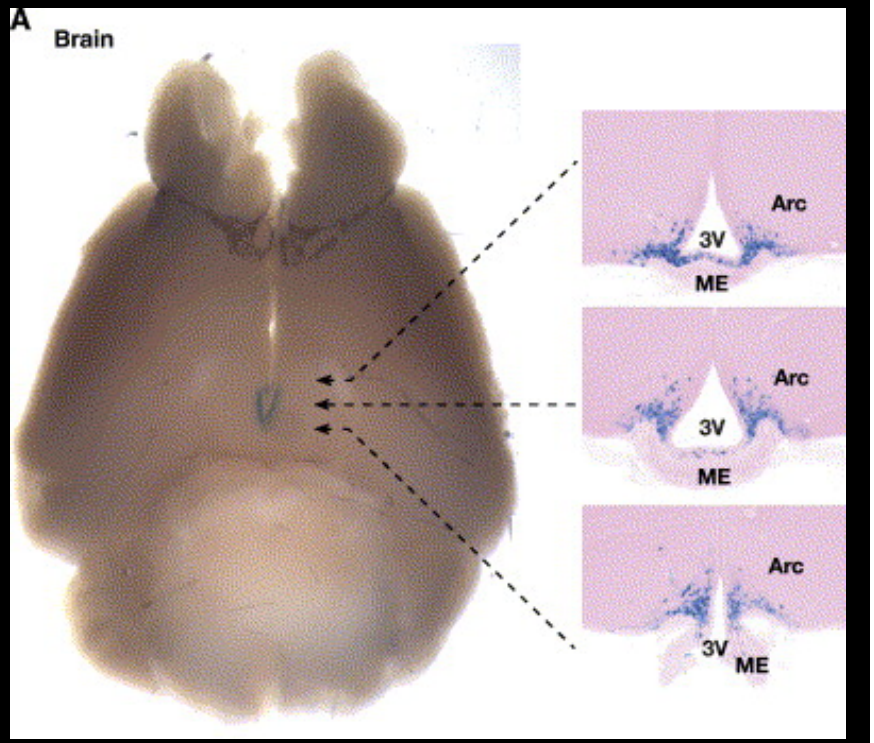
Agrp 在大脑中的表达十分特异

下丘脑区



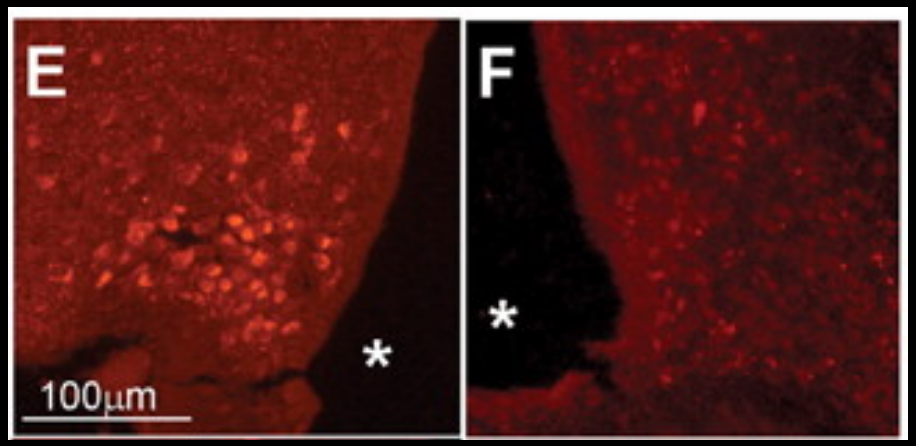
弓形核

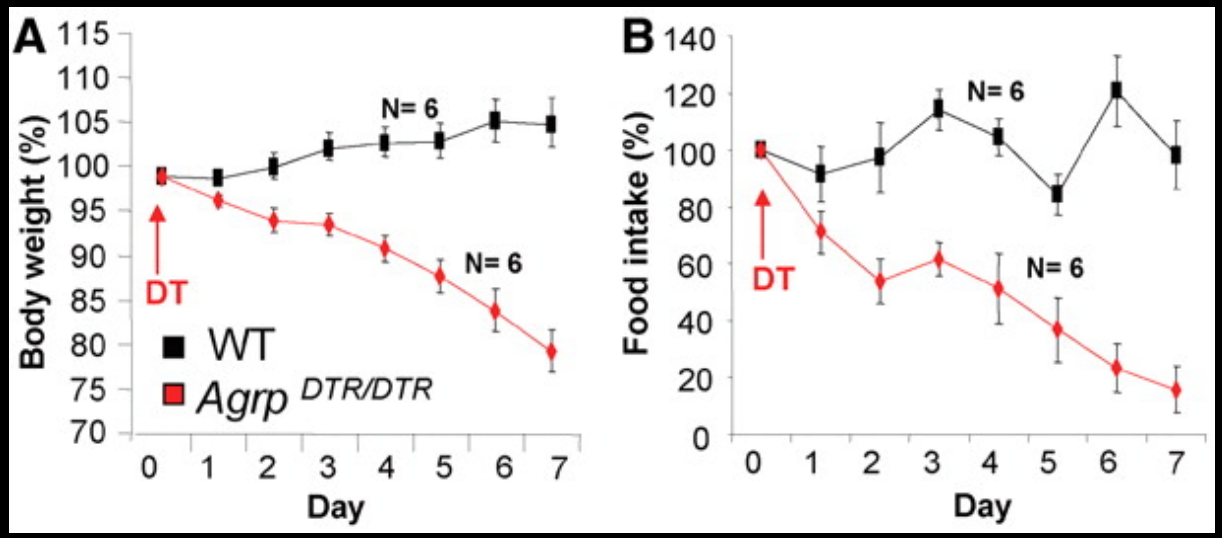




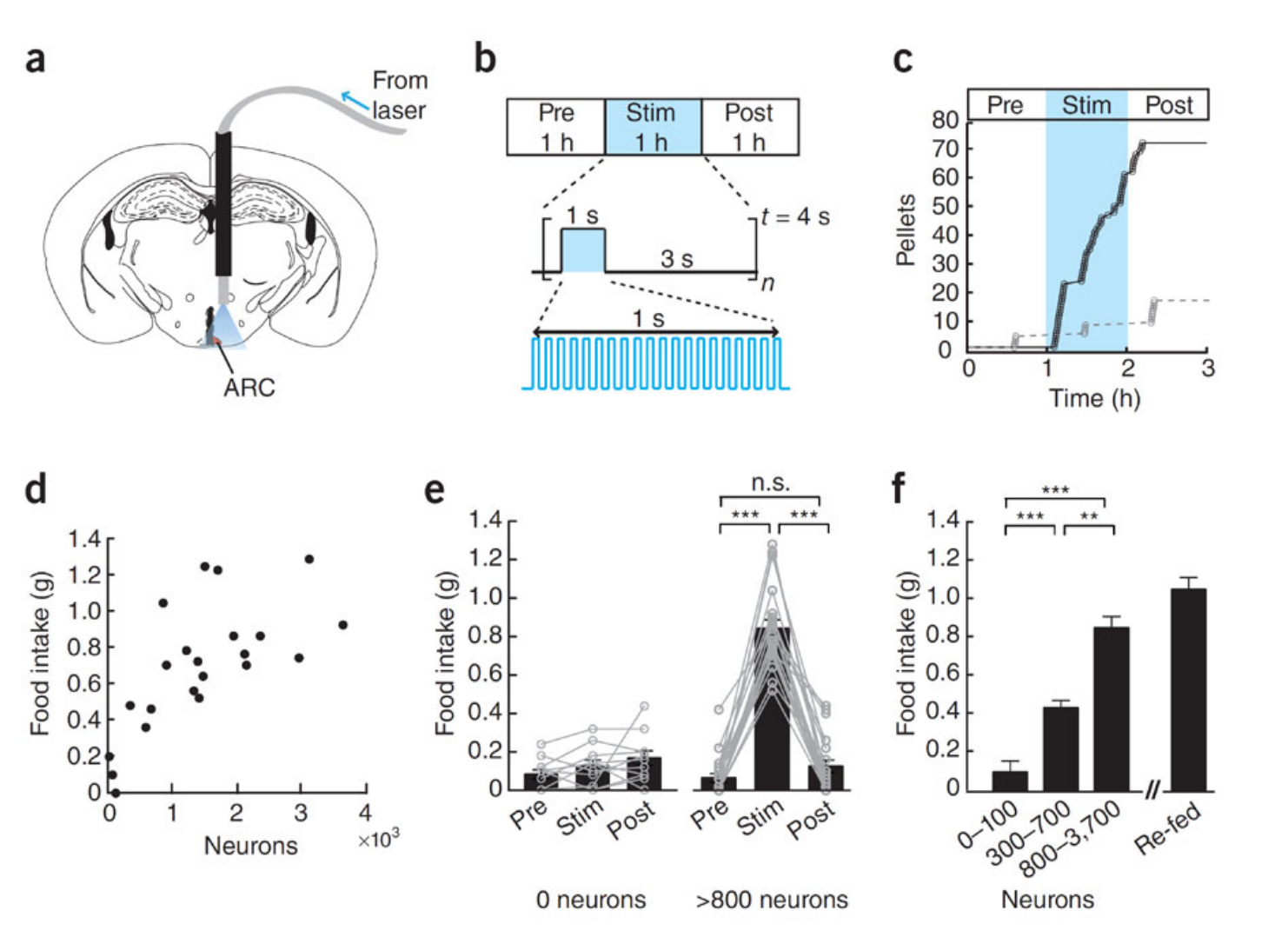
Agrp神经元控制摄食行为

WT　　Agrp－DTR

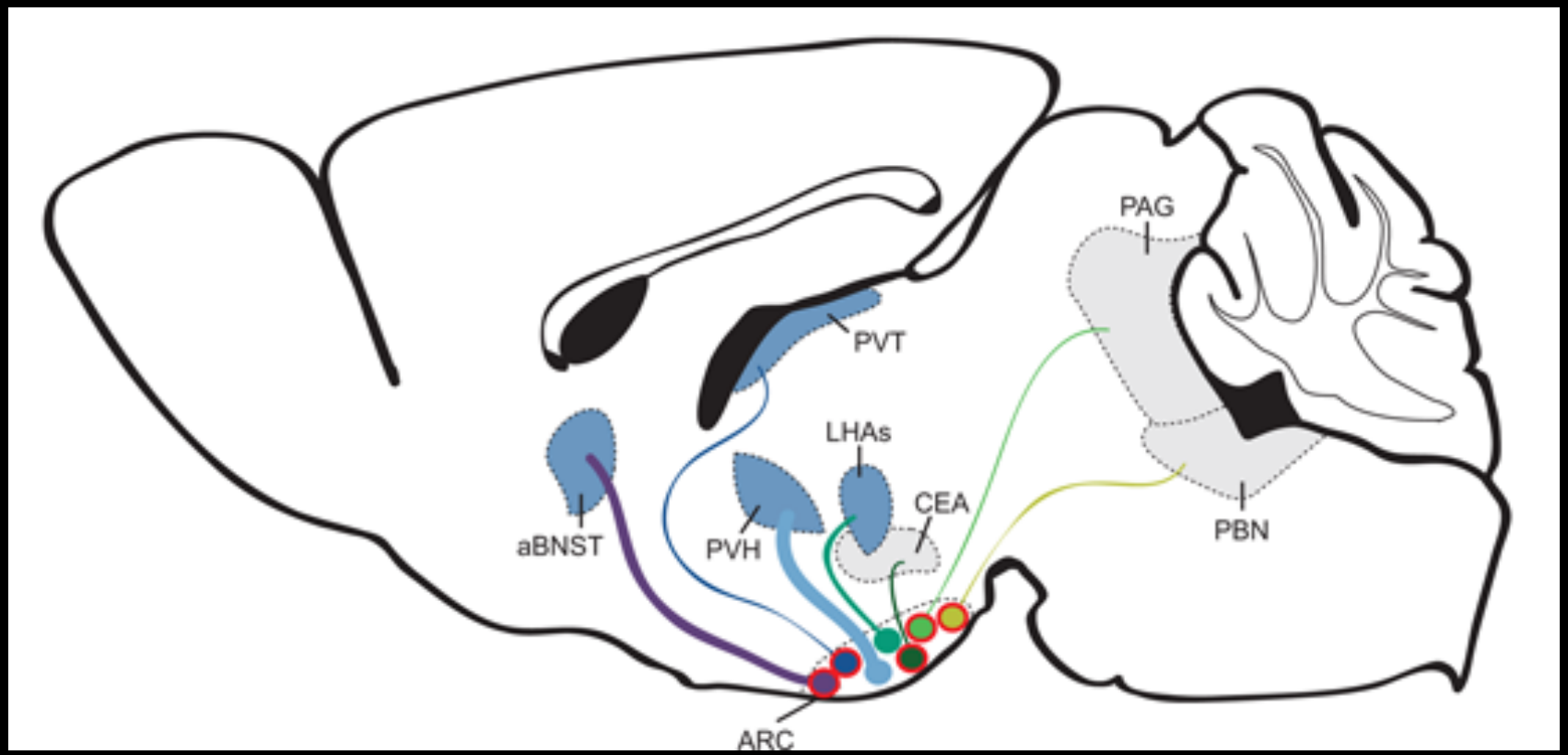




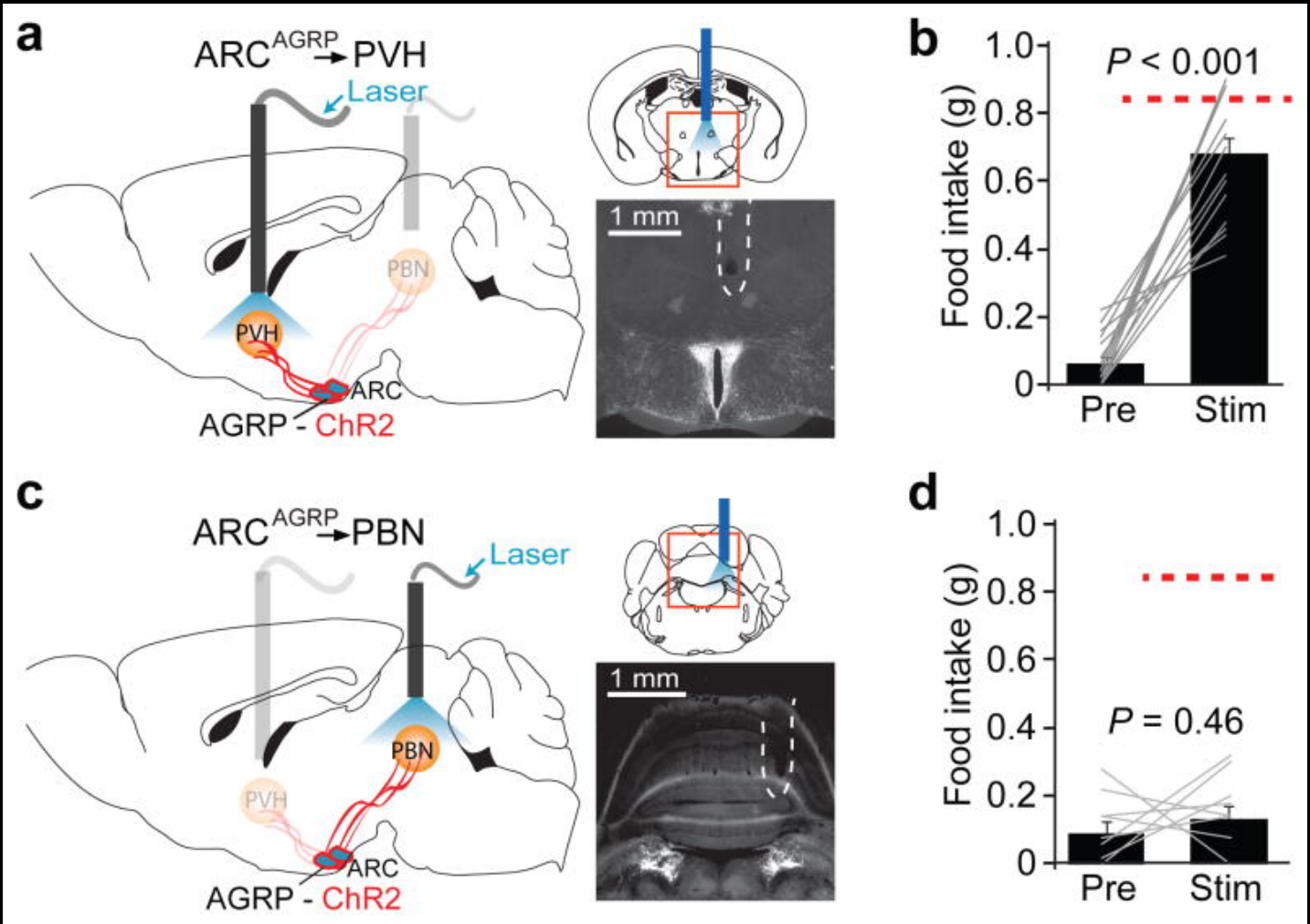
Agrp神经元控制摄食行为



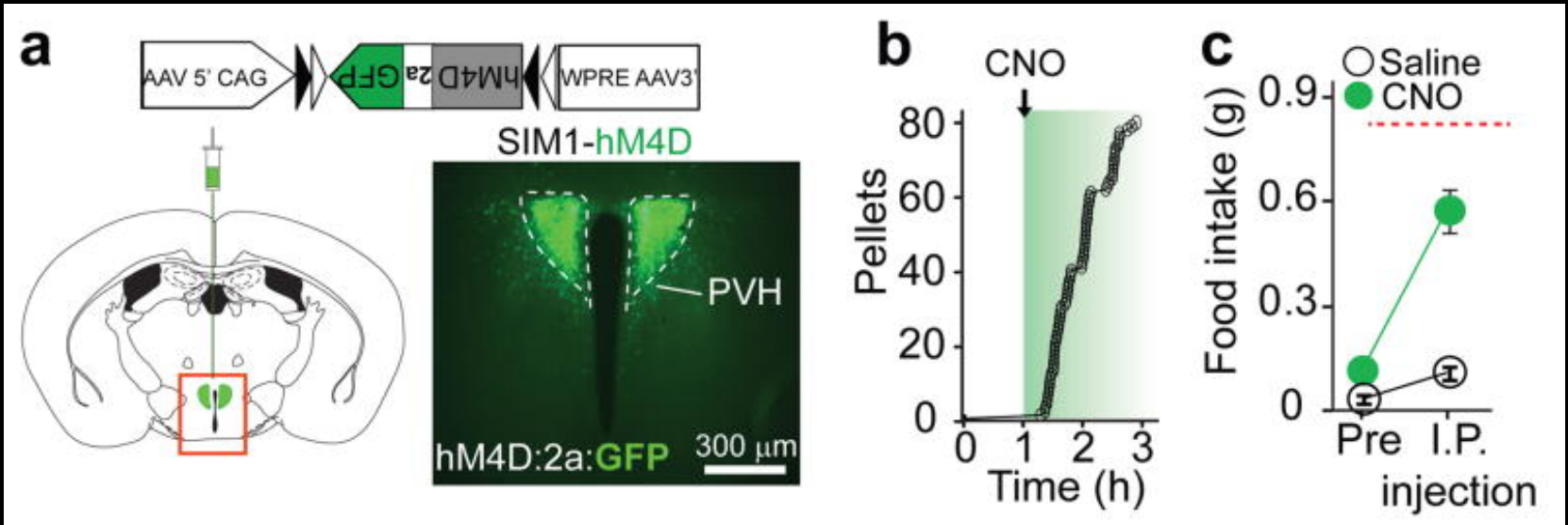
以Agrp神经元为中心的神经环路控制摄食行为



以Agrp神经元为中心的神经环路控制摄食行为

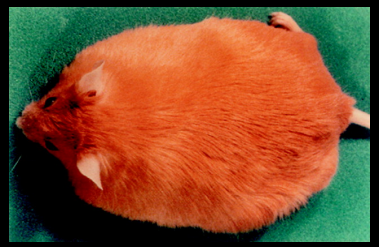


以Agrp神经元为中心的神经环路控制摄食行为



摄食行为的神经基础

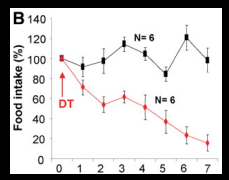
近一个世纪前的发现



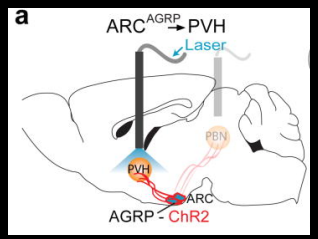
1992－1994　　*Agouti* 及 *Agrp* 基因的克隆

20世纪初　　*Agrp* 神经元定位

2005　　杀死*Agrp* 神经元
小鼠饥饿至死

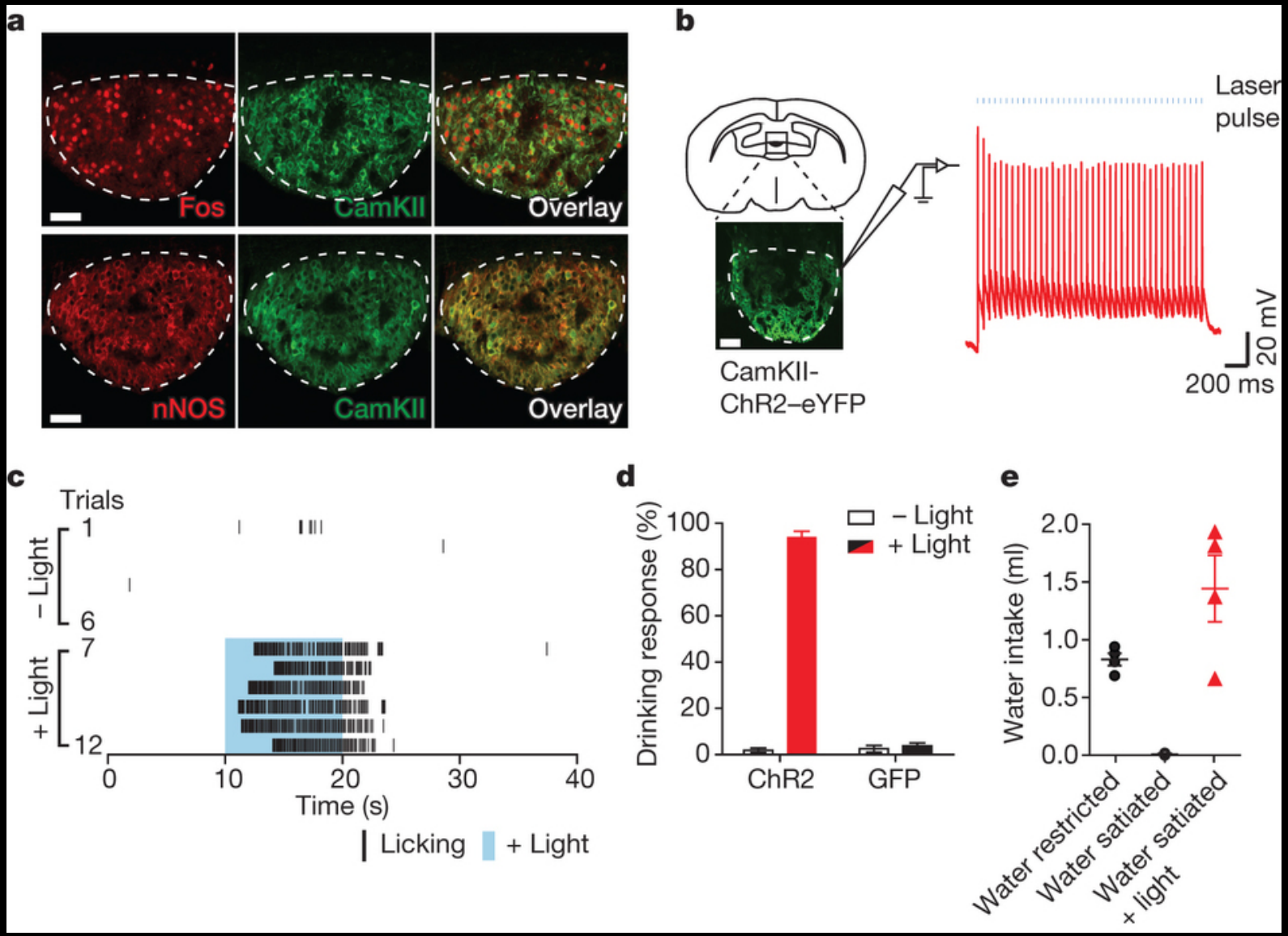


2011　　激活*Agrp* 神经元
小鼠无节制的摄食



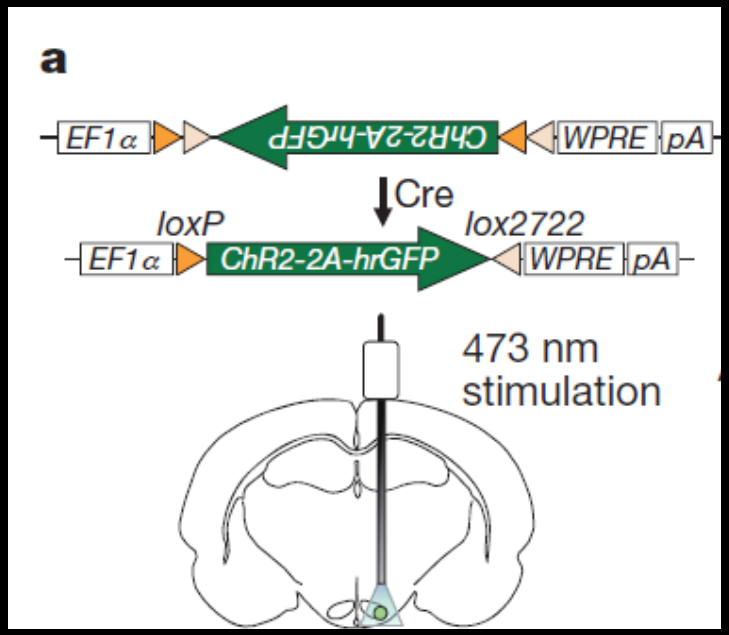
2012-　　激活*Agrp* 神经元所在神经环路
小鼠无节制设施

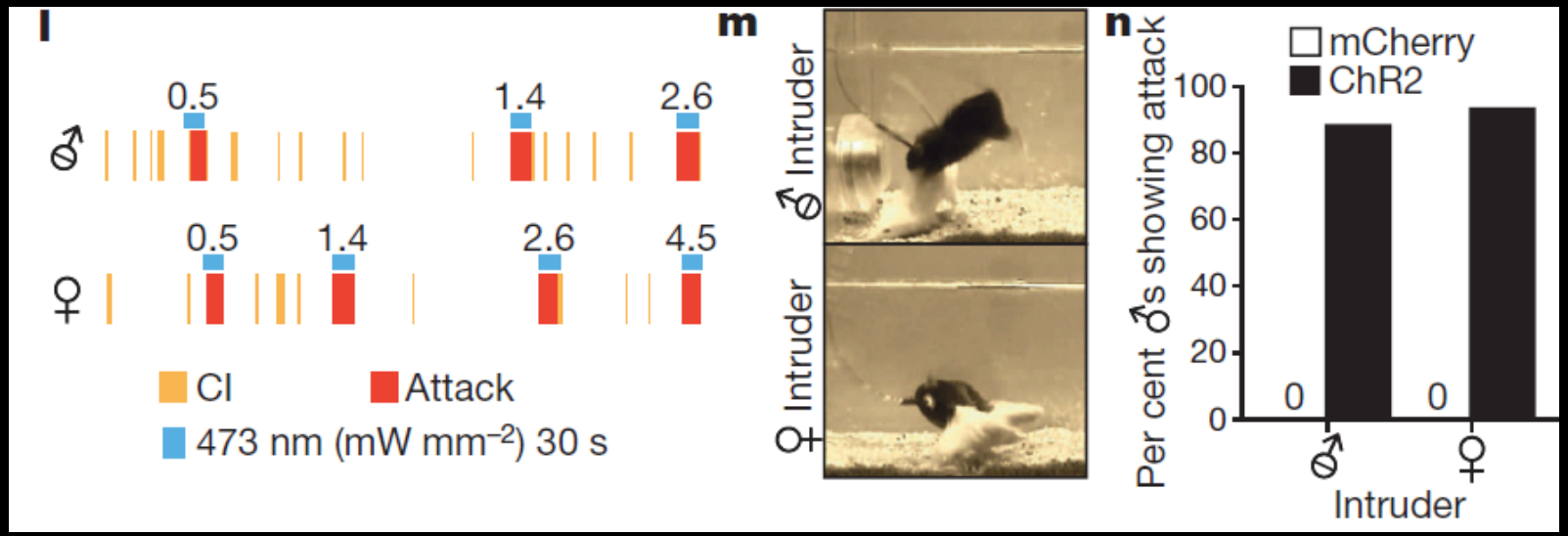
饮水行为的神经基础



SFO: subfornical organ

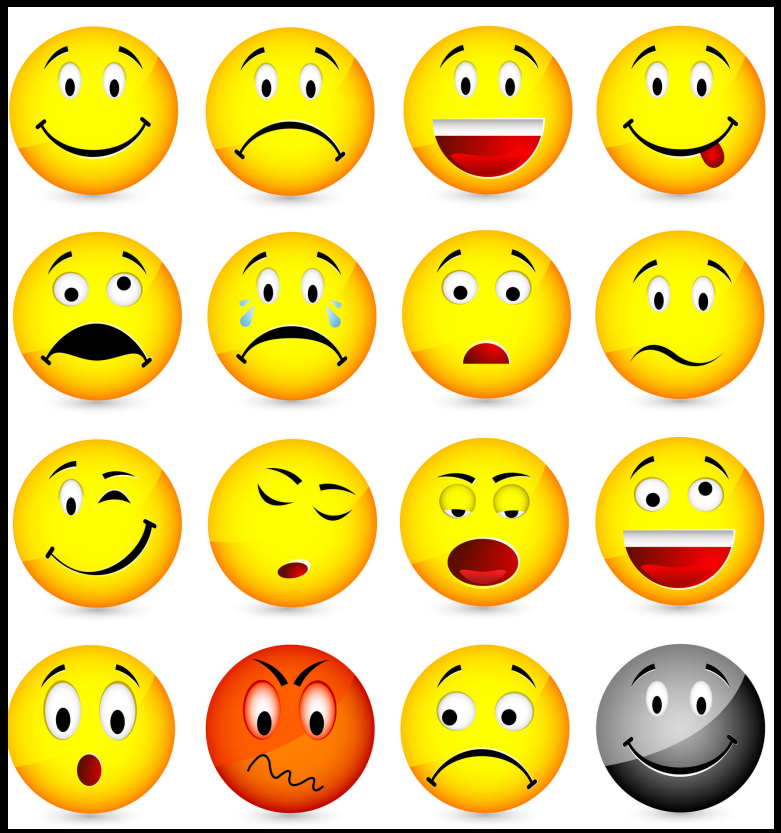
攻击行为的神经基础


a
EF1α
ChR2-2A-hrGFP
WPRE
pA
Cre
loxP
lox2722
EF1α
ChR2-2A-hrGFP
WPRE
pA
473 nm
stimulation


l
0.5
1.4
2.6
0.5
1.4
2.6
4.5
CI
Attack
473 nm (mW mm⁻²) 30 s
m
♂ Intruder
♀ Intruder
n
mCherry
ChR2
Per cent ♂s showing attack
100
80
60
40
20
0
0
0
♂
♀
Intruder

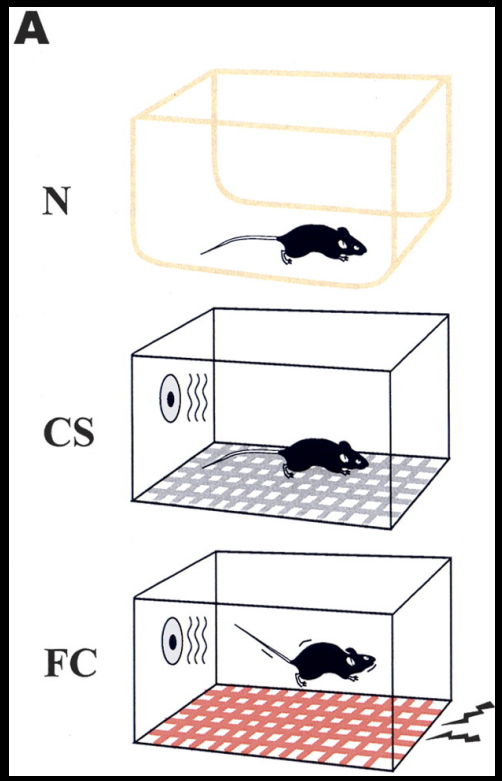
攻击行为的神经基础

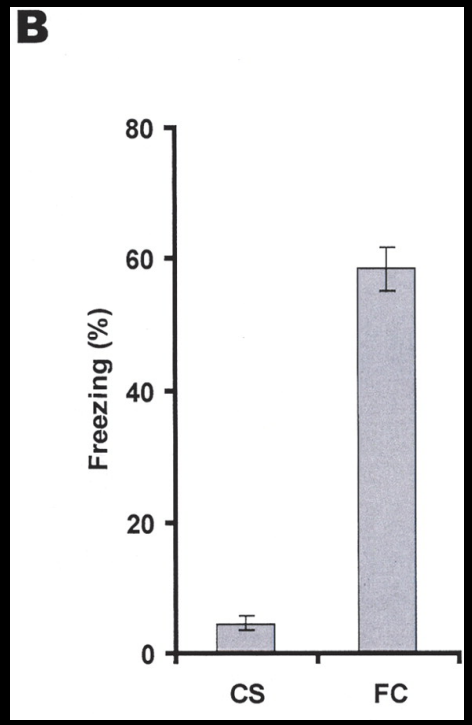
Emotion - an experience that includes a subjective *feeling*, which is a cognitive interpretation, and a *physical reaction*, which is behavioral expression.

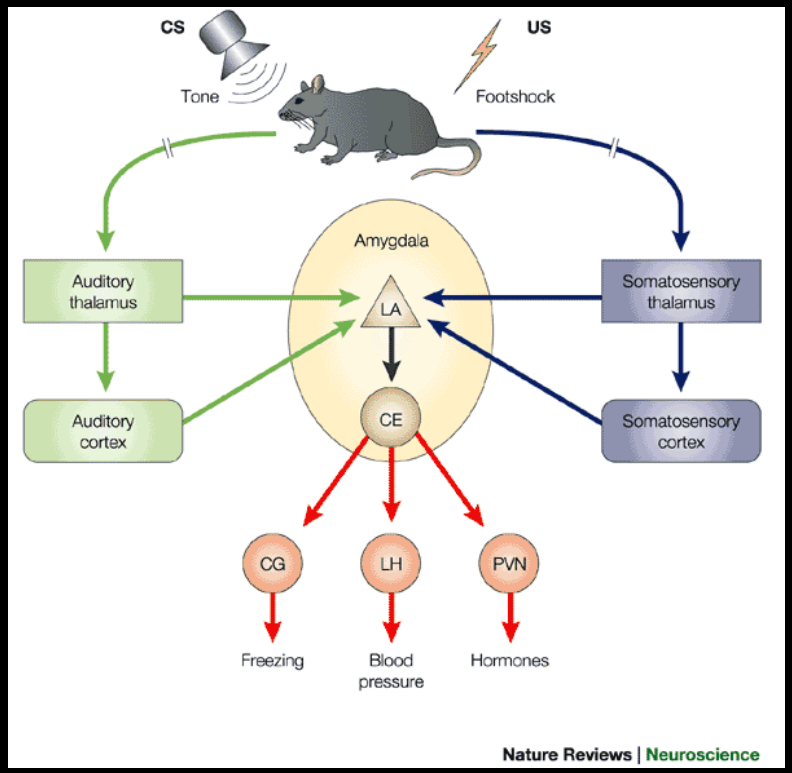


Happiness
Sadness
Anger
Fear
Anxiety
Depression
Confusion
Surprise
…..

恐惧的神经环路基础

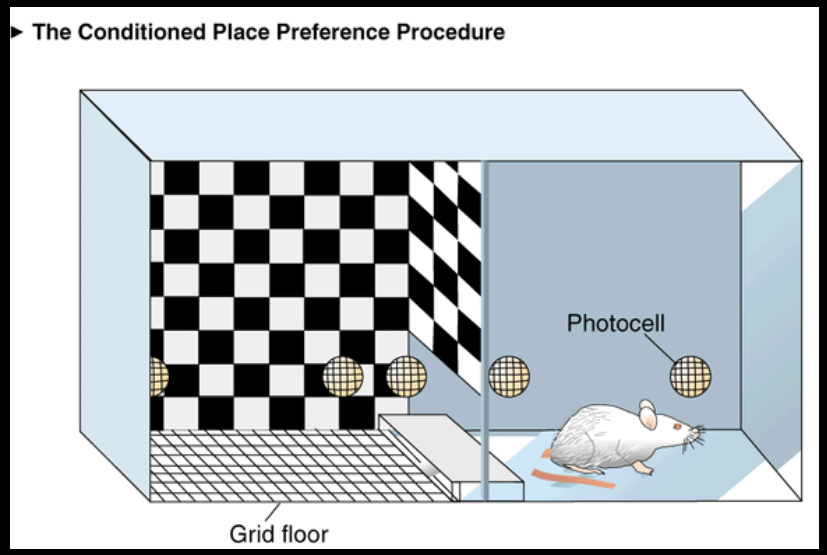

A
N
CS
FC

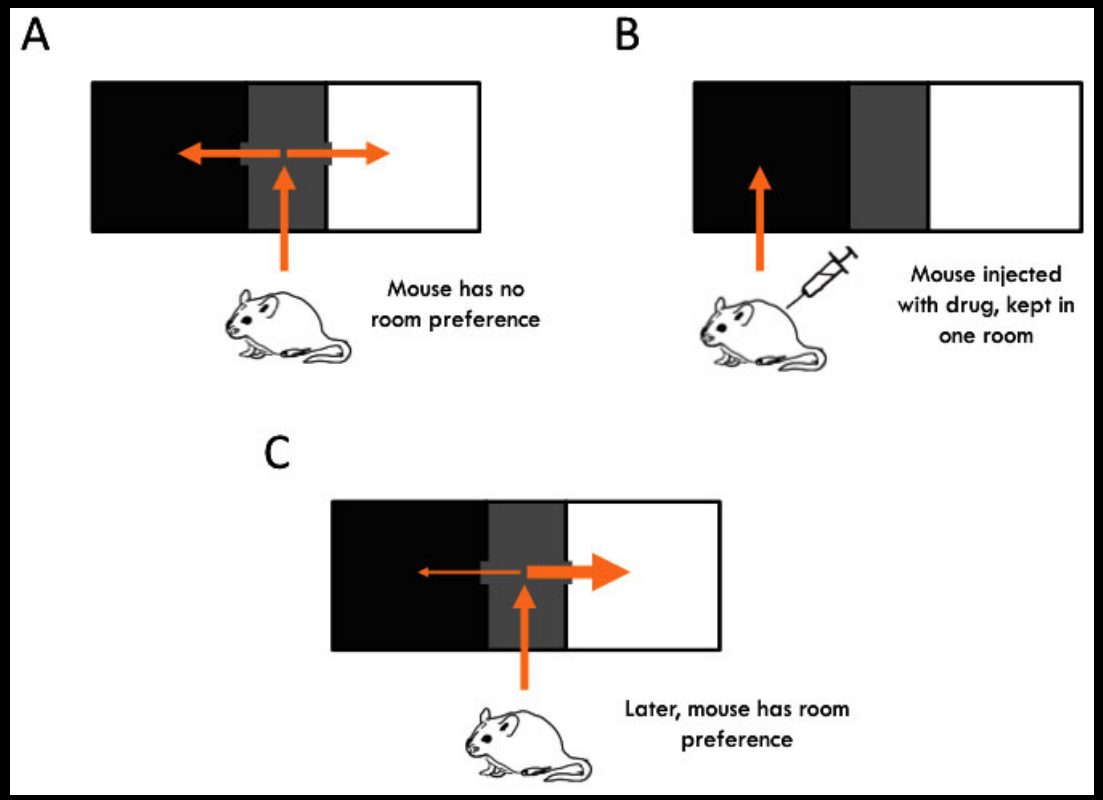

B
Freezing (%)
80
60
40
20
0
CS
FC


CS
Tone
US
Footshock
Amygdala
Auditory thalamus
LA
Somatosensory thalamus
Auditory cortex
CE
Somatosensory cortex
CG
LH
PVN
Freezing
Blood pressure
Hormones
Nature Reviews | Neuroscience

检测动物情绪的行为范式

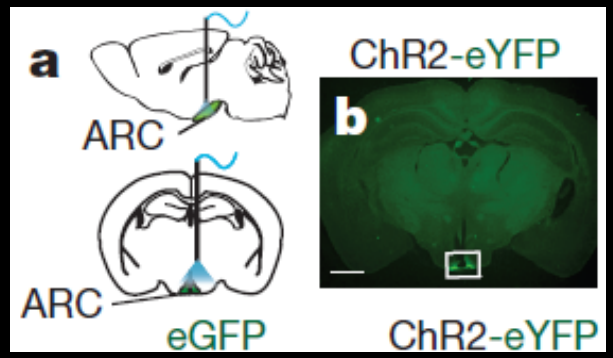
Conditional Place Preference：条件性位置偏好



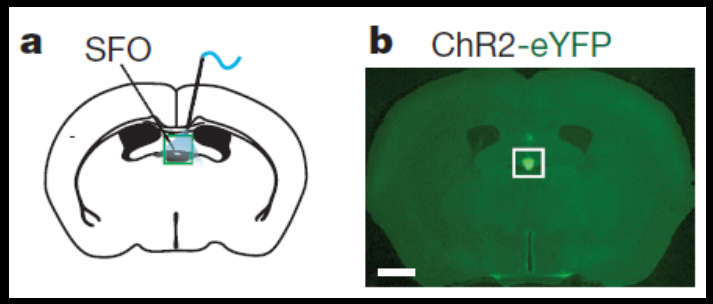


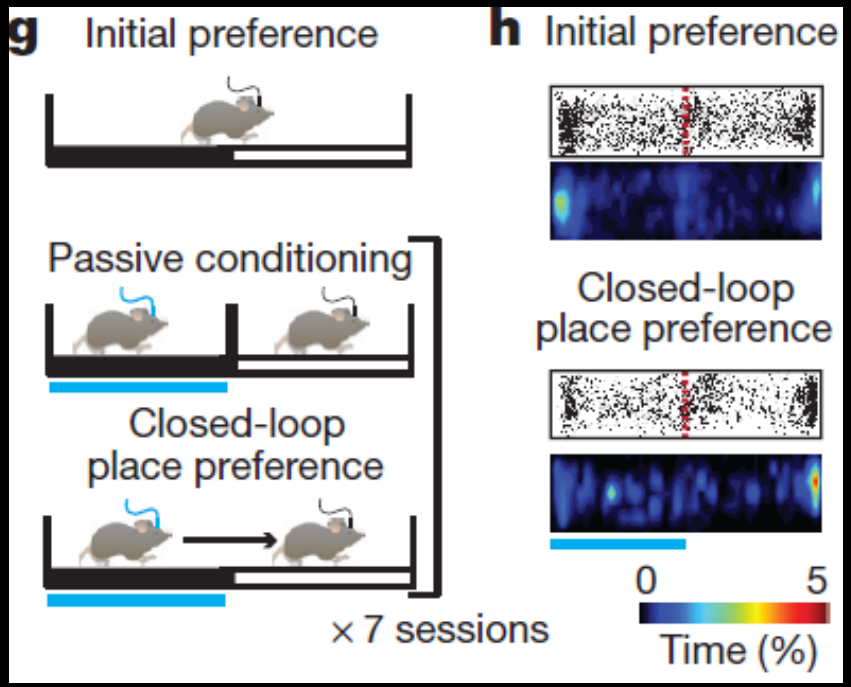
饥饿和渴介导负面情绪

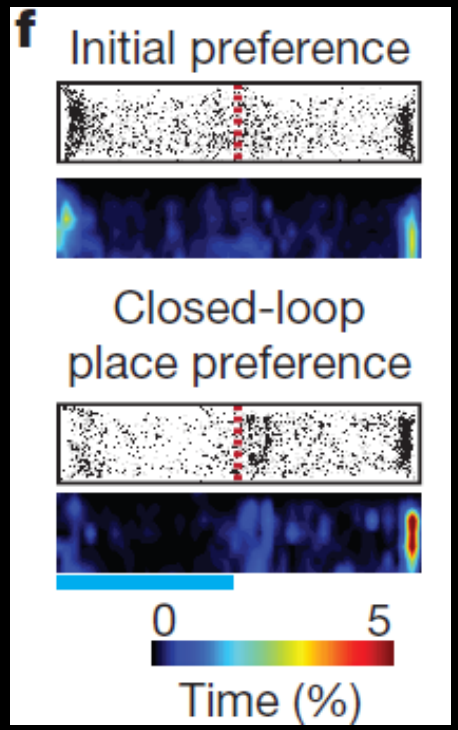
Hunger



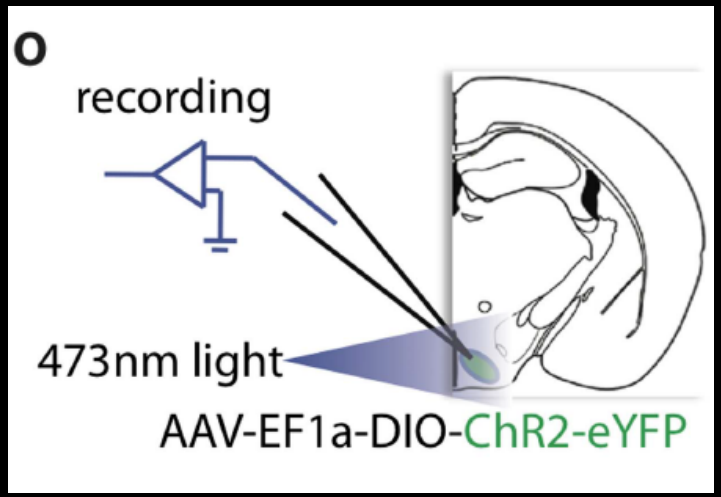
Thirst

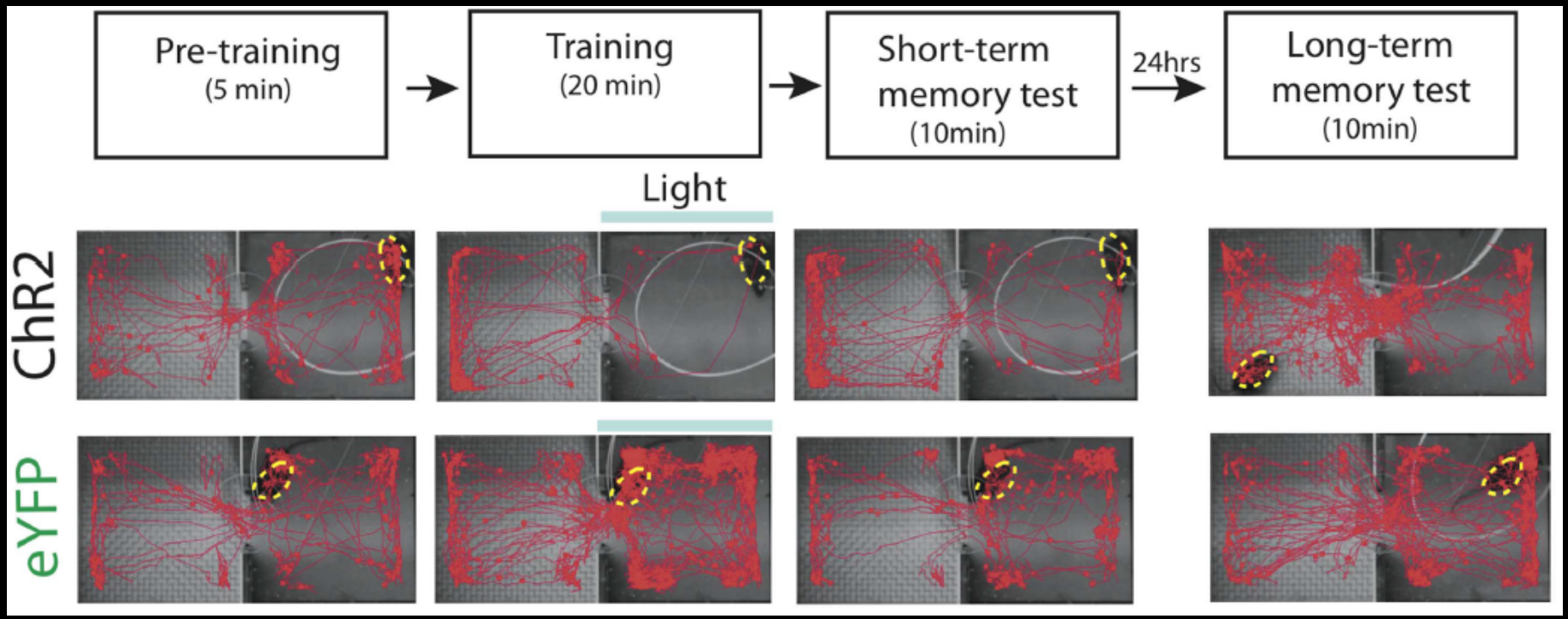




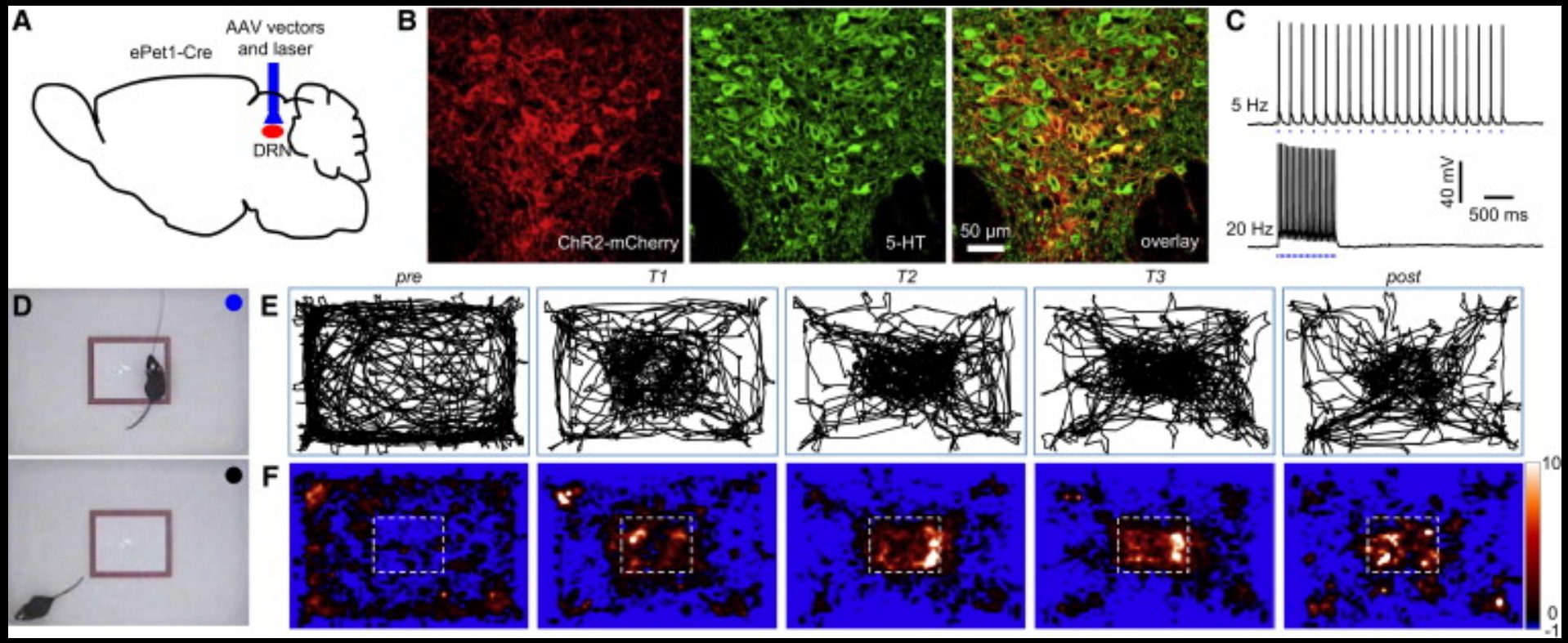


防御心理也是负面情绪

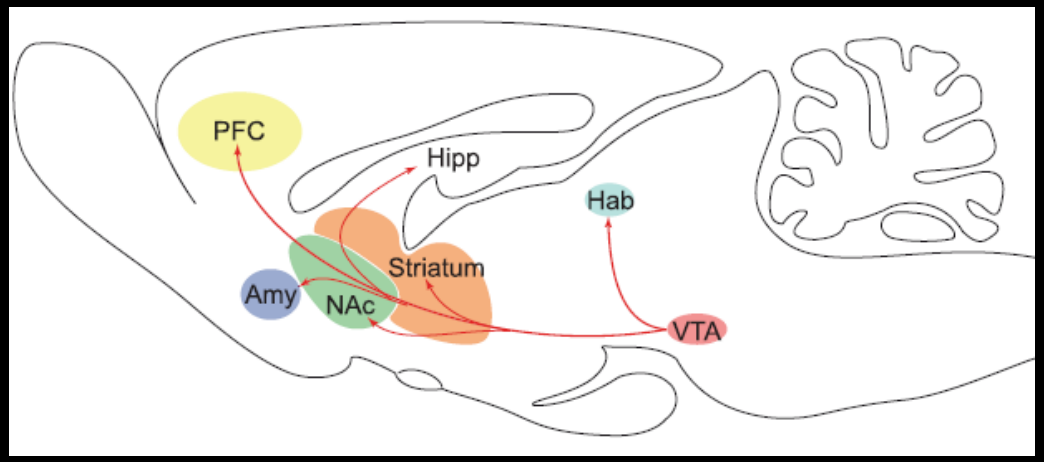

o
recording
473nm light
AAV-EF1a-DIO-ChR2-eYFP

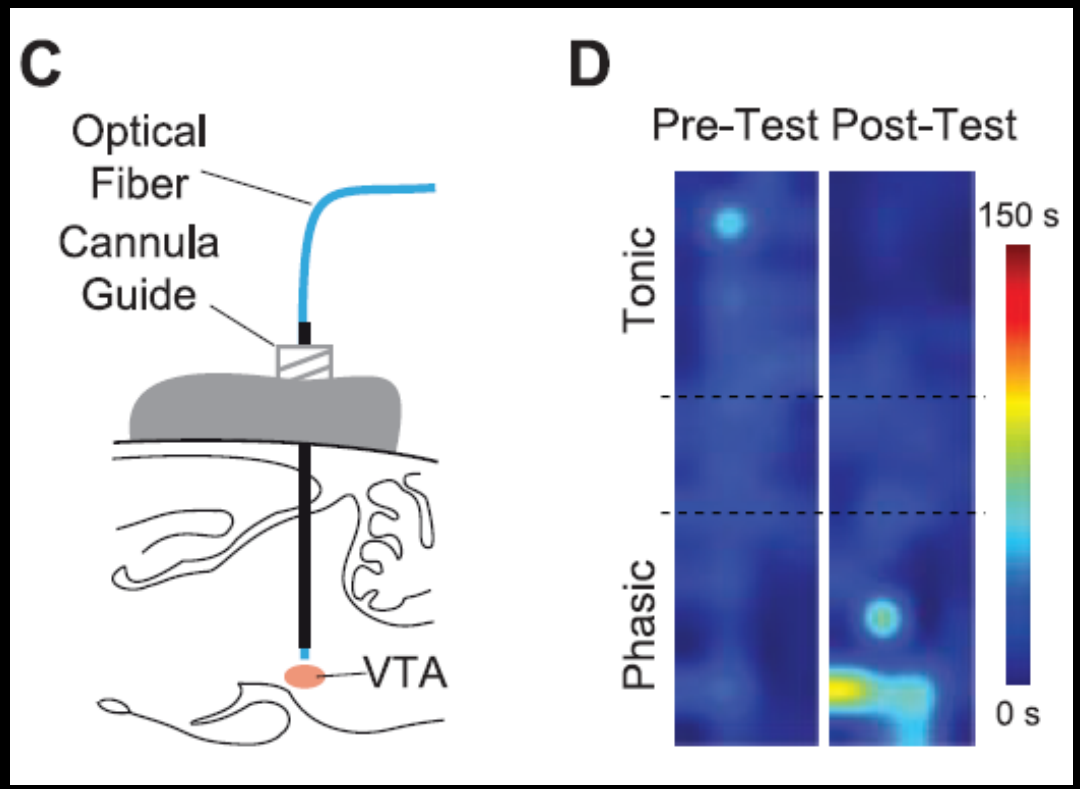

Pre-training
(5 min)
Training
(20 min)
Short-term
memory test
(10min)
24hrs
Long-term
memory test
(10min)
Light
ChR2
eYFP

五羟色胺神经元介导“倍爽”

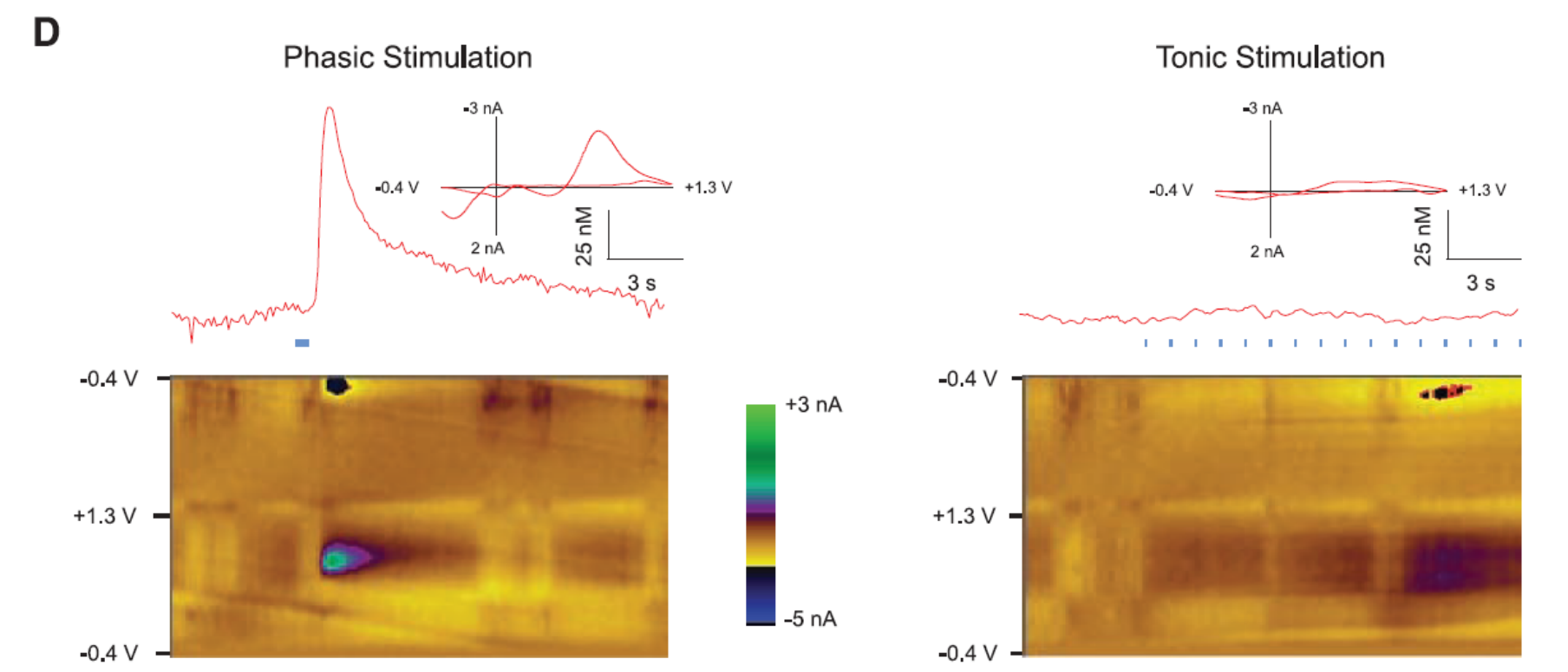


多巴胺神经元：奖赏中枢

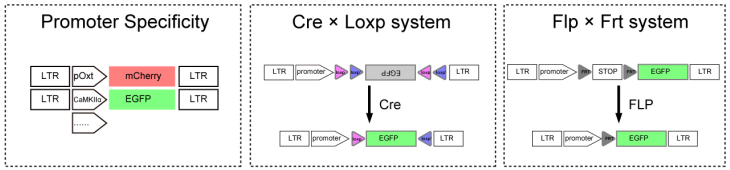
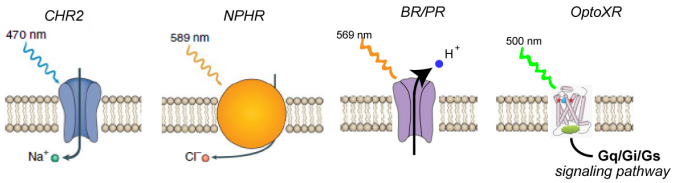
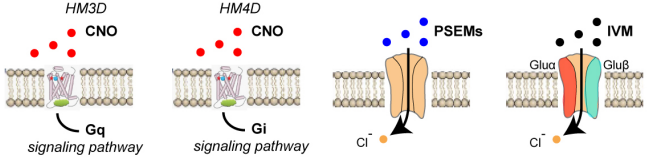
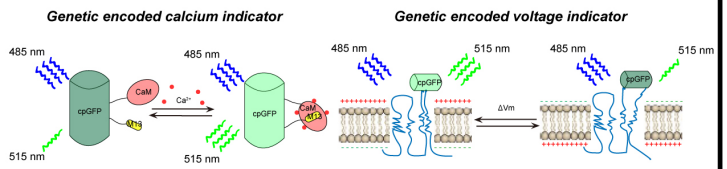
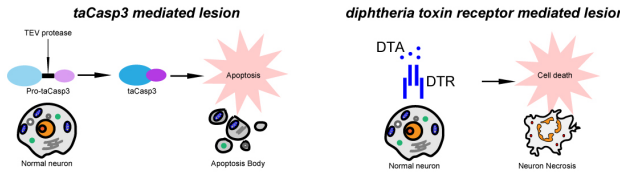
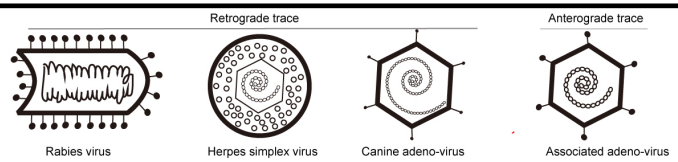

PFC
Hipp
Hab
Striatum
Amy
NAc
VTA


C
Optical
Fiber
Cannula
Guide
VTA
D
Pre-Test Post-Test
Tonic
Phasic
150 s
0 s

多巴胺神经元：奖赏中枢

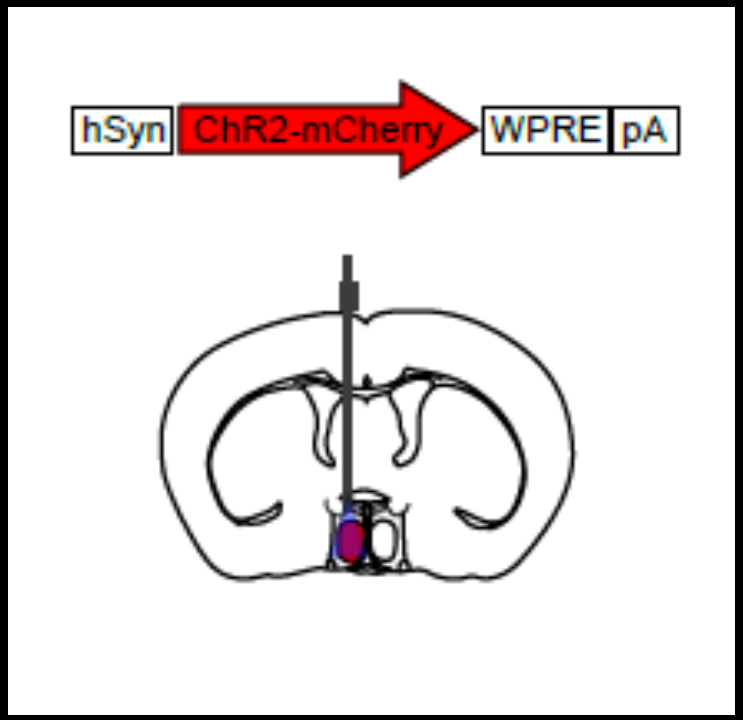

D
Phasic Stimulation
Tonic Stimulation
-3 nA
-0.4 V
+1.3 V
2 nA
25 nM
3 s
-0.4 V
+1.3 V
-0.4 V
+3 nA
-5 nA

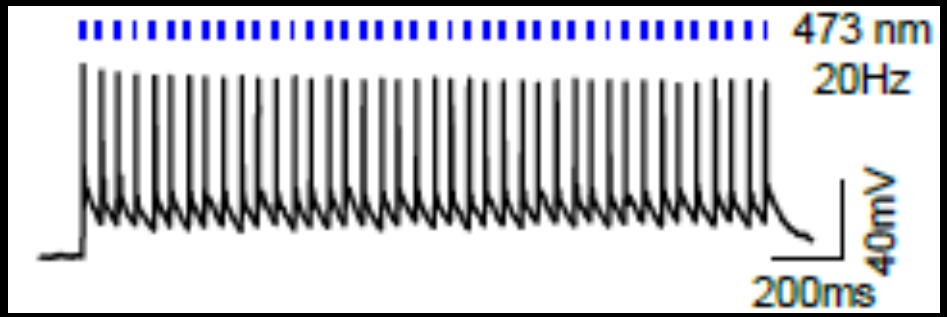
细胞特异性研究手段和方法

Functions	*Commonly used tools*	*References*
Cell specific targeting		Dittgen et al., 2004 Fields et al., 2012 Schlake and Bode, 1994 Sauer and Henderson, 1988
Light activated receptor		Airan et al., 2009 Boyden et al., 2005 Gradinaru et al., 2010
Drug activated receptor		Armbruster et al., 2007 Magnus et al., 2011 Lerchner et al., 2007
Neuronal activity indicator		Nakai et al., 2001 St-Pierre et al., 2014
Cell ablation		Yang et al., 2013 Palmiter et al., 1987 Buch et al., 2005
Circuit tracing		Callaway, 2008 Soudais et al., 2001 Bak et al., 1977 Norgren and Lehman, 1998

谢谢大家！

求偶行为和母性行为的神经基础





求偶行为

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