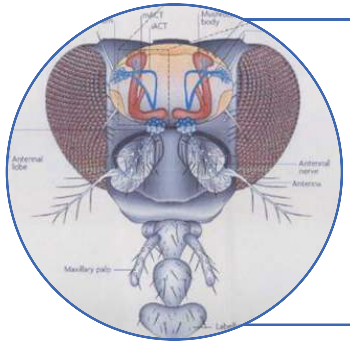
The olfactory learning and memory in *Drosophila*

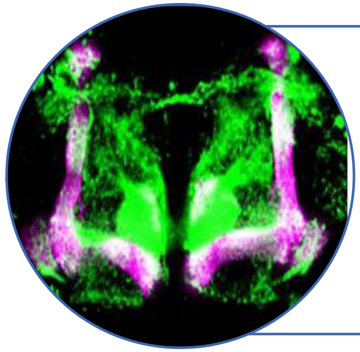
2019/08/30

邢丽敏 孙梦实 苏祥彬



Olfactory transmission and memory in *Drosophila*

--XLM



Olfactory Memory Formation in *Drosophila*

-- SXB

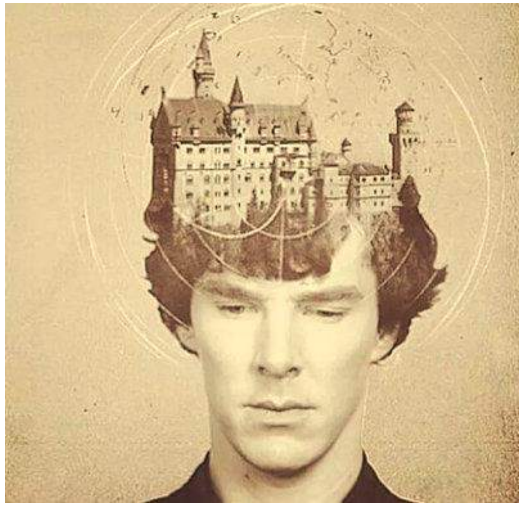
Forgetting and sleep-dependent memory retention in *Drosophila*

--SMS

Olfactory transmission and memory in *Drosophila*

Xing Limin

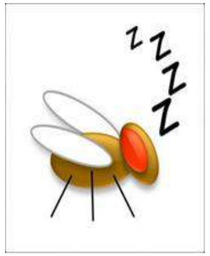
- What is learning and memory?
- How is olfactory information transmitted to the corresponding brain region?
- Functional genes in olfactory learning and memory in *Drosophila*
- Difficulties in olfactory learning and memory research

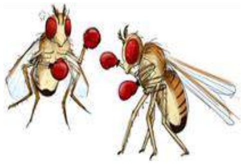


What is learning and memory?

Forget

Sensory information → learning → Short-term memory → consolidation → Long-term memory



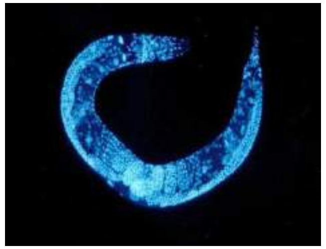


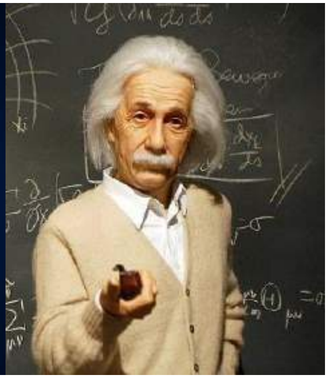
time

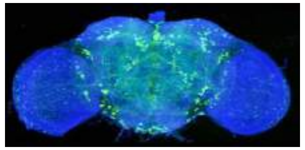
Learning: gain or acquire knowledge of or skill in (something) by study, experience, or being taught.

Memory: the ability for the mind stores and remembers information

Why choose the flies as a model organism?







人类大脑（1000亿个神经元）

老鼠大脑 (1亿个神经元)

果蝇大脑（10万个神经元）

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Current Opinion in Neurobiology

Olfactory learning skews mushroom body output pathways to steer behavioral choice in *Drosophila*

David Owald and Scott Waddell

eLIFE elifesciences.org RESEARCH ARTICLE

Shared mushroom body circuits underlie visual and olfactory memories in *Drosophila*

Katrin Vogt[1†], Christopher Schnaitmann[1†‡], Kristina V Dylla[1§], Stephan Knapek[1], Yoshinori Aso[2], Gerald M Rubin[2], Hiromu Tanimoto[1,3*]

[1]Max-Planck-Institute of Neurobiology, Martinsried, Germany; [2]Janelia Farm Research Campus, Howard Hughes Medical Institute, Ashburn, United States; [3]Graduate School of Life Sciences, Tohoku University, Sendai, Japan

eLIFE elifesciences.org RESEARCH ARTICLE

Gap junction networks in mushroom bodies participate in visual learning and memory in *Drosophila*

Qingqing Liu[1,2†], Xing Yang[3†], Jingsong Tian[1,2], Zhongbao Gao[1,2], Meng Wang[1], Yan Li[1*], Aike Guo[1,3*]

[1]State Key Laboratory of Brain and Cognitive Science, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China; [2]University of Chinese Academy of Sciences, Beijing, China; [3]Institute of Neuroscience, State Key Laboratory of Neuroscience, CAS Center for Excellence in Brain Science and Intelligence Technology, Shanghai Institutes for Biological Sciences, CAS, Shanghai, China

Olfactory learning
CS-US
Anatomically similar to vertebrates
Fewer cells
Powerful genetic analysis tools

Contents lists available at ScienceDirect
Journal of Insect Physiology
journal homepage: www.elsevier.com/locate/jinsphys

Review

Odor-taste learning in *Drosophila* larvae

Annekathrin Widmann[b], Katharina Eichler[b,c], Mareike Selcho[a], Andreas S. Thum[b,d,*,1], Dennis Pauls[a,*,1]

[a] Department of Neurobiology and Genetics, Theodor-Boveri-Institute, Biocenter, University of Würzburg, D-97074 Würzburg, Germany
[b] Department of Biology, University of Konstanz, D-78464 Konstanz, Germany
[c] HHMI Janelia Research Campus, 19700 Helix Drive, Ashburn, VA 20147, USA
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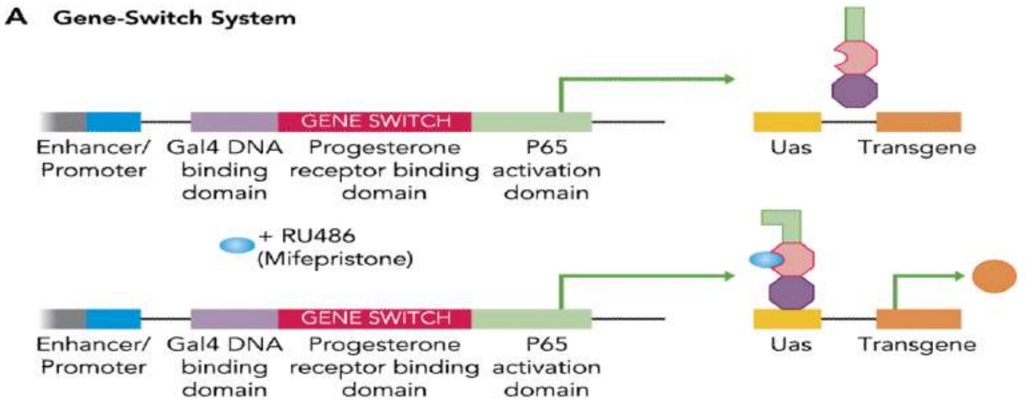
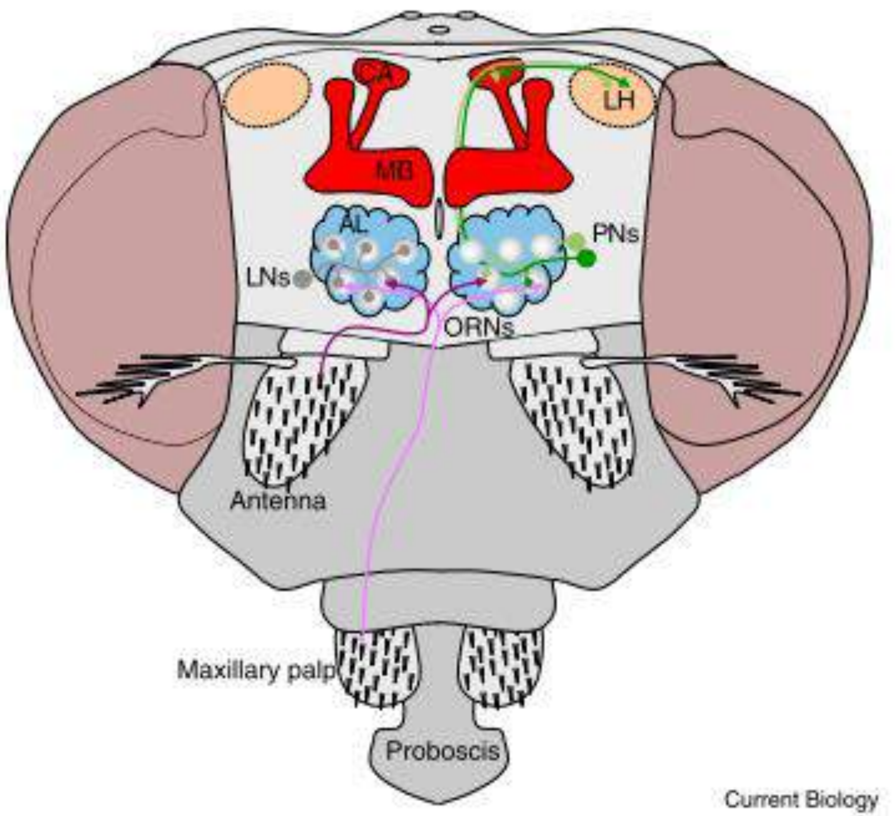
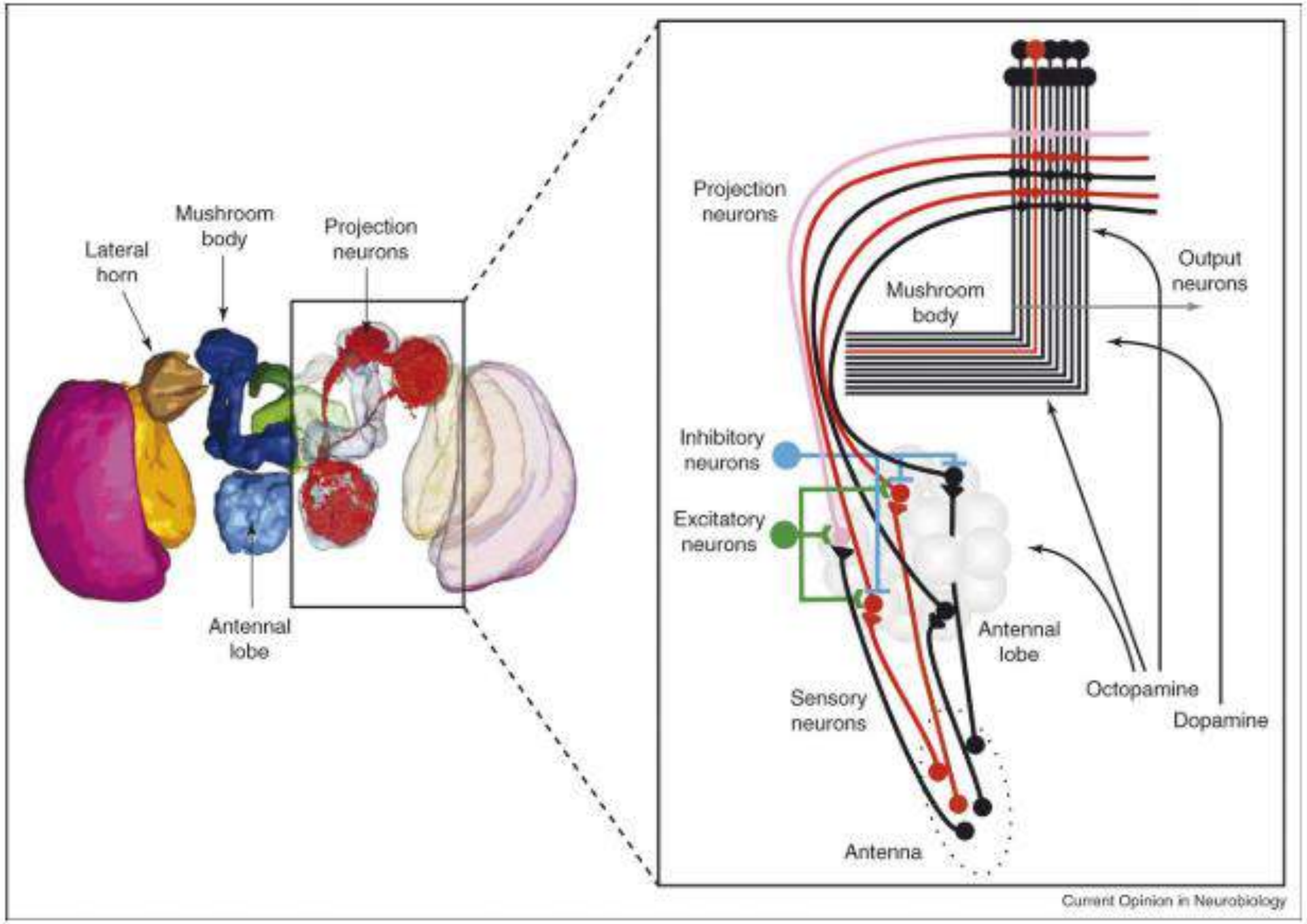


How is olfactory information transmitted to the corresponding brain regions?

The *Drosophila* olfactory pathway

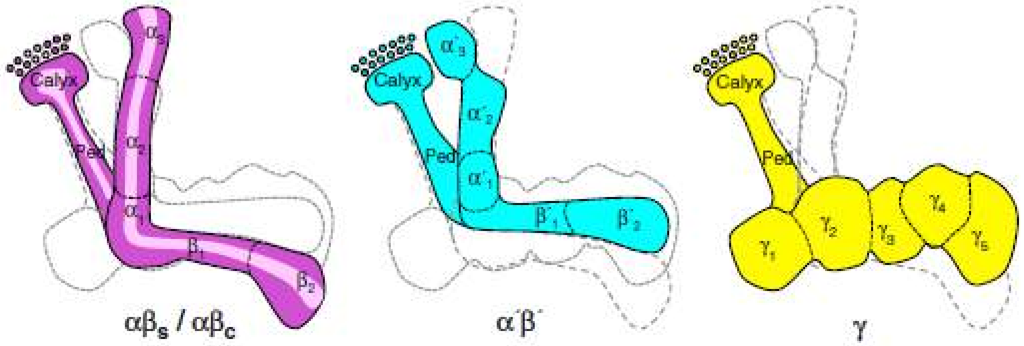


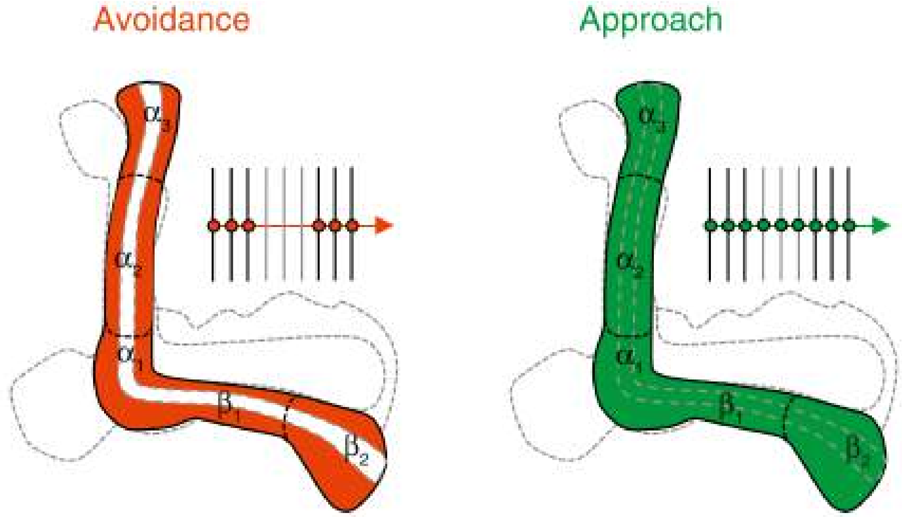


Olfactory receptor neurons (ORNs) in sensillae on the 3rd antennal segments and the maxillary palps project their axons bilaterally into individual glomeruli in the antennal lobe (AL).

Perisse, E. *et al*. 2013. Fiala, A. 2007

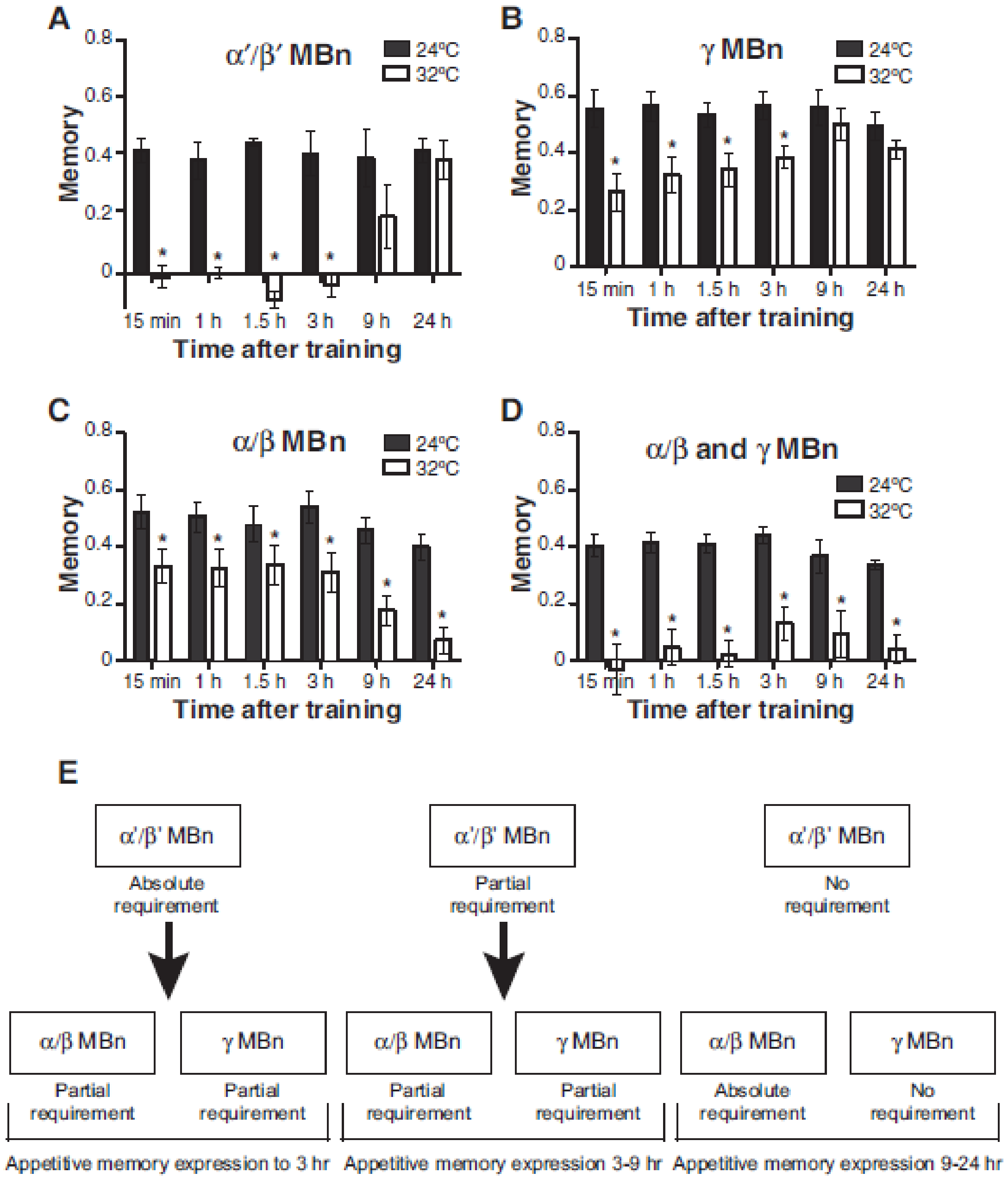
Functional classes of kenyon cells in the mushroom body



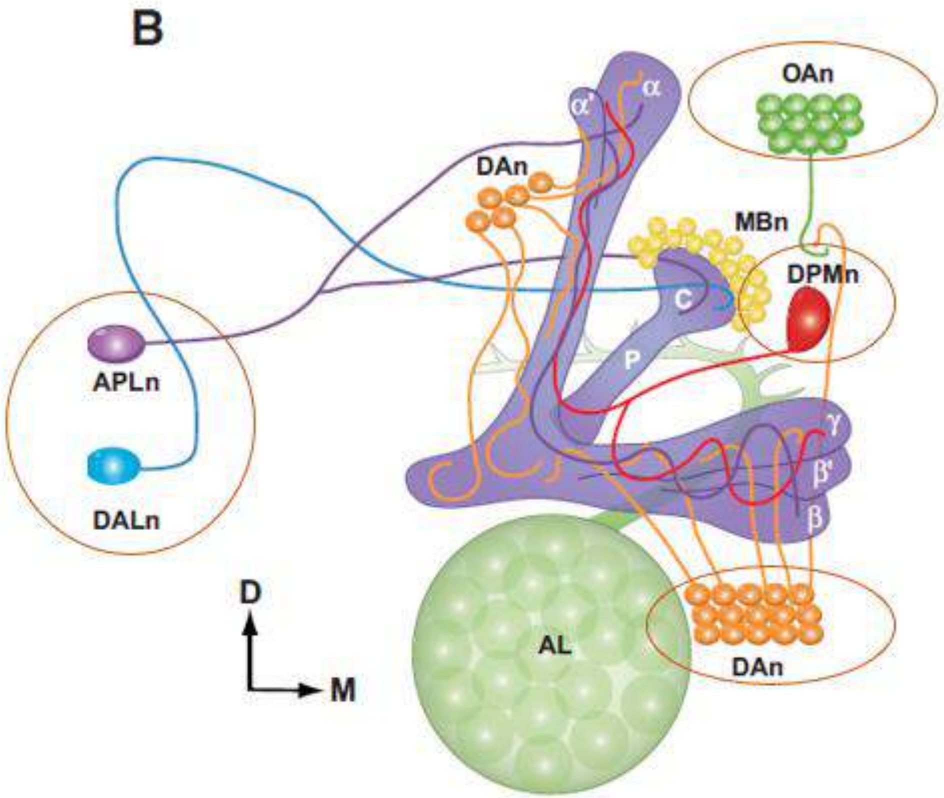


αβs

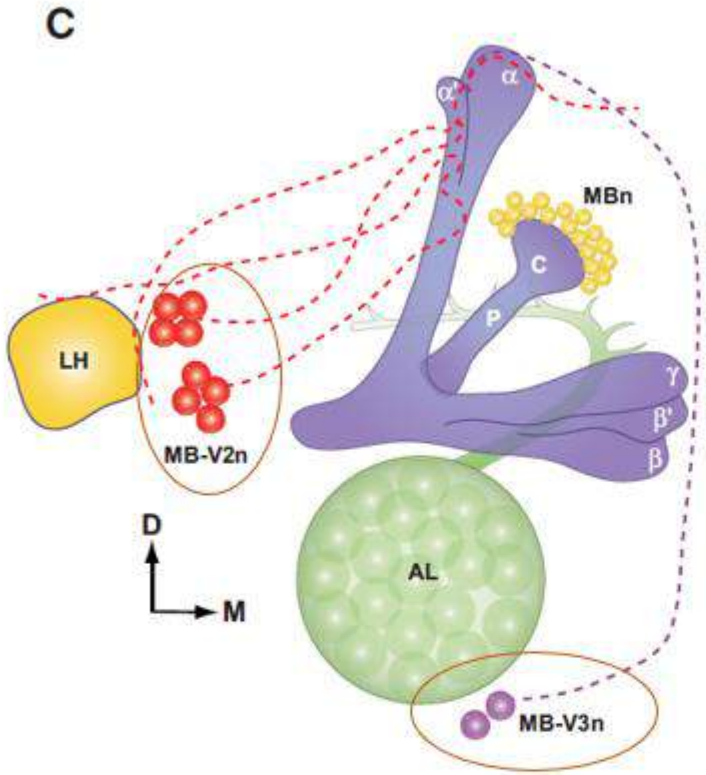
αβs and αβc,



Tugba Guven-Ozkan and Ronald L. Davis. 2014



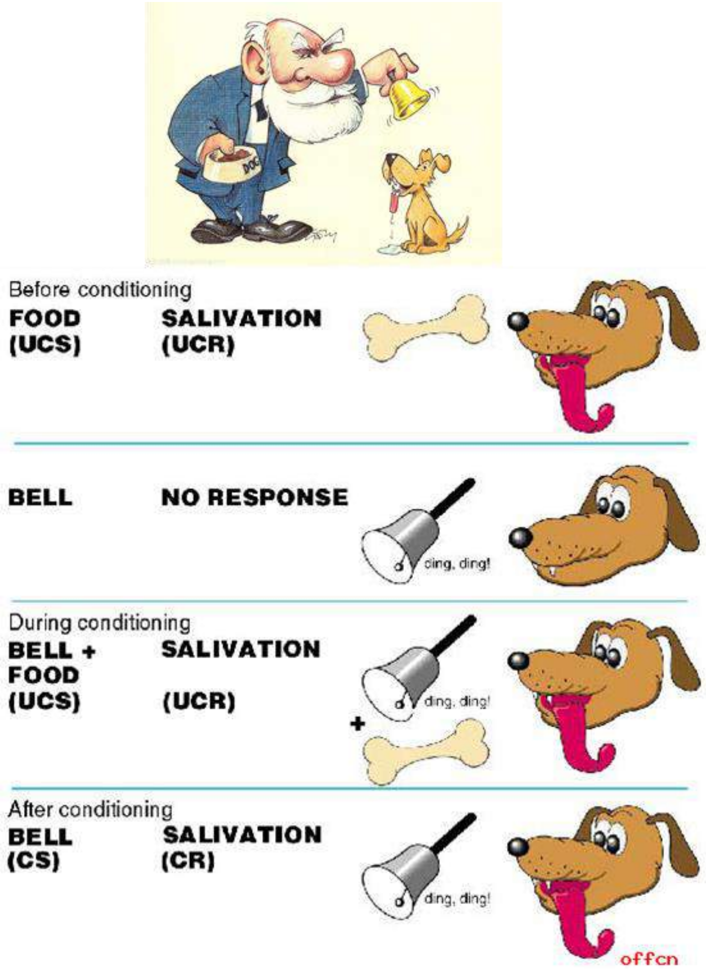
MB extrinsic neurons that are involved in learning and memory.



Output neurons of the MBn.

Tugba Guven-Ozkan and Ronald L. Davis. 2014

Ways to train *Drosophila*



Aversive memory

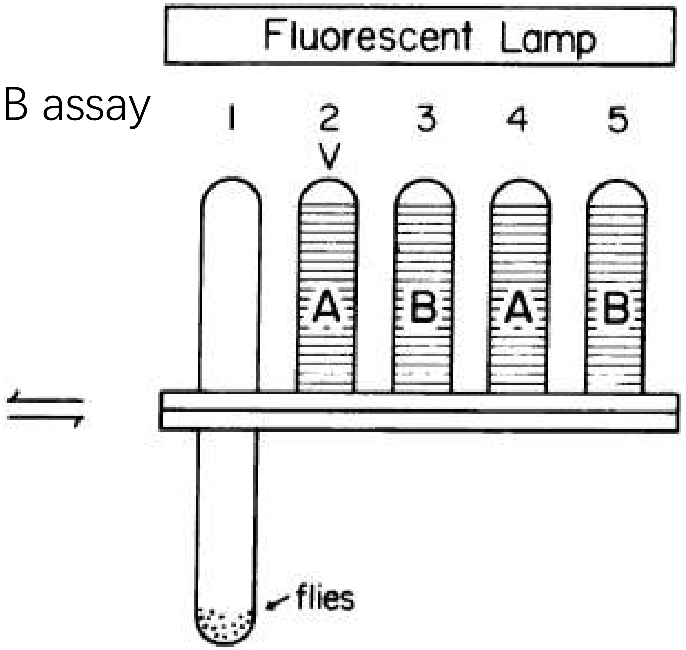
Appetitive memory

The same features: acquisition, extinction, CS/US saliency, order dependence, temporal specificity, conditioned excitation, conditioned inhibition and CS/US preexposure effects

Ways to train *Drosophila*

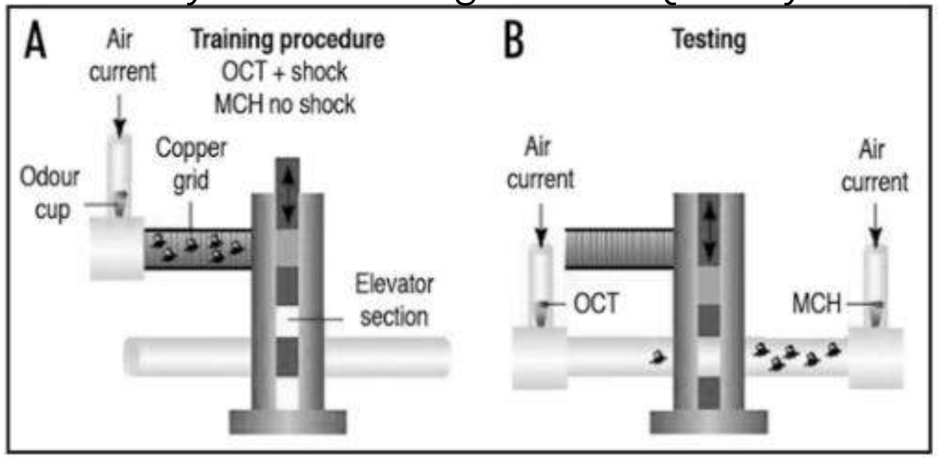
Olfactory avoidance learning

QHB assay

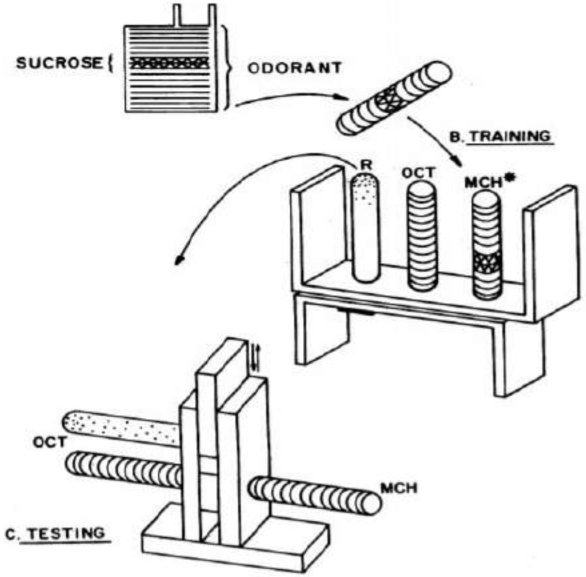


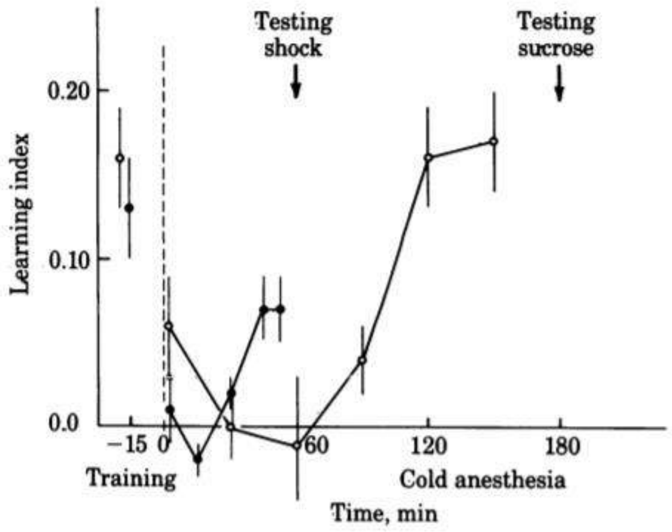
$$\text{learning index}=\frac{\text{avoided the CS}^{-}\text{ - avoided the CS}^{+}}{\text{total number of flies}}$$

Olfactory conditioning in the TQ assay.



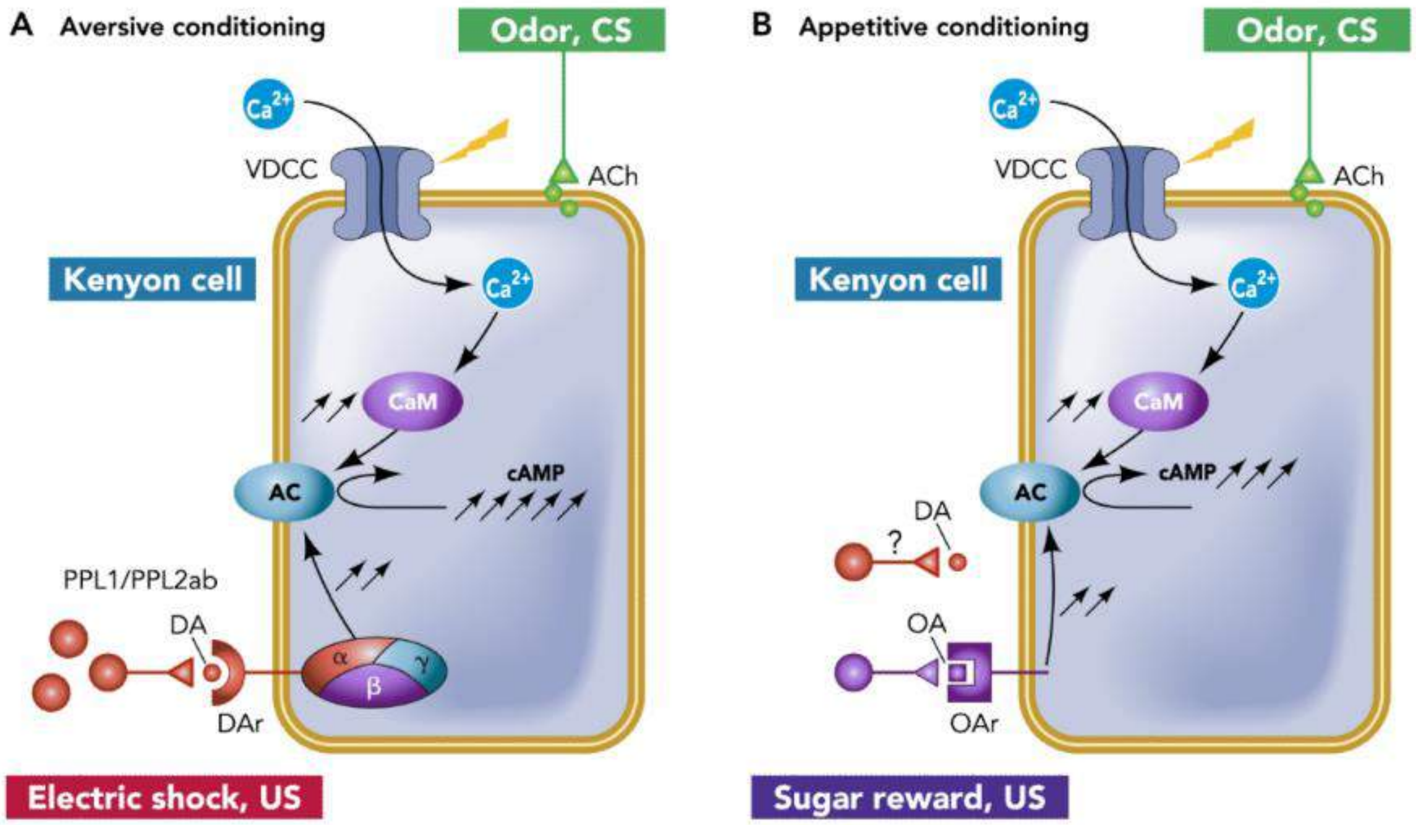
Olfactory appetitive conditioning

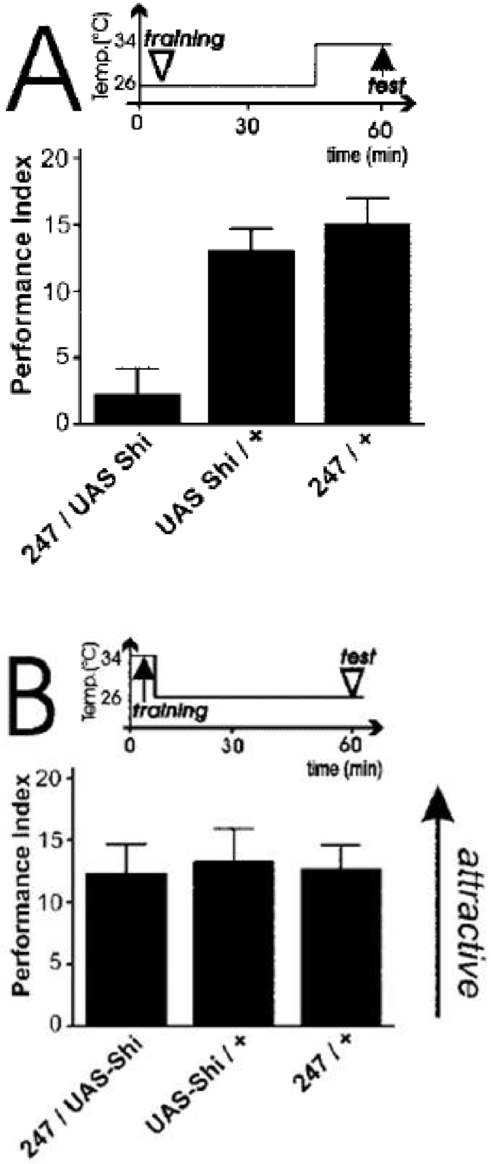




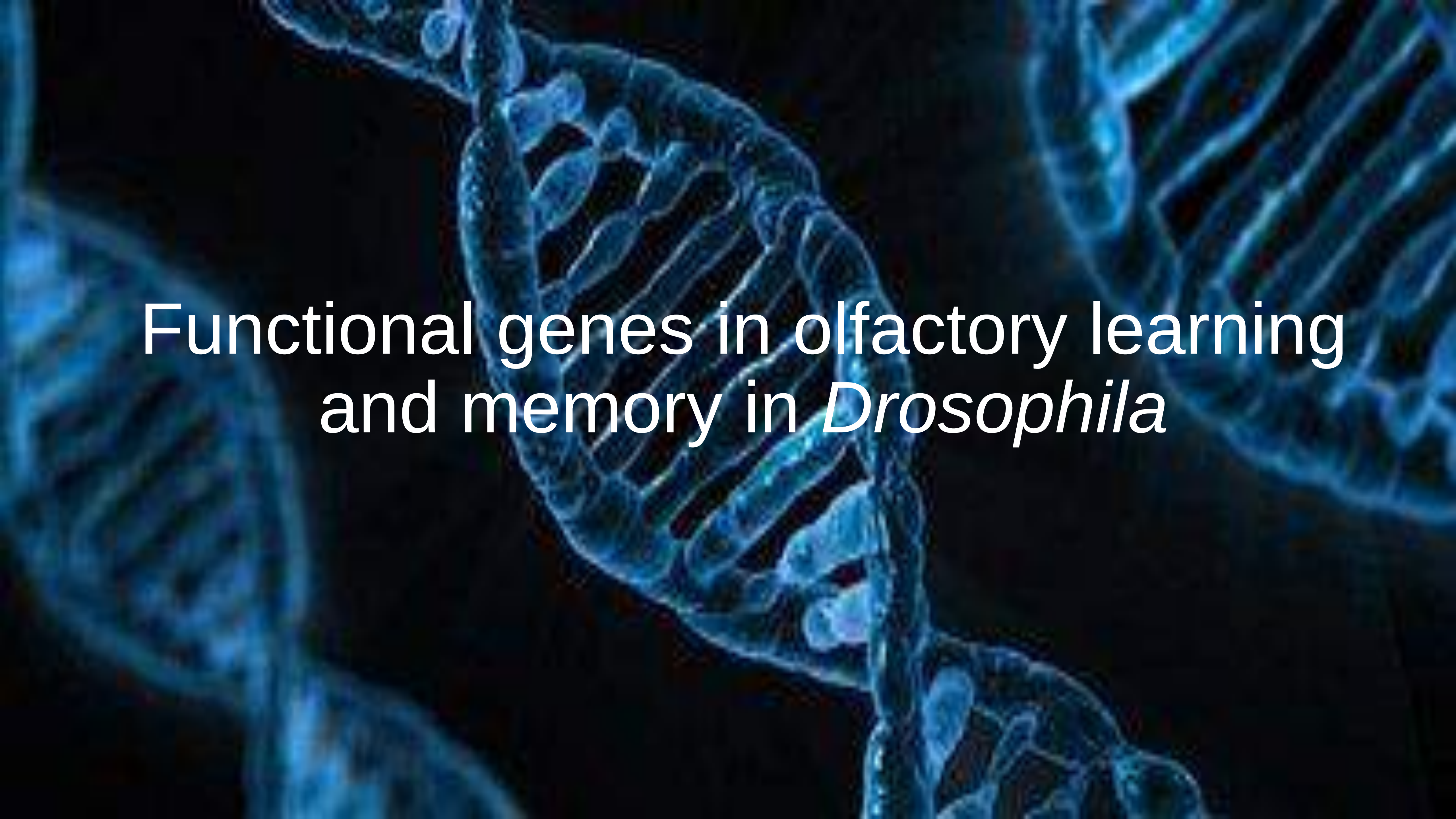
Quinn WG, *et al*. 1974. Tully T, Quinn WG. 1985. Tempel BL, *et al*. 1983

Schematic representation of some of the molecular mechanisms involved in aversive and appetitive olfactory conditioning

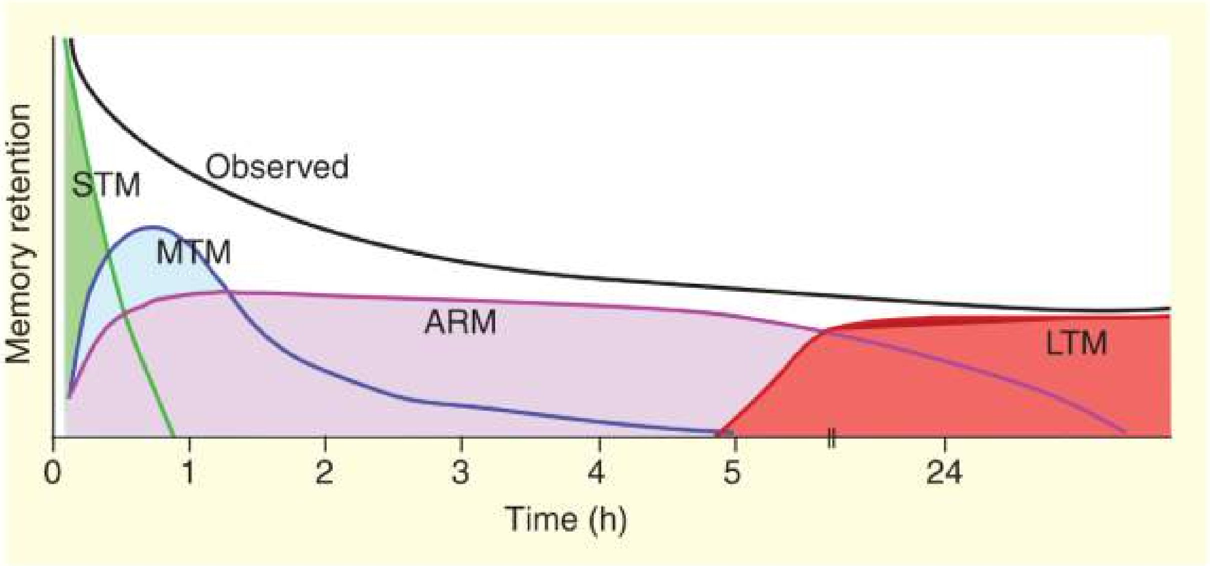




Germain U. Busto., *et al*. 2010



Functional genes in olfactory learning and memory in *Drosophila*



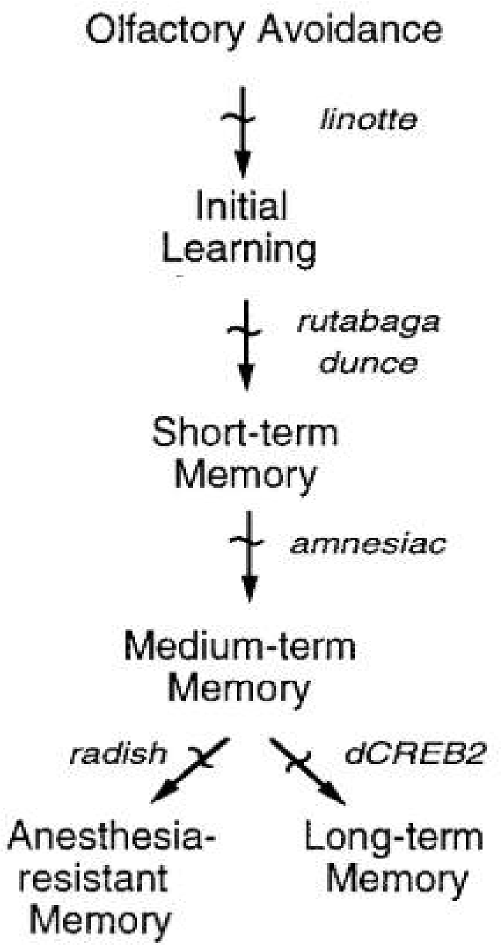


Figure 2. Pathways of Learning Genes
Data are from Tully et al., 1990, 1994; Siegel and Hall, 1979; Gailey et al., 1984; Griffith et al., 1993, 1994.

Genes and genetic technologies

Table 1 | **Genes reported, or suspected, to be involved in *Drosophila melanogaster* memory**

Mutant/transgene (gene)	Abbreviation	Product	Expression
amnesiac	*amn*	Putative neuropeptide	High in DPM
dunce	*dnc*	cAMP phosphodiesterase	High in MBs
rutabaga	*rut*	Type I adenylyl cyclase	High in MBs
turnip	*tur*	ND	ND
radish	*rsh*	No obvious functional homologue	High in MBs
DC0	*DC0*	PKA catalytic subunit	High in MBs
PKA-RI	*PKA-RI*	PKA regulatory subunit	High in MBs
G-sα60A	*G-sα60A*	Stimulatory G protein	ND
Neurofibromin	*NF1*	Ras-GTPase activating protein (GAP)	ND
leonardo	*leo*	14-3-3ζ	High in MBs*
volado (scab)	*scb*	α-integrin	High in MBs*
fasciclin II	*fasII*	Neural cell adhesion molecule	High in MBs*
damb	*damb*	Dopamine receptor in MBs	High in MBs
dDA1/DMDOP1	*dDA1*	Dopamine receptor	High in MBs
oamb	*oamb*	Octopamine receptor in MBs	High in MBs
mushroom body miniature	*mbm*	Transcription factor	High in MBs‡
mushroom bodies deranged	*mbd*	ND	ND
ignorant (S6KII)	*S6KII*	Ribosomal S6 kinase	ND
latheo	*lat*	Origin recognition complex	ND

Table 2 | **Useful genetic technology for *Drosophila melanogaster* neurobiology**

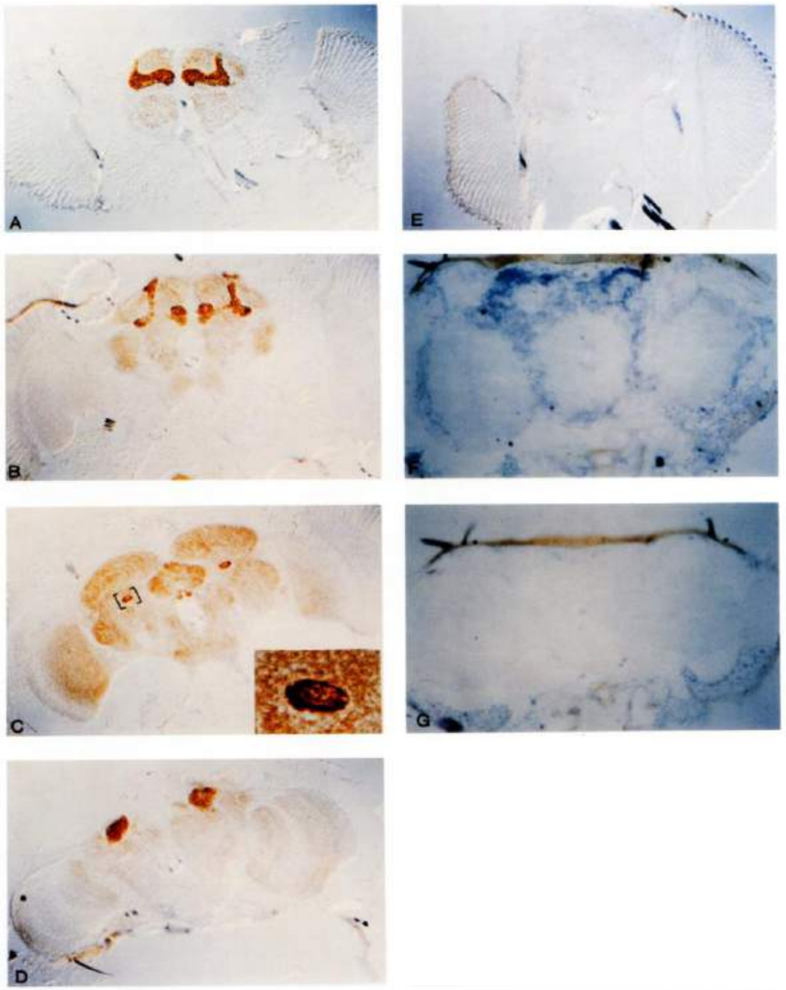
Tool	Description	Refs
Expression control		
GAL4	Yeast transcription factor used to drive expression of transgenes downstream of the GAL4 upstream activating sequence (UAS_{GAL4})	181
UAS_{GAL4}	Promoter driven by GAL4; any gene cloned downstream can be driven in a cell-specific manner when combined with a region-restricted GAL4	181
GAL80	Yeast repressor of GAL4, can be used to spatially limit GAL4 activity	72
GAL80ts	A temperature sensitive GAL80 used in the TARGET system to provide user-determined temporal control of spatially restricted GAL4 activity	135
GeneSwitch	A steroid-hormone activated GAL4, allowing user-determined temporal control of spatially restricted GAL4 activity	136
OR[GAL4]	Olfactory receptor gene promoter-driven GAL4	
TH[GAL4]	Tyrosine hydroxylase gene promoter-driven GAL4, to control transgene expression in dopaminergic neurons	109
TDC2[GAL4]	Tyrosine *decarboxylase 2* gene-promoter driven GAL4, to control transgene expression in octopaminergic (and tyraminergic) neurons	117
MB[GAL4]	There are many [GAL4] enhancer-trap lines that permit transgene expression in subsets of MB neurons	83,99,134,137
DPM[GAL4]	Several [GAL4] enhancer-trap lines that permit transgene expression in DPM neurons	148,153
FLP–FRT	A site-specific recombination system that can be used to limit the expression of reporter genes so that single neurons can be labelled	71
MARCM	Mosaic analysis with a repressible cell marker, a sophisticated genetic trick using GAL80 that allows single (wild-type or mutant) neurons to be labelled	72
LexA/LexAop	Binary transcription factor system based on the bacterial LexA transcription factor. LexA transactivates promoters containing the LexAop sequence. This system is independent of GAL4 but variants have been engineered that can be repressed by GAL80. Dual use of LexA/LexAop and GAL4/UAS allows one to simultaneously manipulate different neurons	162
Reporters		
UAS–Cameleon 2.1	A ratiometric fluorescent reporter of intracellular Ca^{2+}	96
UAS–SpH	Synaptophluorin, a pH-sensitive fluorescent reporter of synaptic transmission	58
UAS–GCaMP	A high signal-to-noise fluorescent reporter of intracellular Ca^{2+}	59
Effectors		
UAS–*TNT*	Tetanus toxin light chain; blocks neurotransmitter release	182
UAS–*shibire*^{ts1}	A temperature-sensitive blocker of synaptic transmission resulting from a block of endocytosis and therefore synaptic vesicle recycling	5
UAS–*P2X2*	A rat ionotropic ATP receptor that permits direct stimulation of genetically marked neurons following photoactivation of caged ATP	7
UAS–*VR1*	A rat vanilloid receptor that permits direct stimulation of genetically marked sensory receptors with capsaicin	6,8
UAS–*ChR2*	Channelrhodopsin 2, an algal blue-light-activated cation channel that permits direct stimulation of genetically marked neurons with light	9–11
UAS–PTX	Pertussis toxin; inhibitor of G_o signalling	183
UAS–*PACα*	Photoactivated adenylyl cyclase, a flagellate adenylate cyclase that permits stimulation of cAMP synthesis in genetically marked neurons with blue light	18

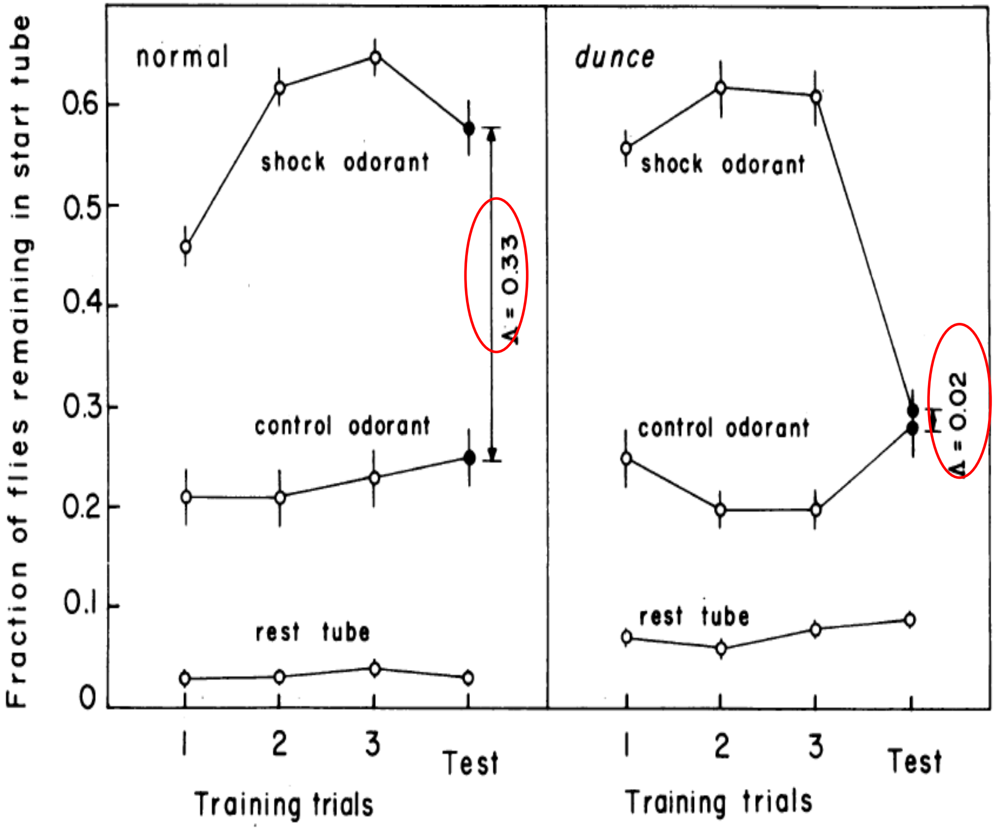
cAMP, cyclic AMP; DPM, dorsal paired medial; MB, mushroom body; UAS, upstream activating sequence.

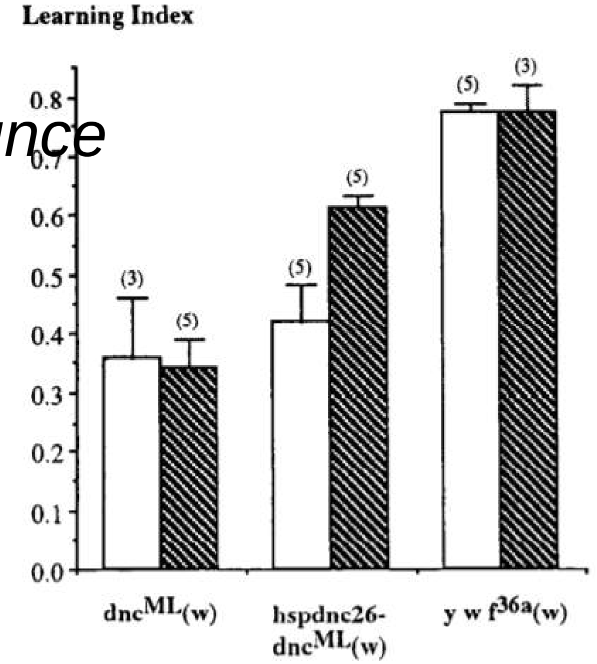
Alex C. Keene and Scott Waddell. 2007

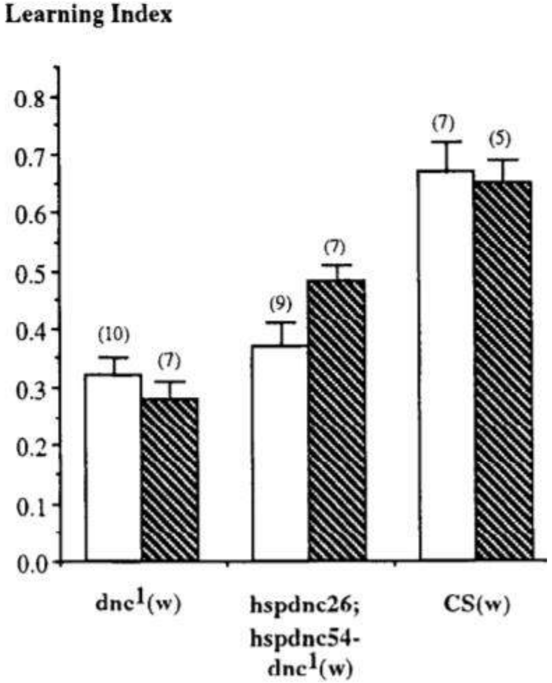
Genes relate to STM: *dunce*

The first learning and memory mutant to be isolated was *dunce*





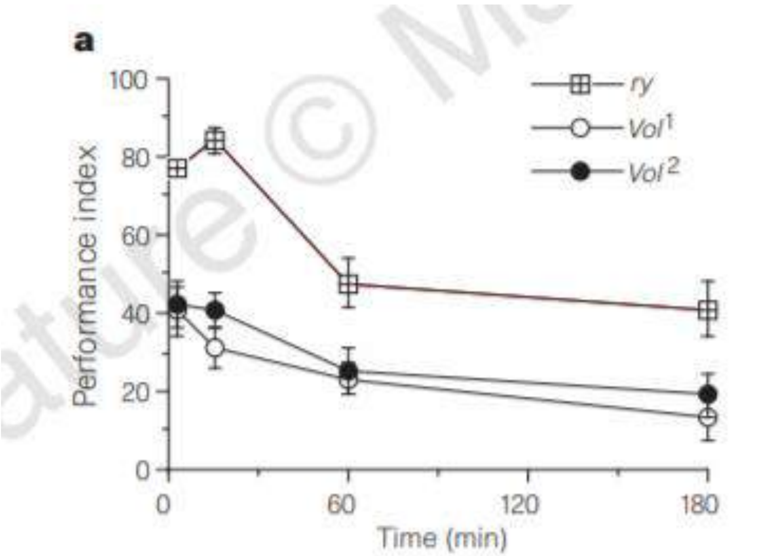


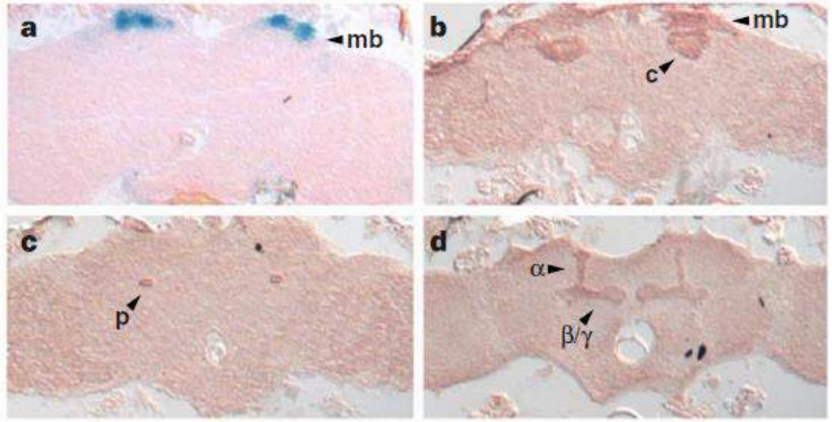


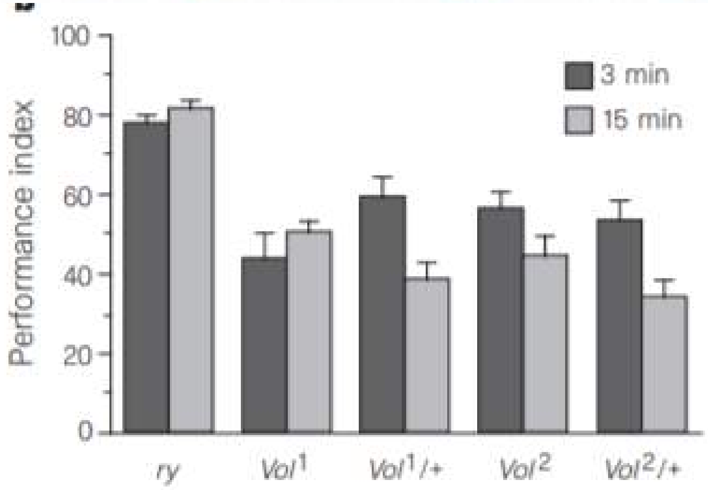
Yadin Dudai., *et al*. 1976. Alan Nighorn., *et al*. 1991. Chun-nan Chen. *et al*.1986

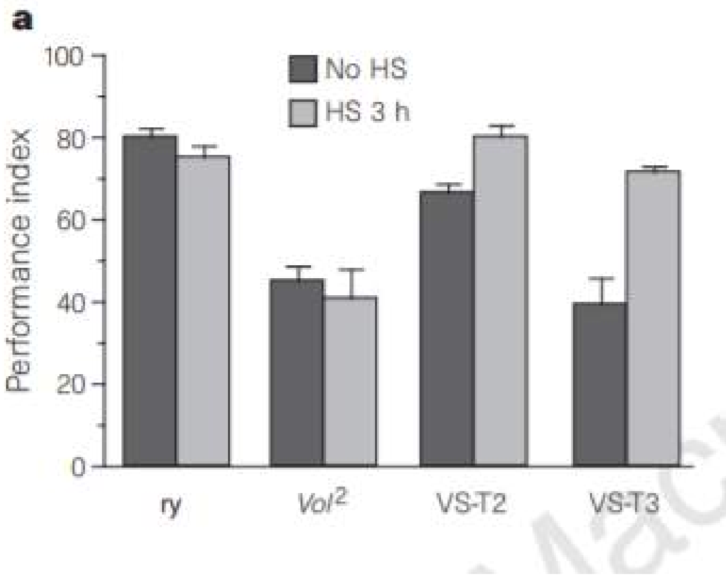
Genes relate to STM: *vol*

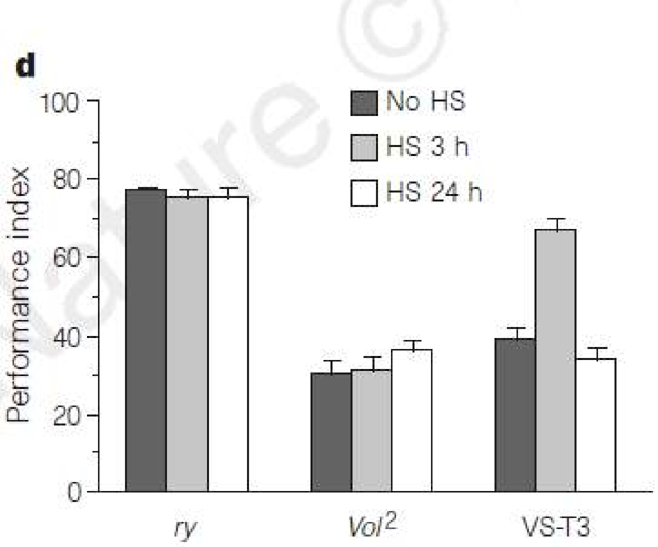
Volado mutants display impaired olfactory memories within **3min** of training, indicating that the **integrin** is required for short-term memory processes.











Michael S. Grotewiel.,*et al*. 1998

Gene relate to MTM: *amn*

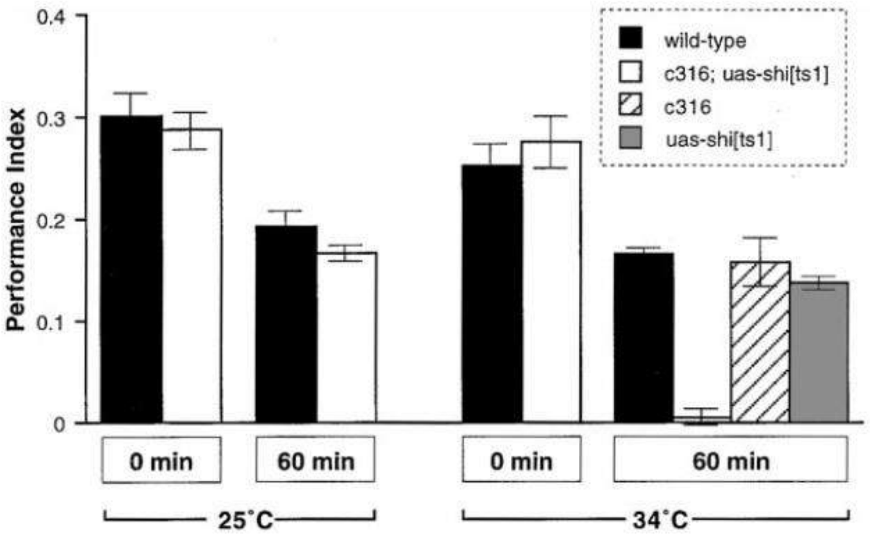
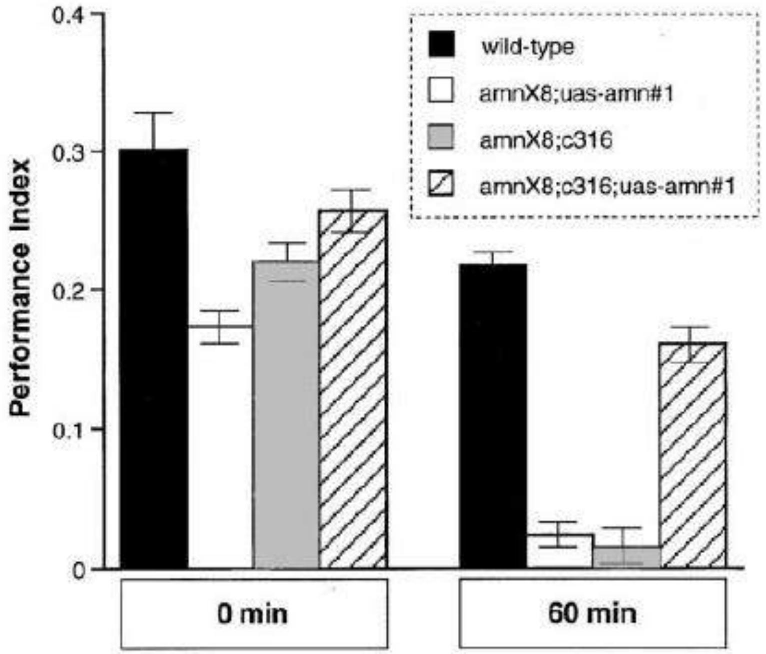
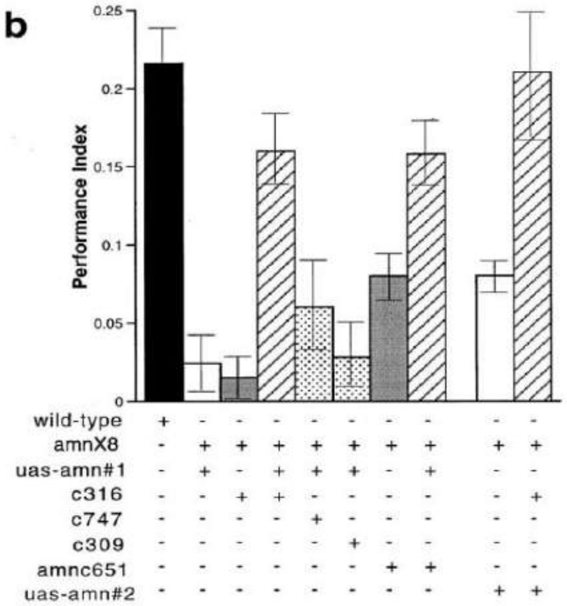
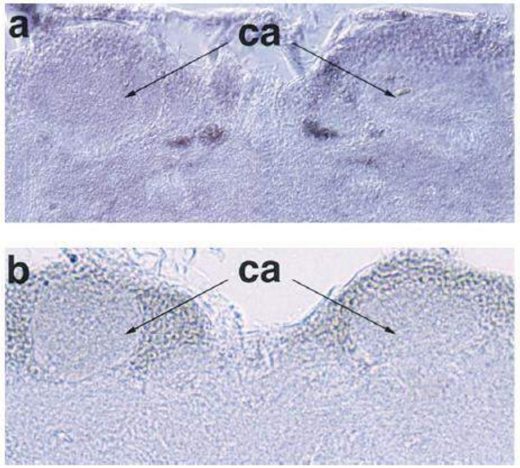


Table 1. List of Strains Used in This Study

Mutant	Chromosomal Location/Description	Tissue Specificity	References
amn^{chpd}	X chromosome, 19A P{lacW} element	*amn* gene pattern	Moore et al. (1998)
amn^{c651}	X chromosome, 19A P{GAL4} element	*amn* gene pattern	This report
amn^{28A}	X chromosome, 19A P{GAL4} element	*amn* gene pattern additional widespread expression	Moore et al. (1998), DeZazzo et al. (1999)
amn^{X8}	X chromosome, 19A *amn* gene deletion		Moore et al. (1998), DeZazzo et al. (1999)
c316	3rd chromosome P{GAL4} element	Largely DPM-cell restricted	This report
c747 (= c772)	2nd chromosome, 41F P{GAL4} element	Widespread, higher in mushroom bodies	Yang et al. (1995), Connolly et al. (1996), Armstrong et al. Flytrap
c309	P {GAL4} element	Widespread, higher in mushroom bodies	Connolly et al. (1996), Armstrong et al. Flytrap



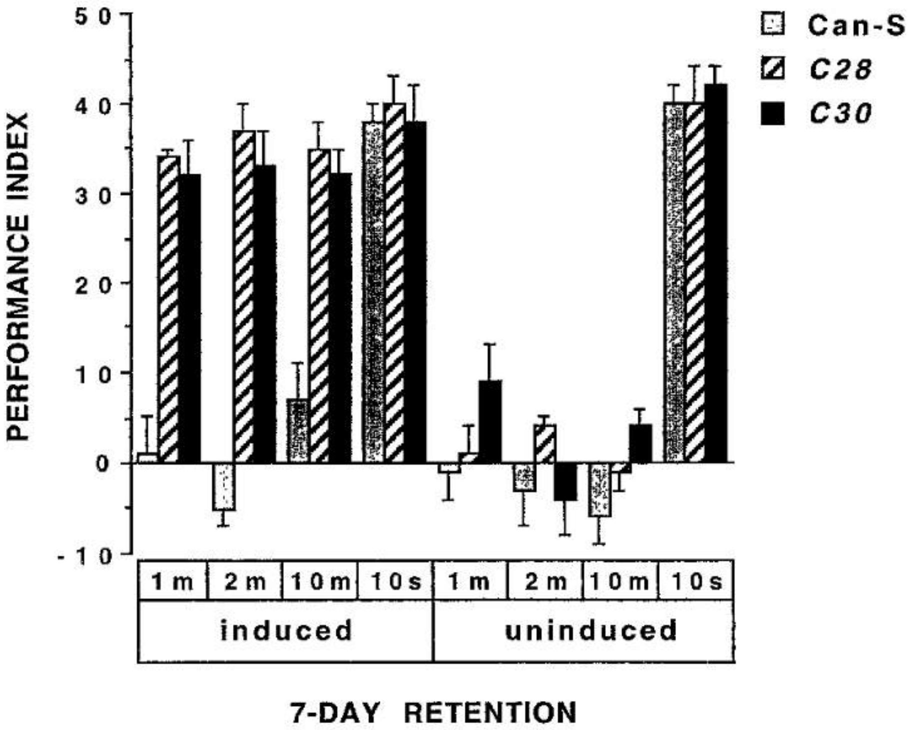


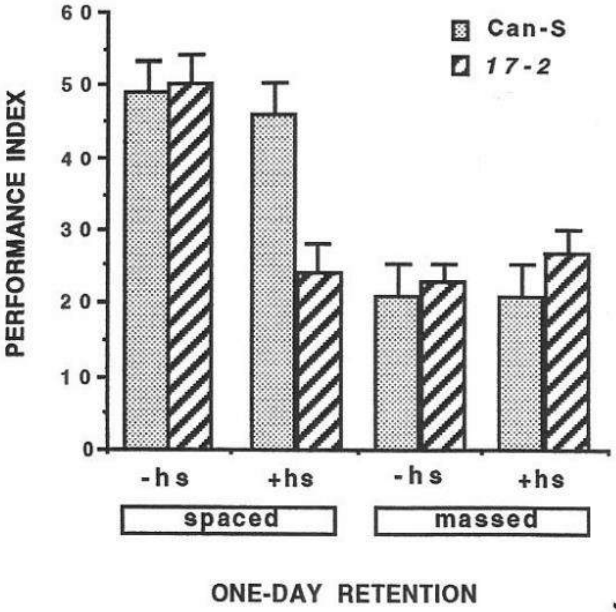


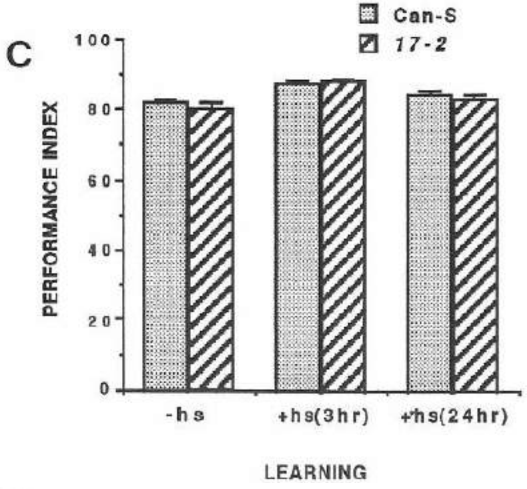
DPM

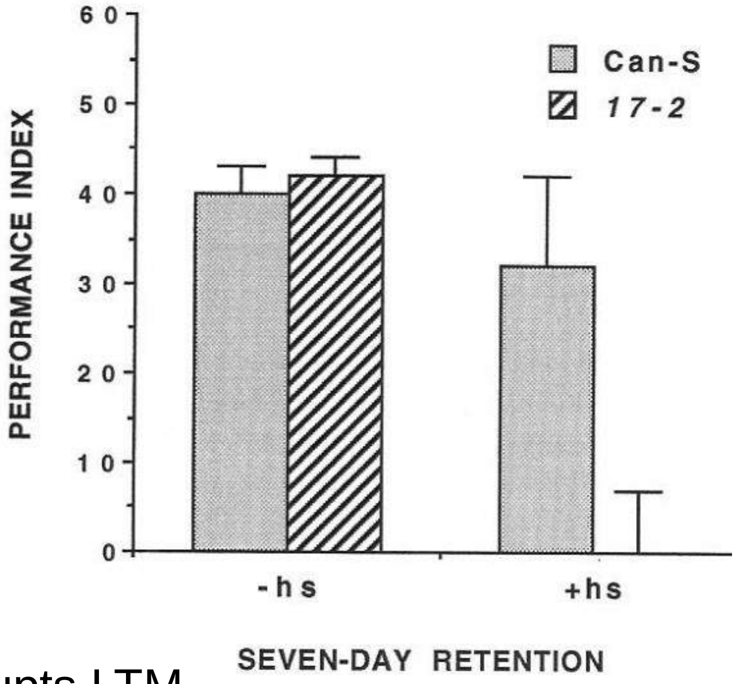
Scott Waddell. *et al*. 2000

The function of cAMP-responsive element-binding protein (CREB) in LTM formation









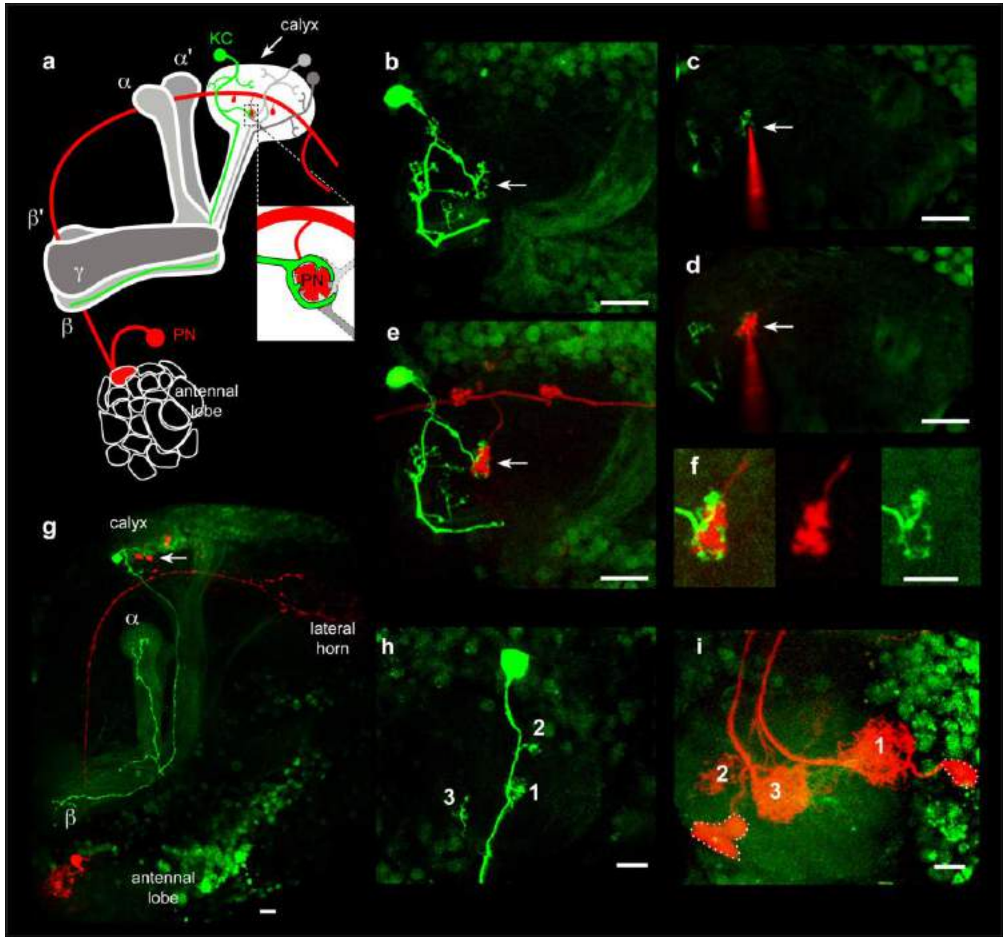
LTM formation was enhanced in transgenic flies after heat-shock induction of the hs-dCREB2-a transgene.

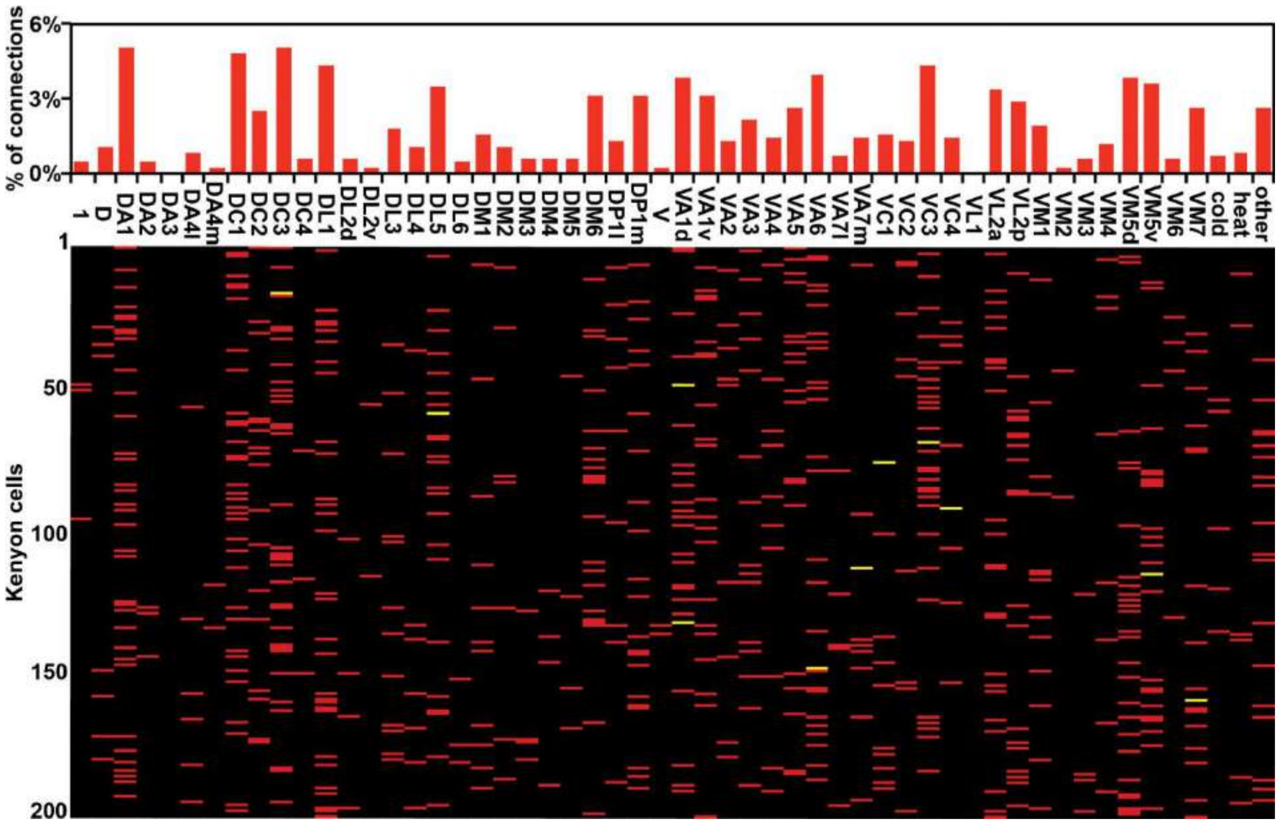
Induction of hs-dCREB2-b disrupts LTM

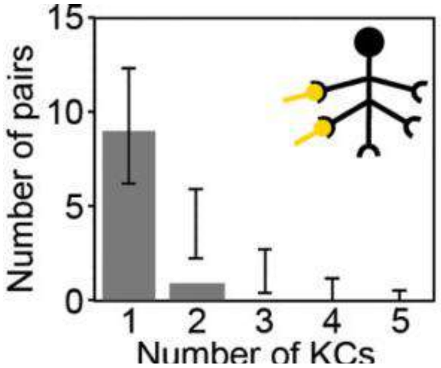
Yin. et al., 1994, 1995

Difficulties in olfactory learning and memory research: individual differences

Part of the olfactory system is randomly wired

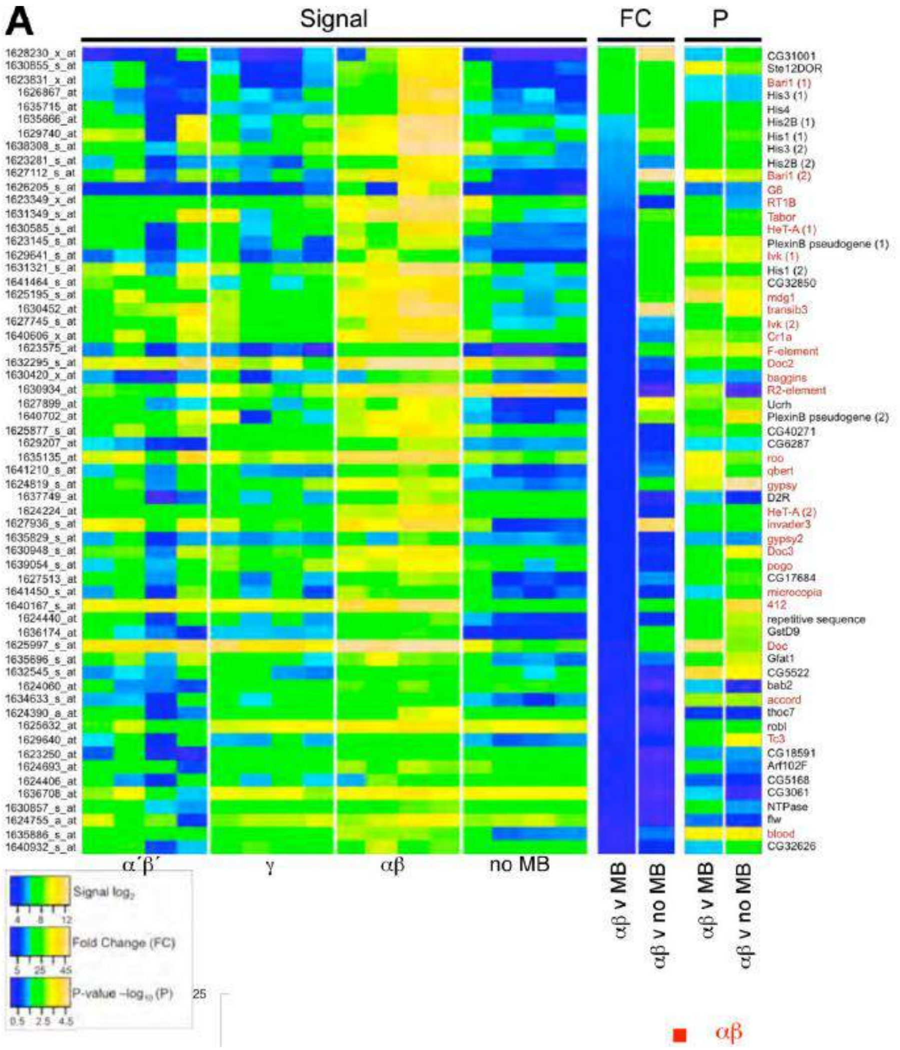


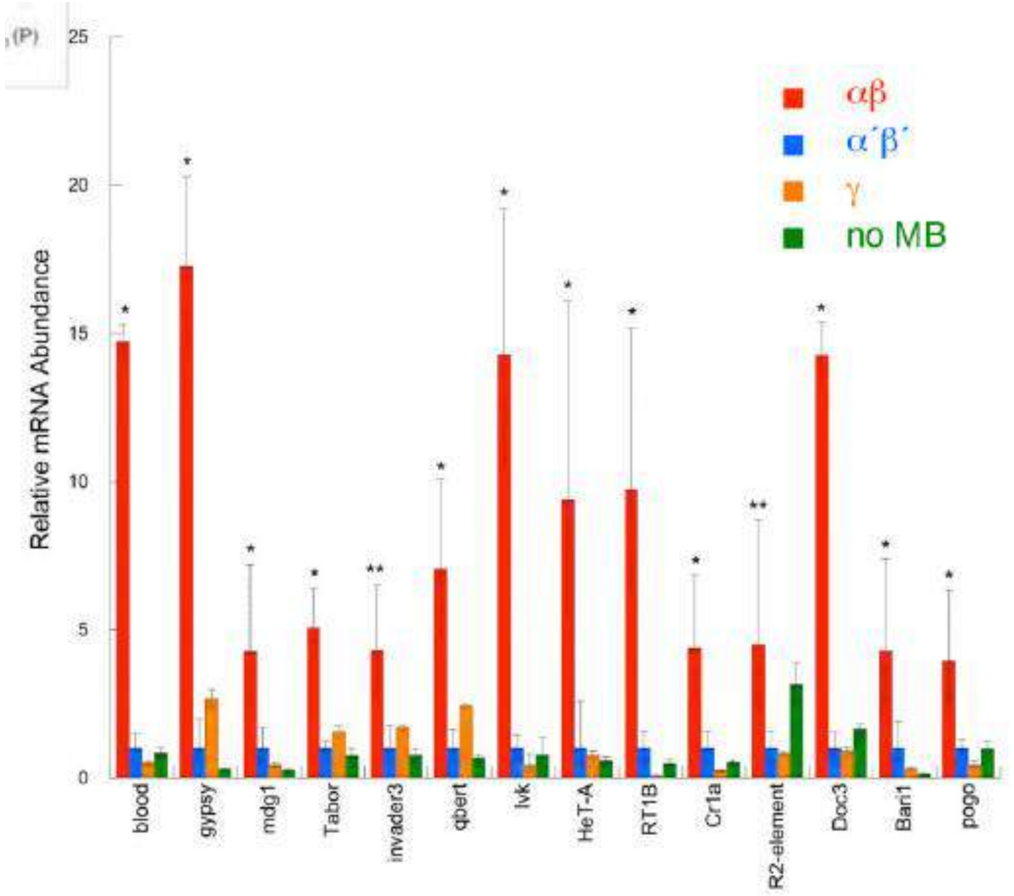




an individual KC claw receives input from only a single glomerulus

Stochastic transposition in neural genomes leads to genetic heterogeneity in the brain

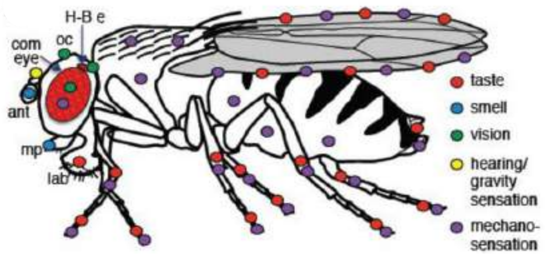


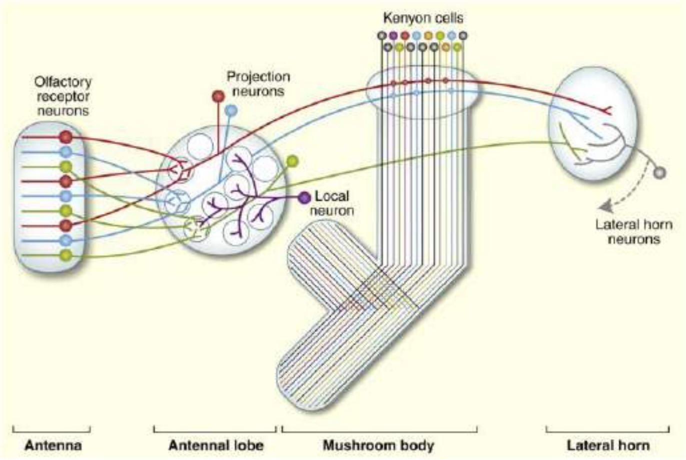


QRT-PCR validation of increased transposon mRNA levels in αβ neurons

Scott Waddell. *et al*. 2013

Summary





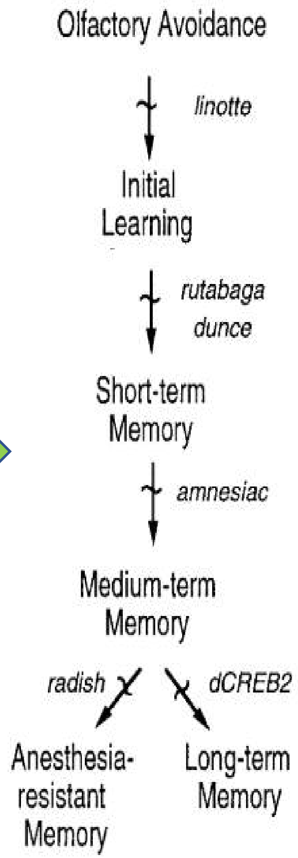


Figure 2. Pathways of Learning Genes

Data are from Tully et al., 1990, 1994; Siegel and Hall, 1979; Gailey et al., 1984; Griffith et al., 1993, 1994.

Output behaviors

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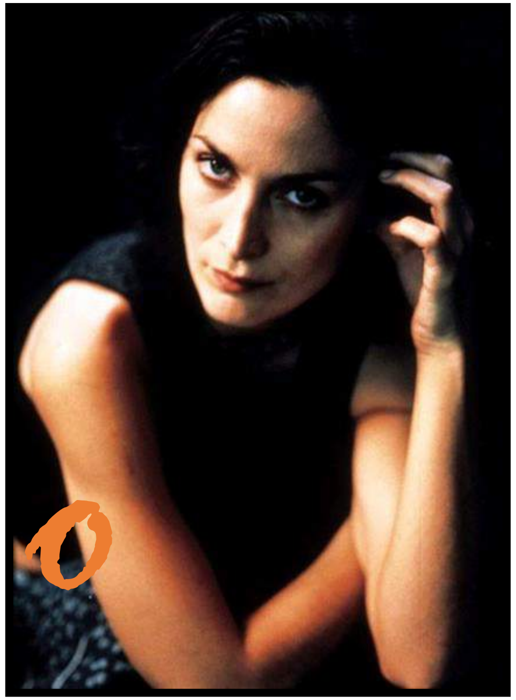
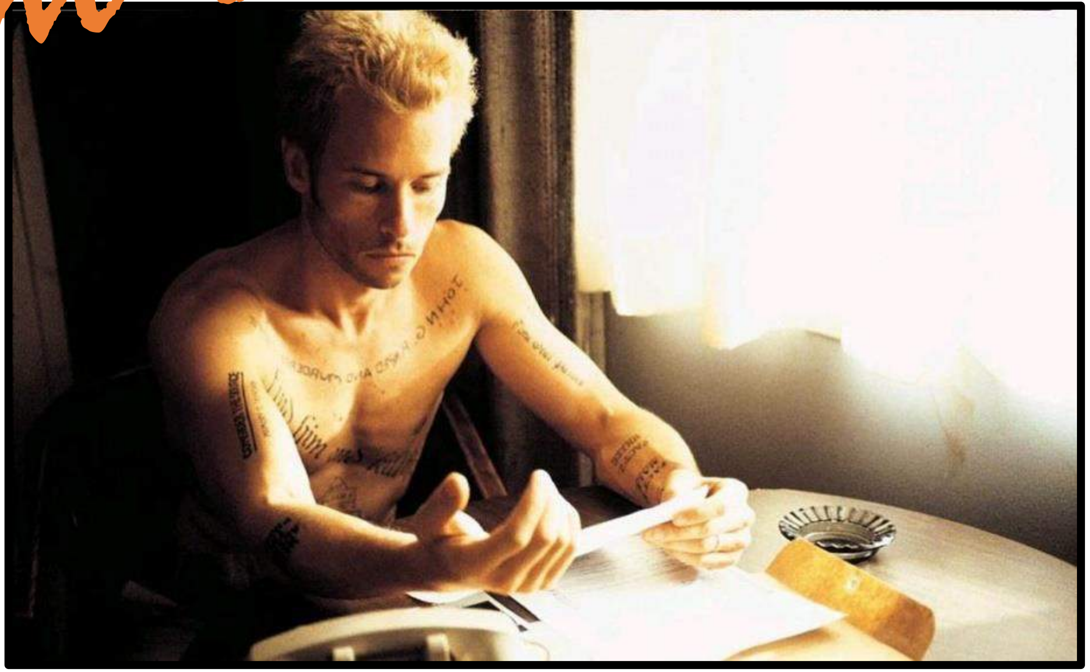
MEMENTO
(official selection - Toronto Film Festival)
(official selection - Venice Film Festival)
(official selection - Sundance Film Festival)
GUY PEARCE
CARRIE-ANNE MOSS
JOE PANTOLIANO
MEMENTO



Memento



Olfactory Memory Formation in *Drosophila*

Su XB

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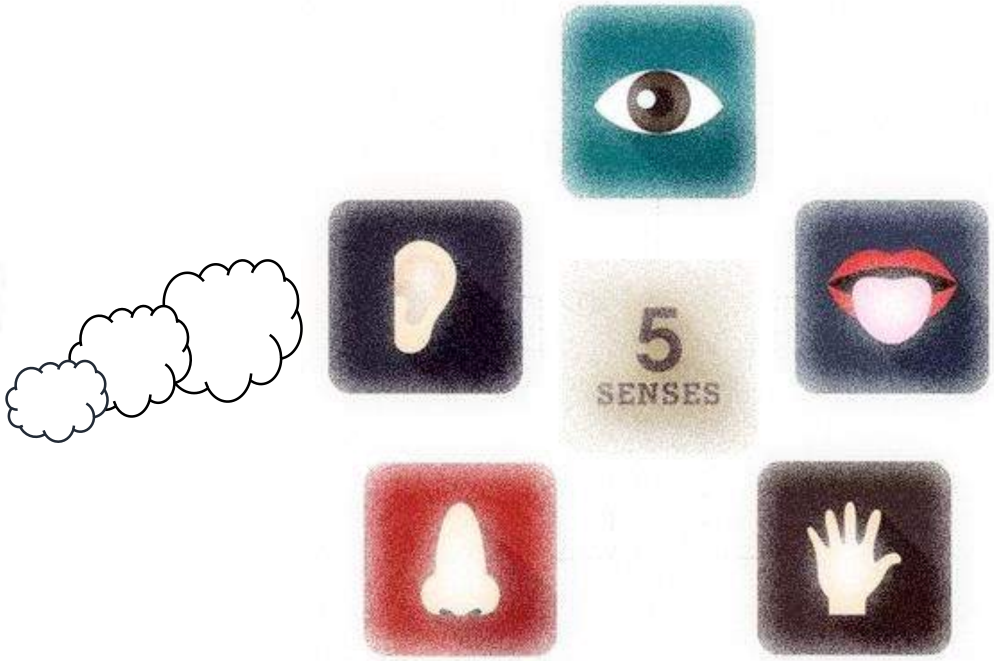

5
SENSES

Three critical questions about olfactory memories

1, What is the complete neural circuitry extending from the site(s) of acquisition to the site(s) controlling memory expression ?

2, Which neurons in the olfactory nervous system mediate memory formation ?

3, How is information processed across this circuit ?

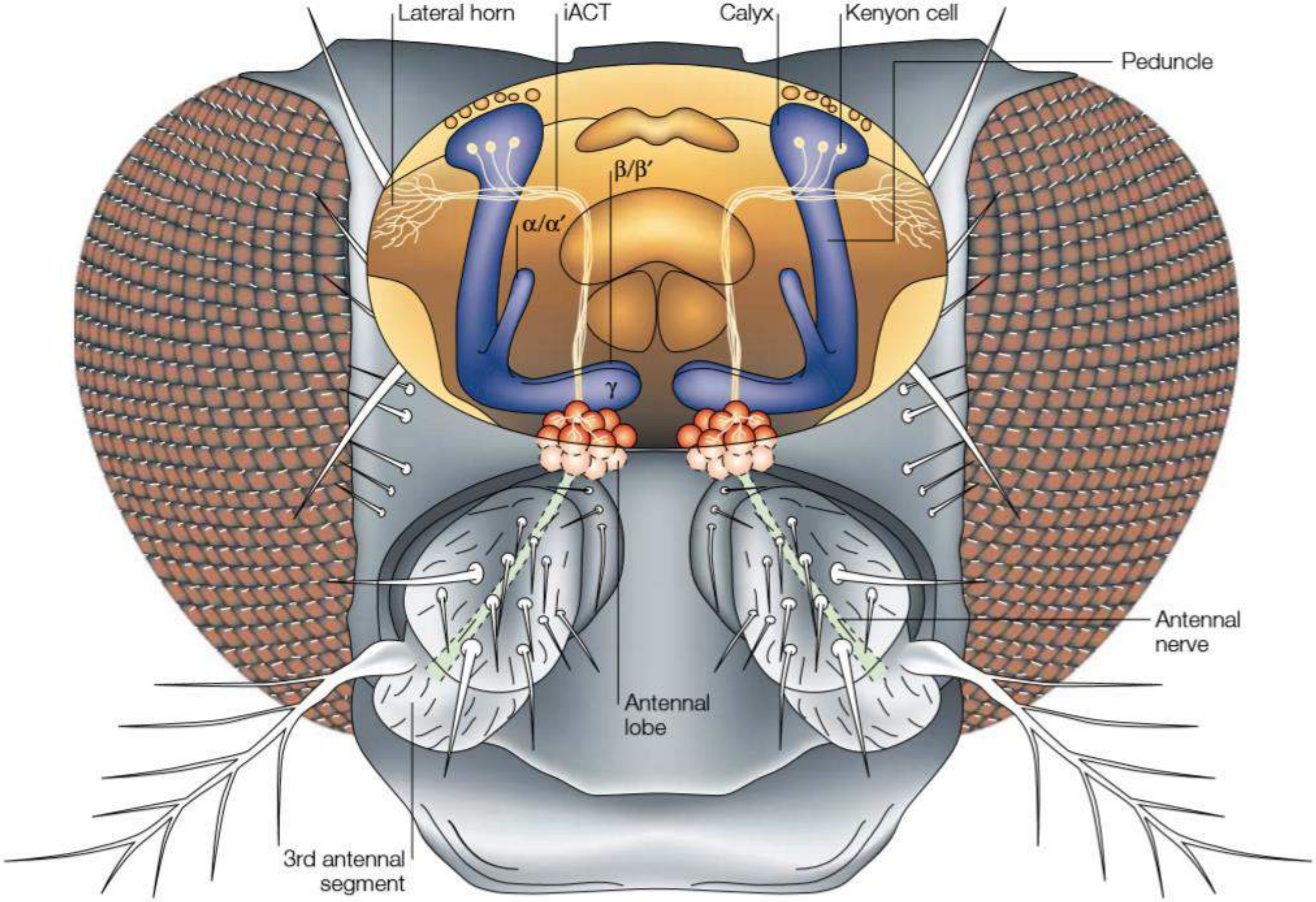
Olfactory Memory Formation in *Drosophila*

1, The perception and transmission of olfactory information.

2, Neurons that mediate olfactory memory formation.

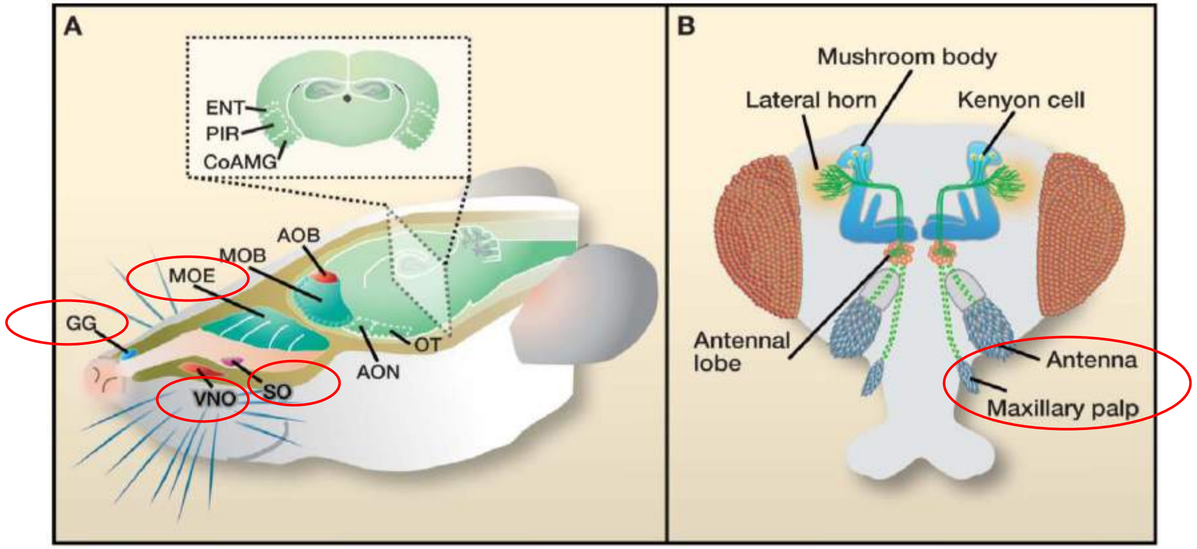
3, Molecular model for olfactory memory formation.

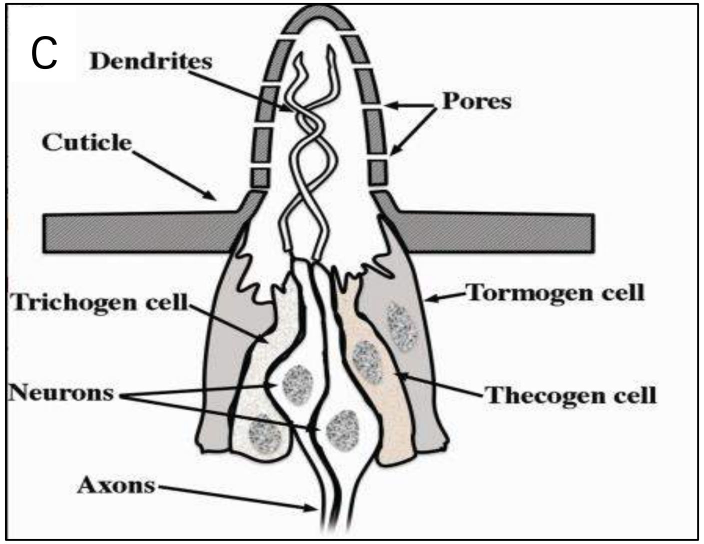
1 The perception and transmission of olfactory information



Martin Heisenberg. Nat Rev Neurosc. 2003

The perception site of olfactory information



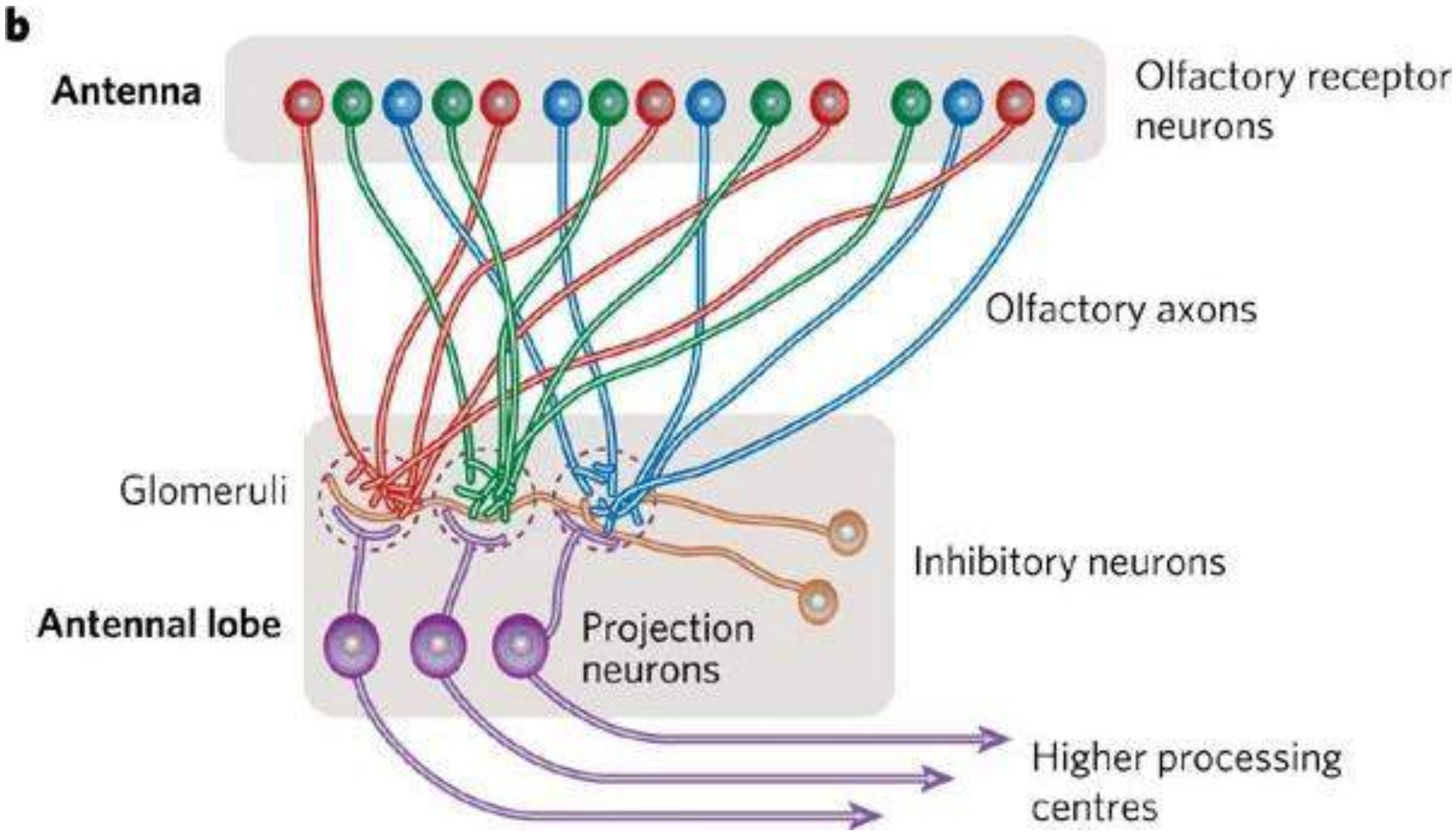


(A) Sagittal view of a rodent head, showing four olfactory organs.
(B) Frontal view of a *Drosophila* head.
(C) Structure and components of typical sensilla.

Su CY et al. Cell. 2009

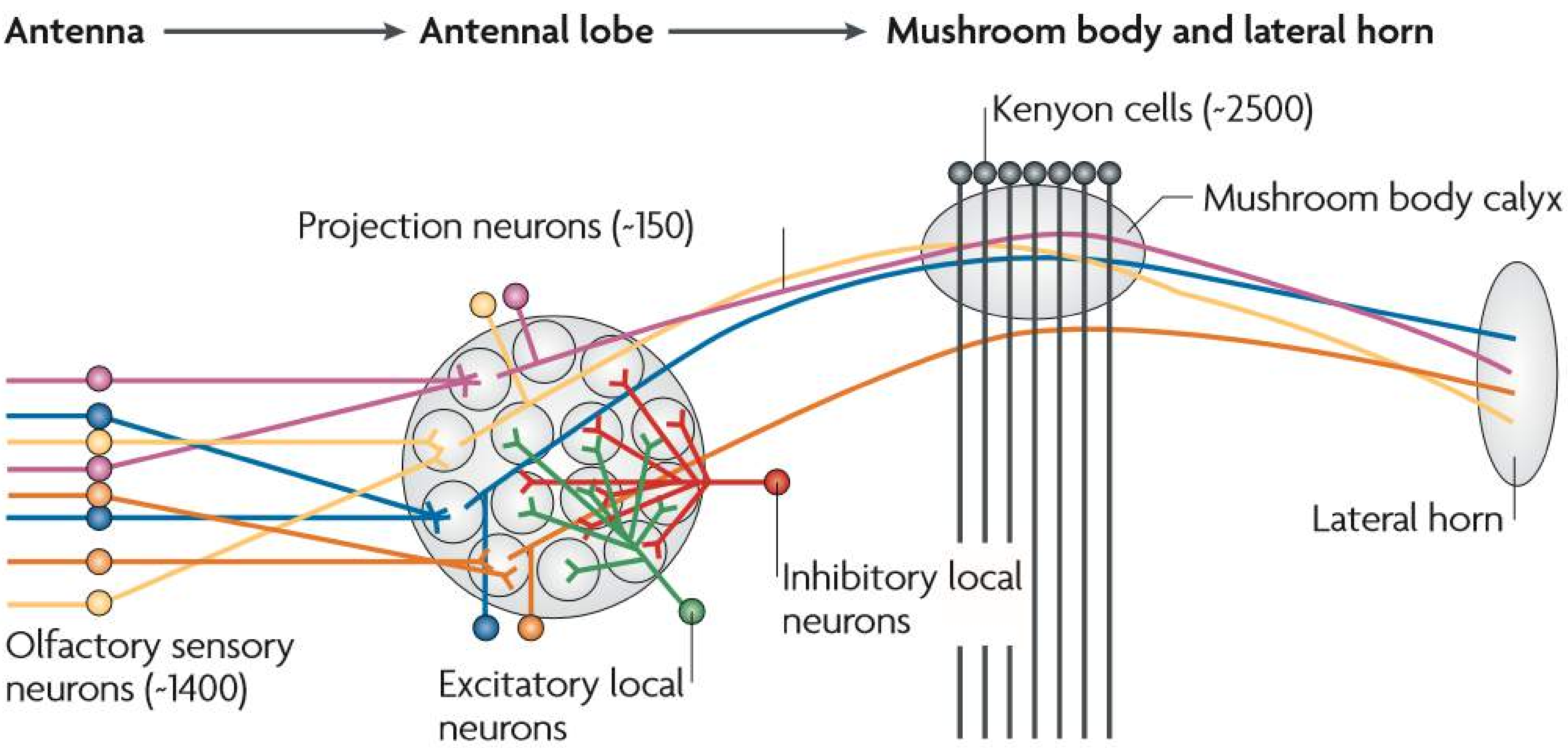
Martin F et al. Anat Rec (Hoboken). 2013

Second-order coding of olfactory information



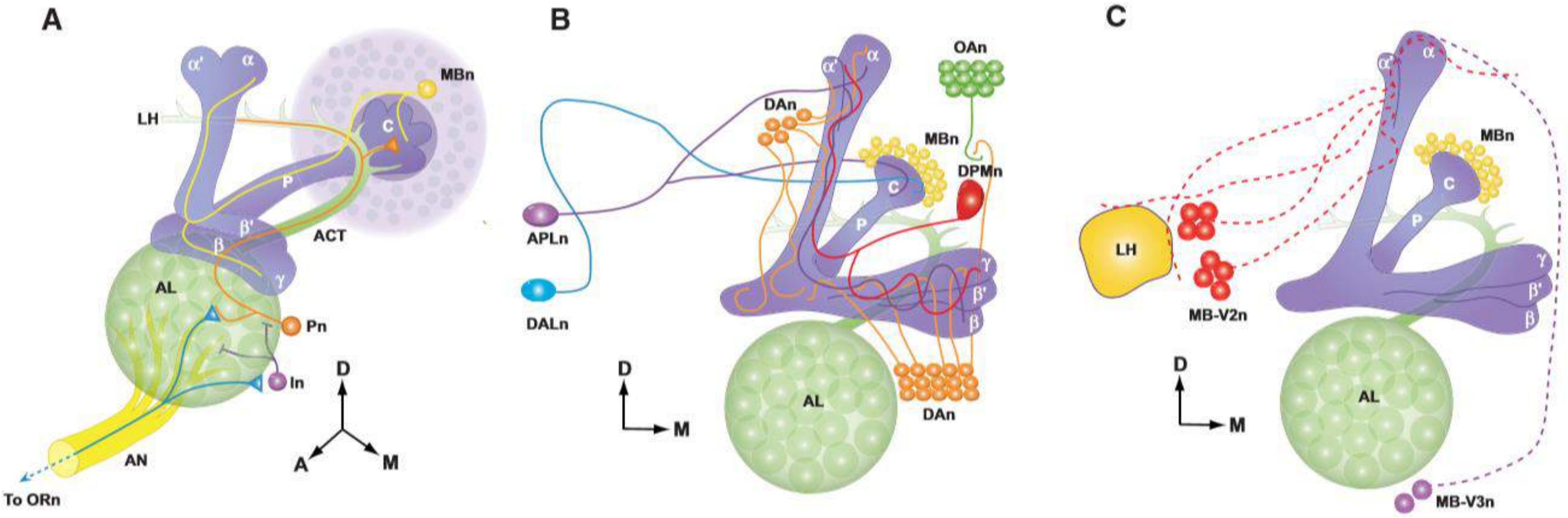
Cornelia I. Bargmann. Nature. 2016

Schematic of the adult fly olfactory system circuit



Keene AC. Nat Rev Neurosci. 2007

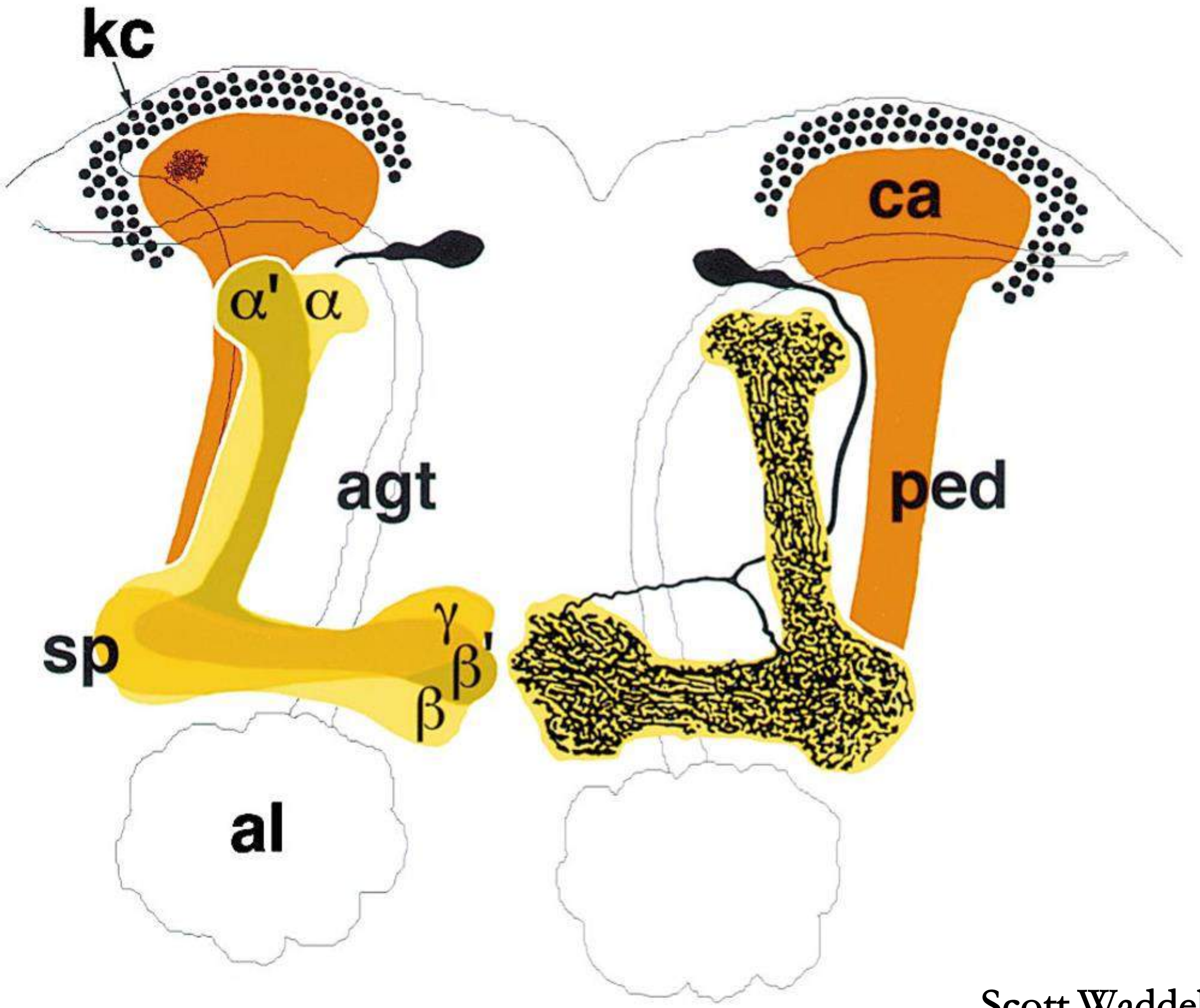
2 Neurons that mediate olfactory memory formation



Tugba Guven-Ozkan and Ronald L. Davis. Learn Mem. 2014

MBs are a primary brain center for *Drosophila* olfactory memory formation

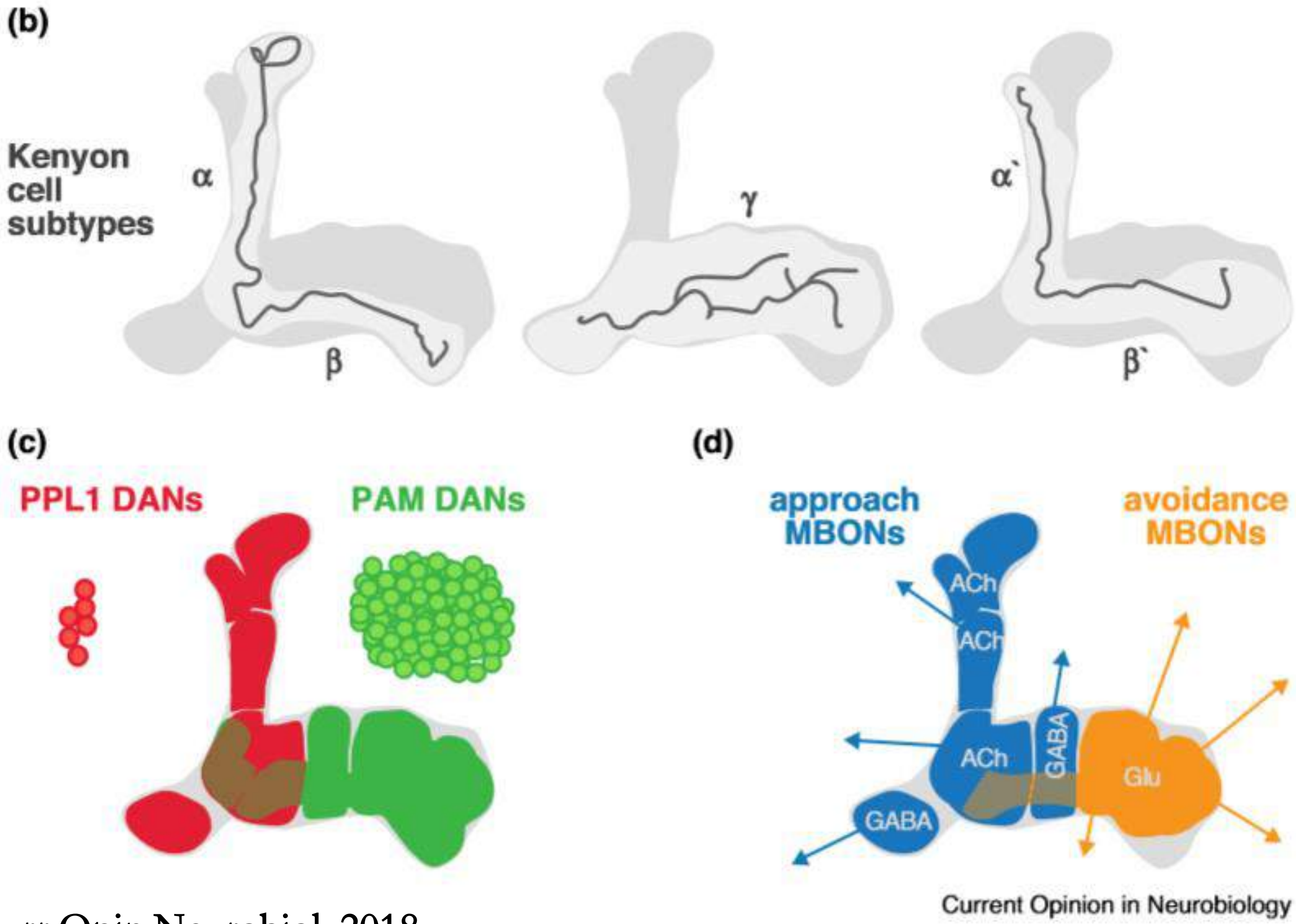
The processing site of olfactory information—Mushroom Bodies



- al, antennal lobes
- agt, antennoglomerular tract
- ca, calyces
- kc, Kenyon cell bodies
- ped, pedunculus
- sp, spur

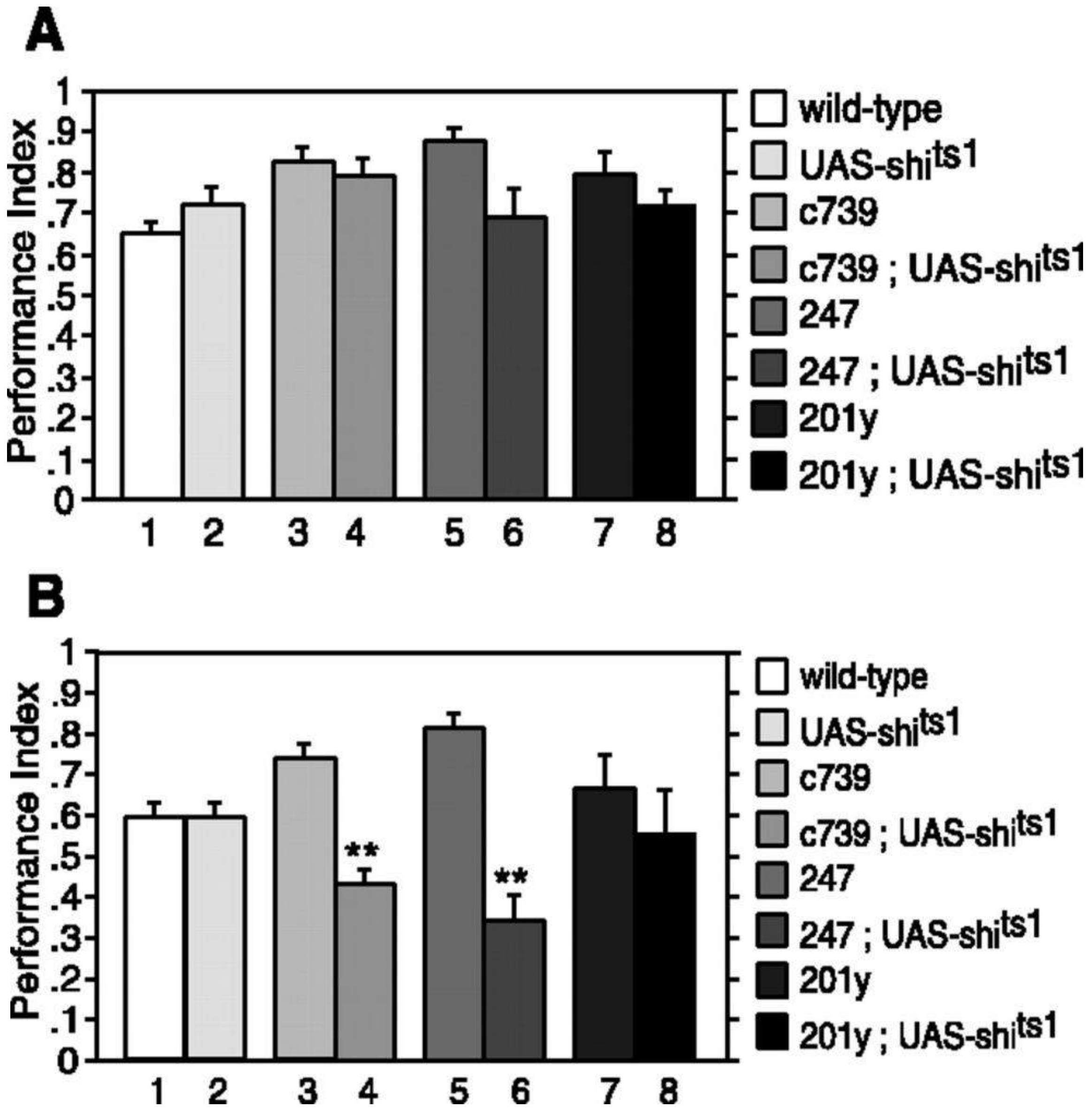
Scott Waddell, et al. Cell. 2000

The mushroom body is the center for associative learning



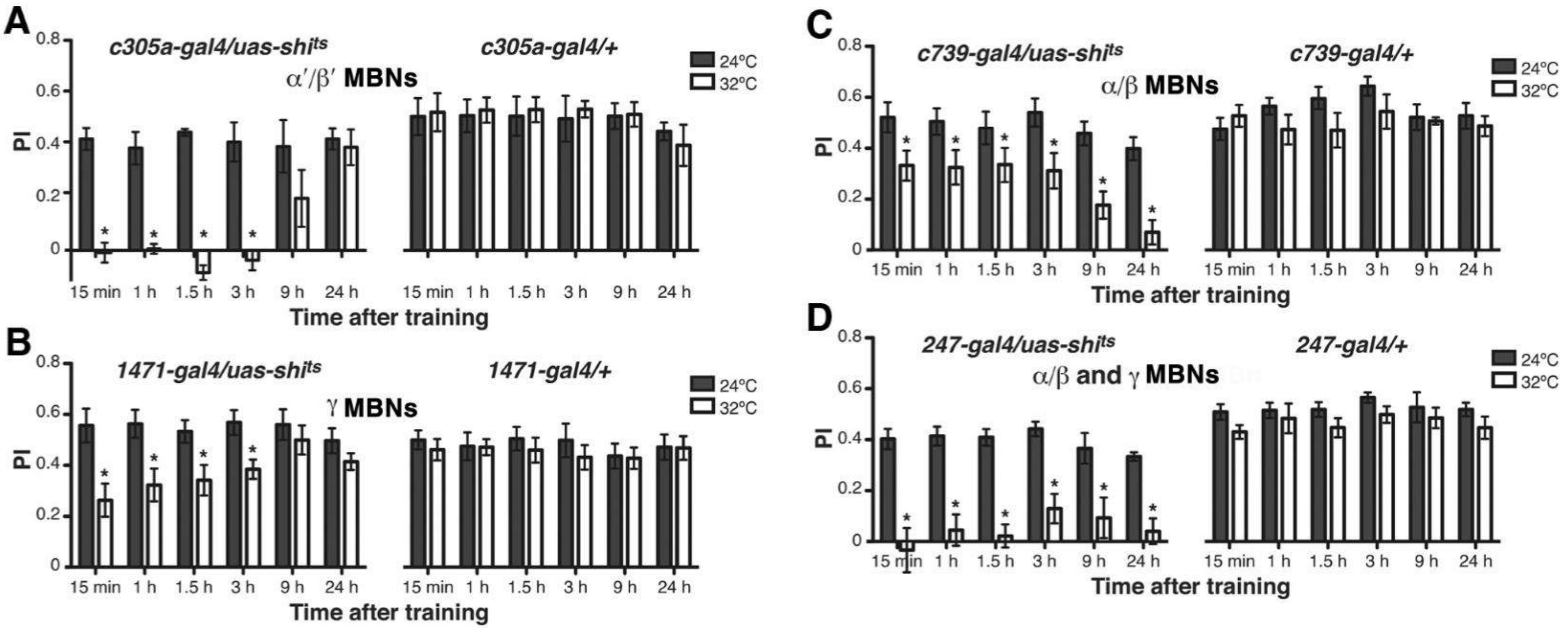
Paola Cognigni. Curr Opin Neurobiol. 2018

Disruption of memory at 3 min when MB signaling is blocked.



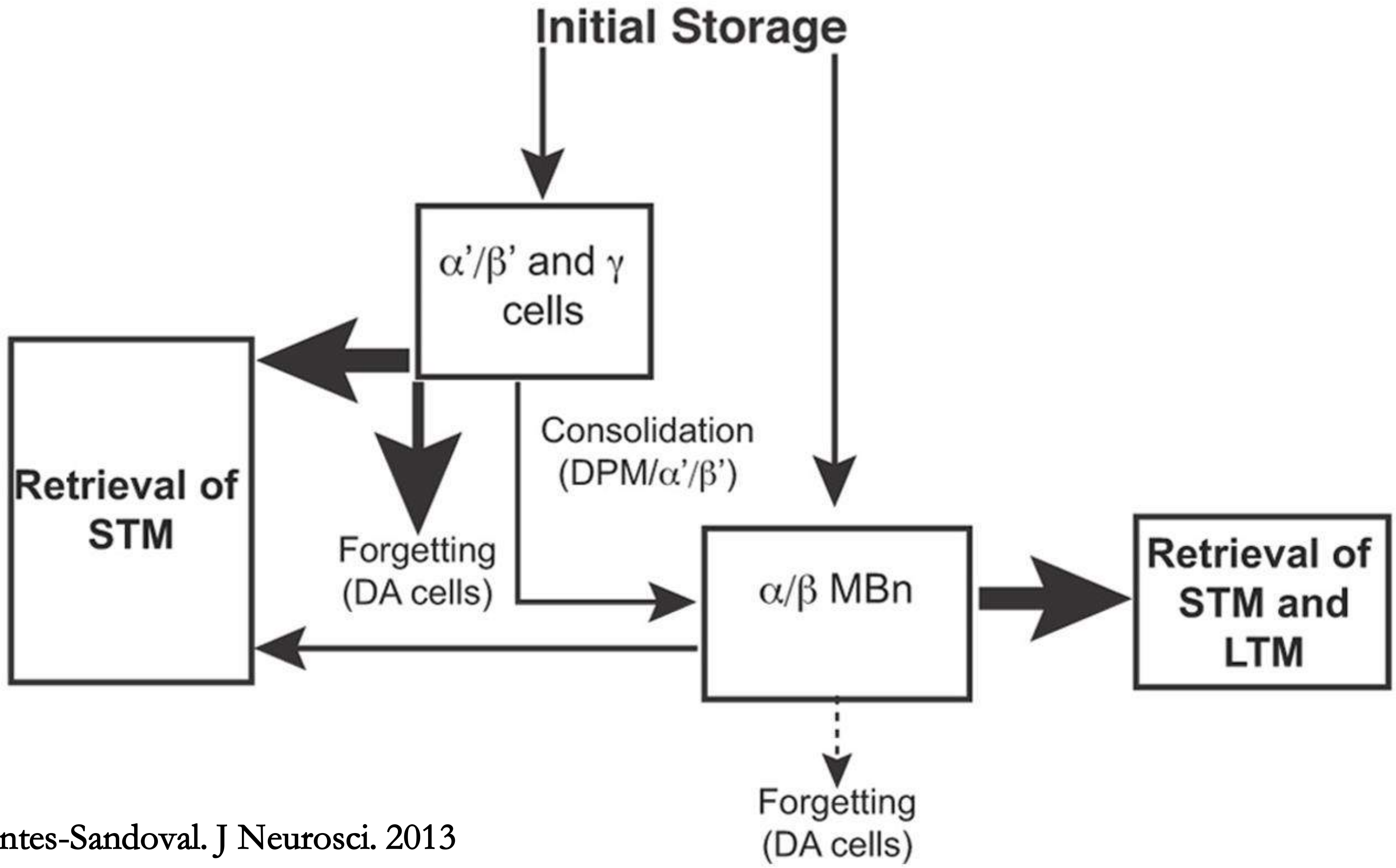
McGuire SE. Science. 2001

Time requirements for synaptic output from MBN subsets for the retrieval of appetitive olfactory memory



Isaac Cervantes-Sandoval. J Neurosci. 2013

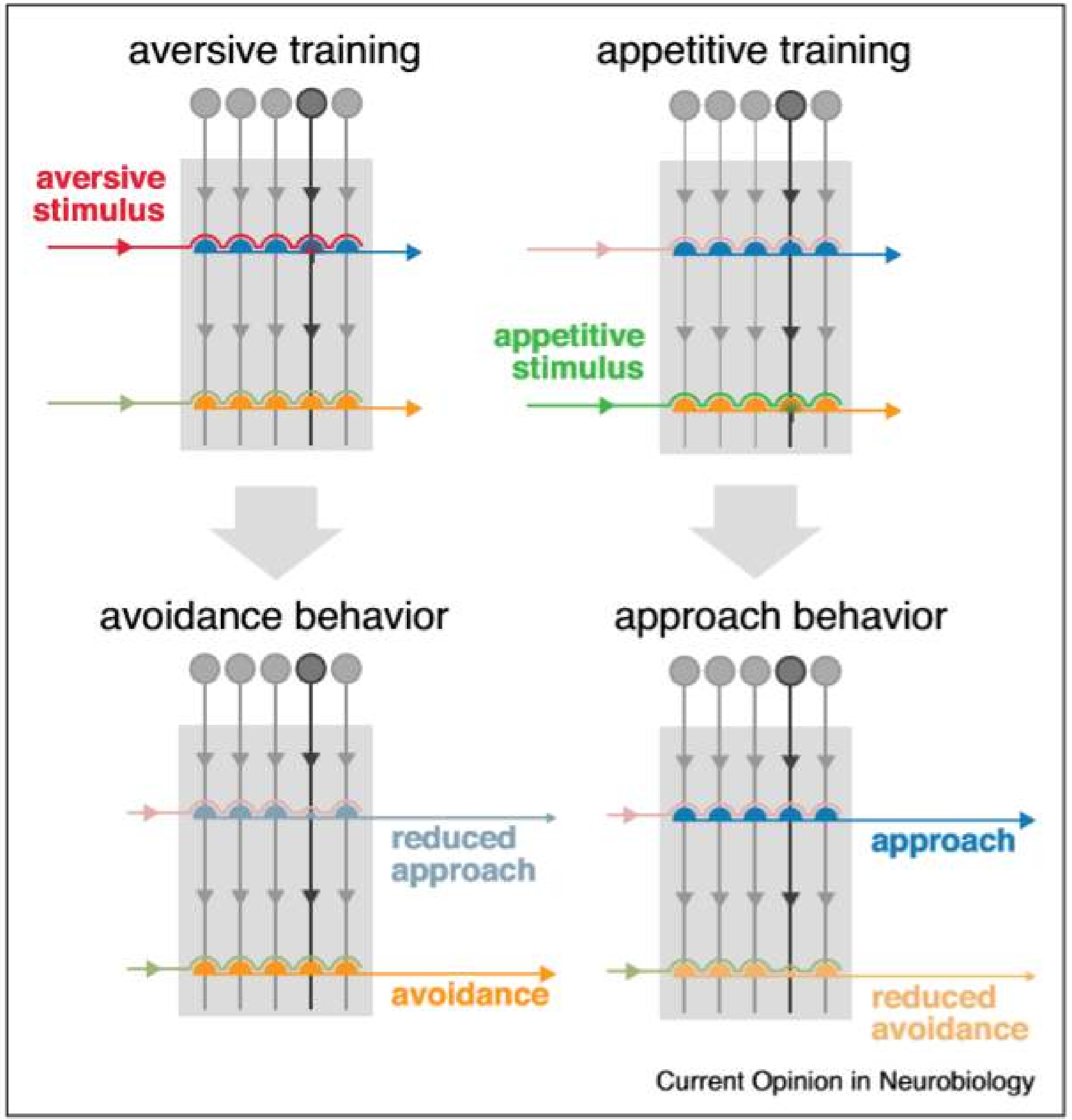
Drosophila-adapted, standard model of system consolidation



Isaac Cervantes-Sandoval. J Neurosci. 2013

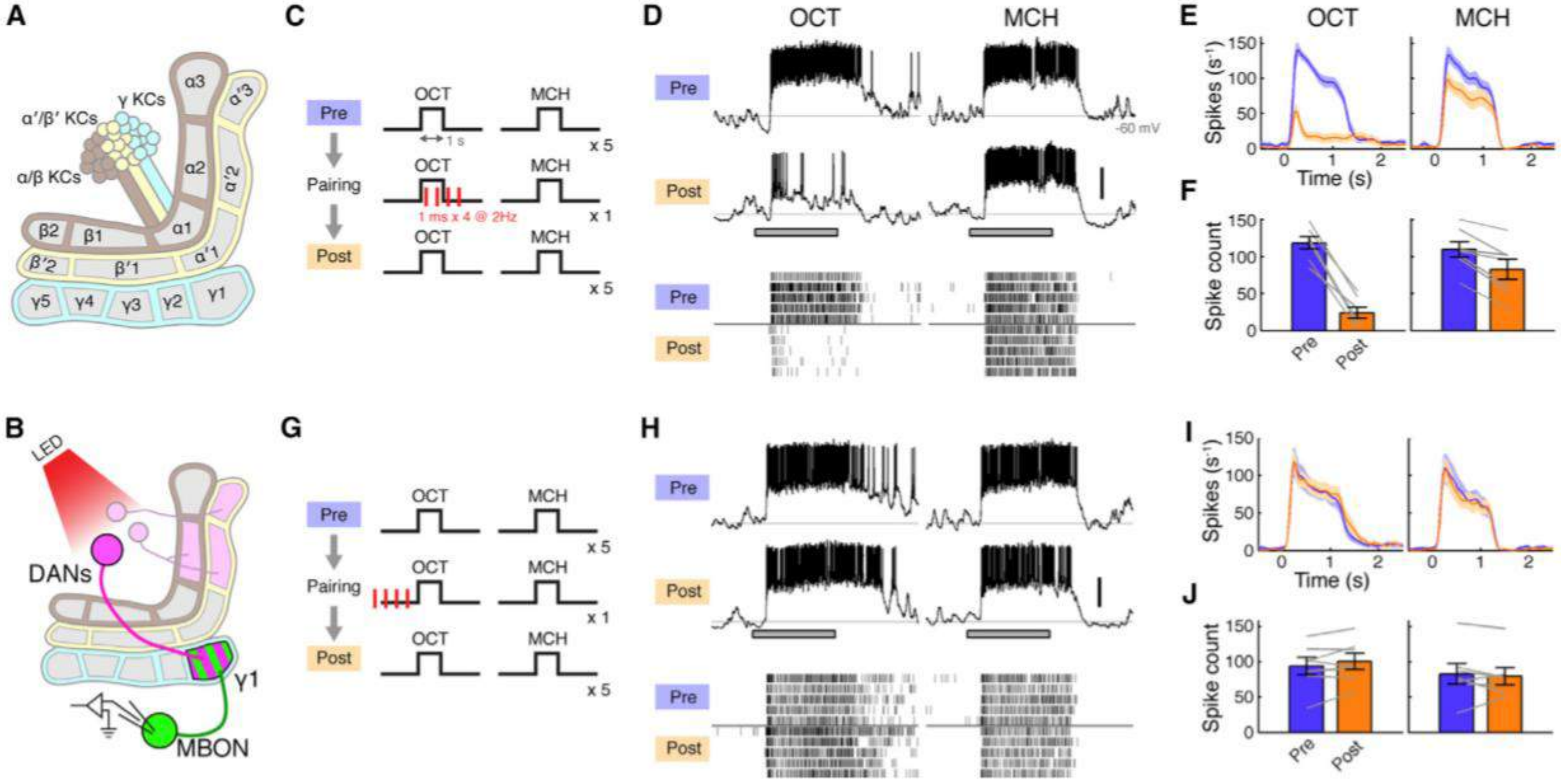
Dopaminergic rules of engagement for memory in *Drosophila*

Dopamine drives plasticity at KC output synapses to alter behavior upon learning



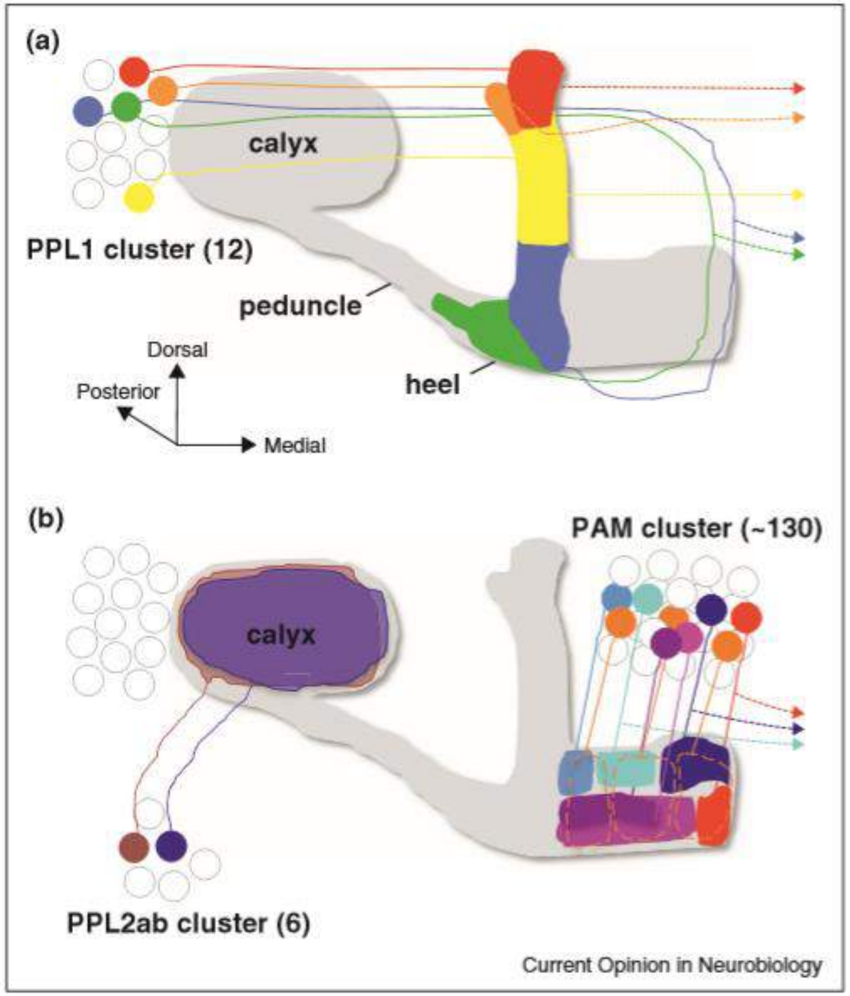
Paola Cognigni. Curr Opin Neurobiol. 2018

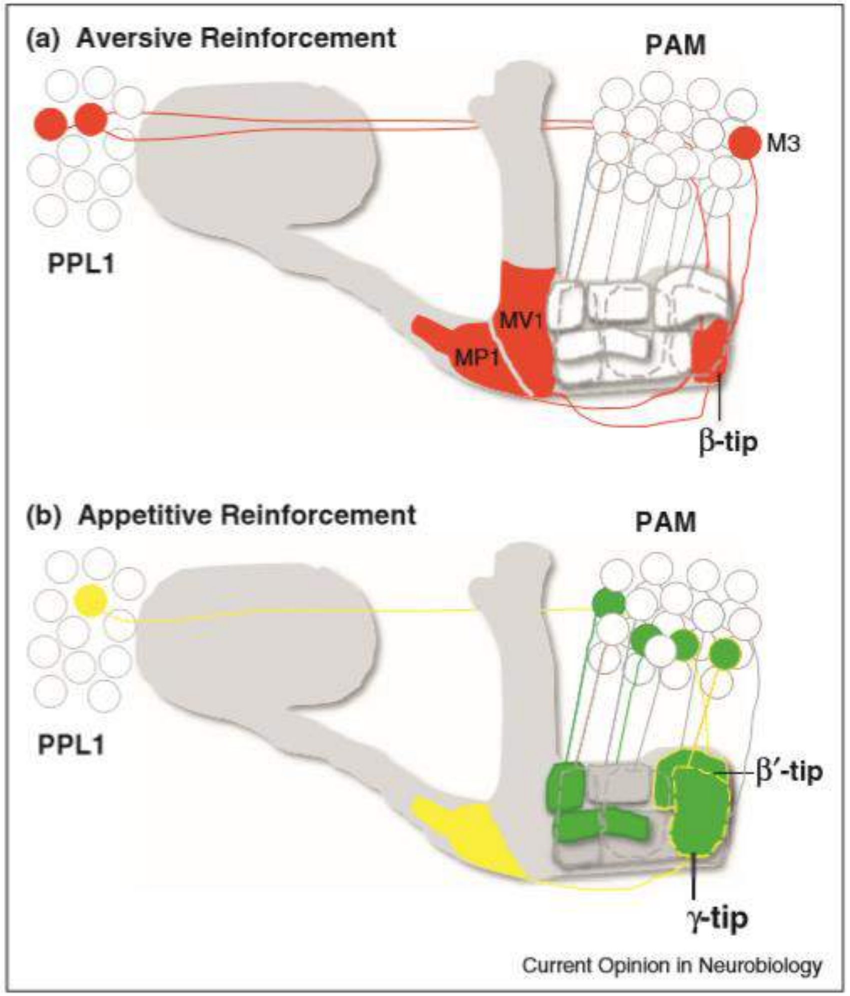
Forward Pairing of Odor and DAN Activation Induces Long-Lasting Suppression in the g1 Compartment



Toshihide Hige. Neuron. 2015

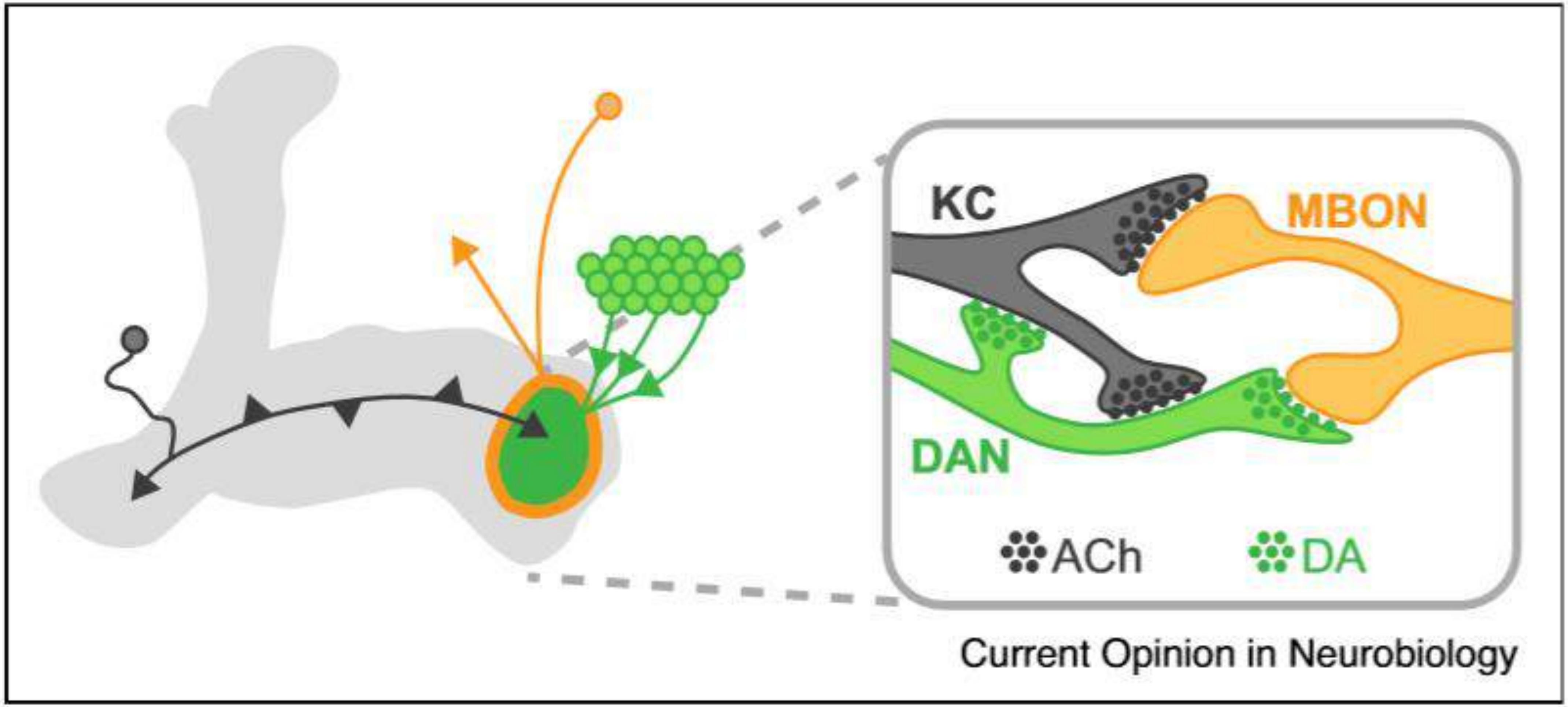
Dopamine signals aversive reinforcement





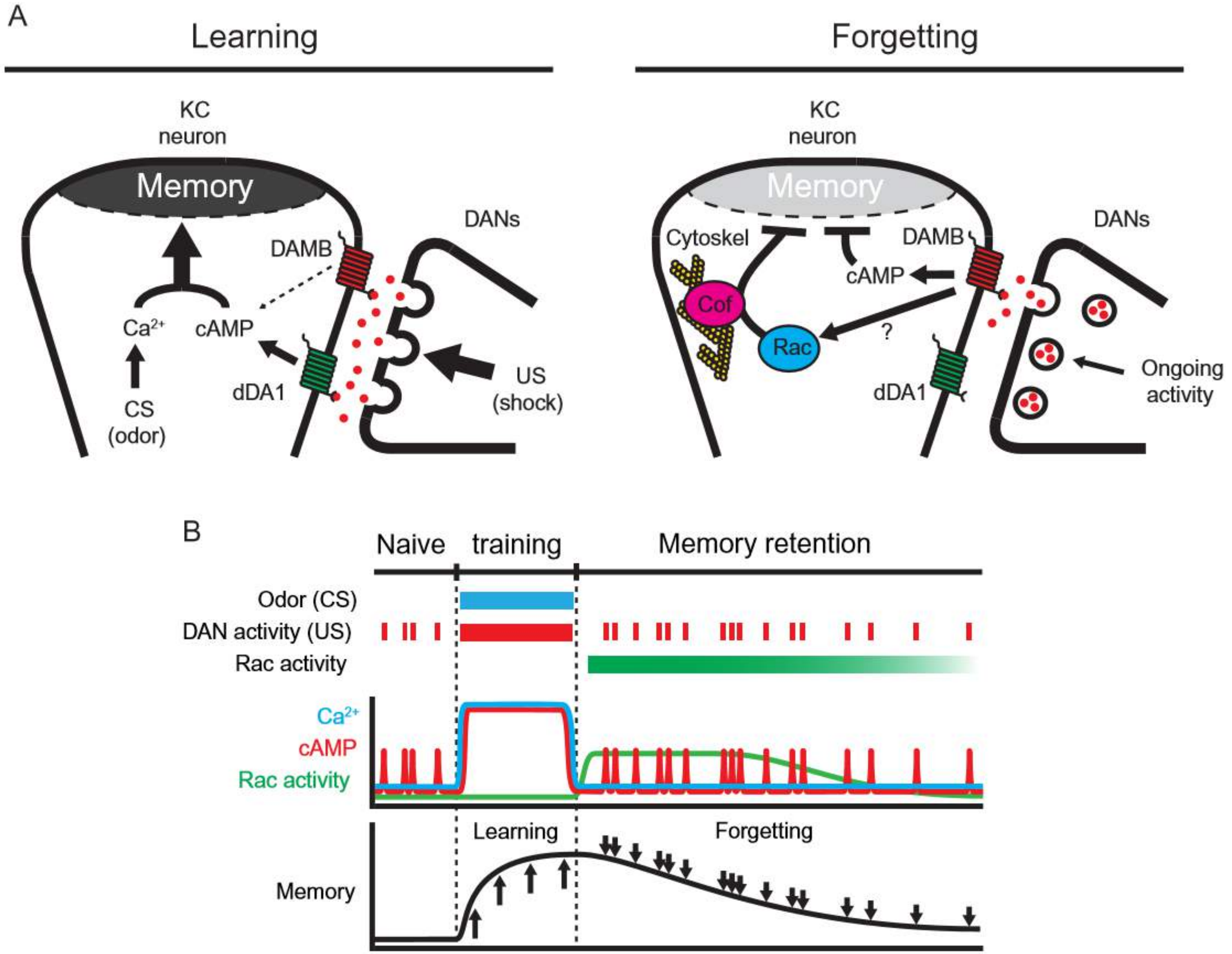
Scott Waddell. Curr Opin Neurobiol. 2013

KCs, MBONs and DANs form microcircuits within a compartment



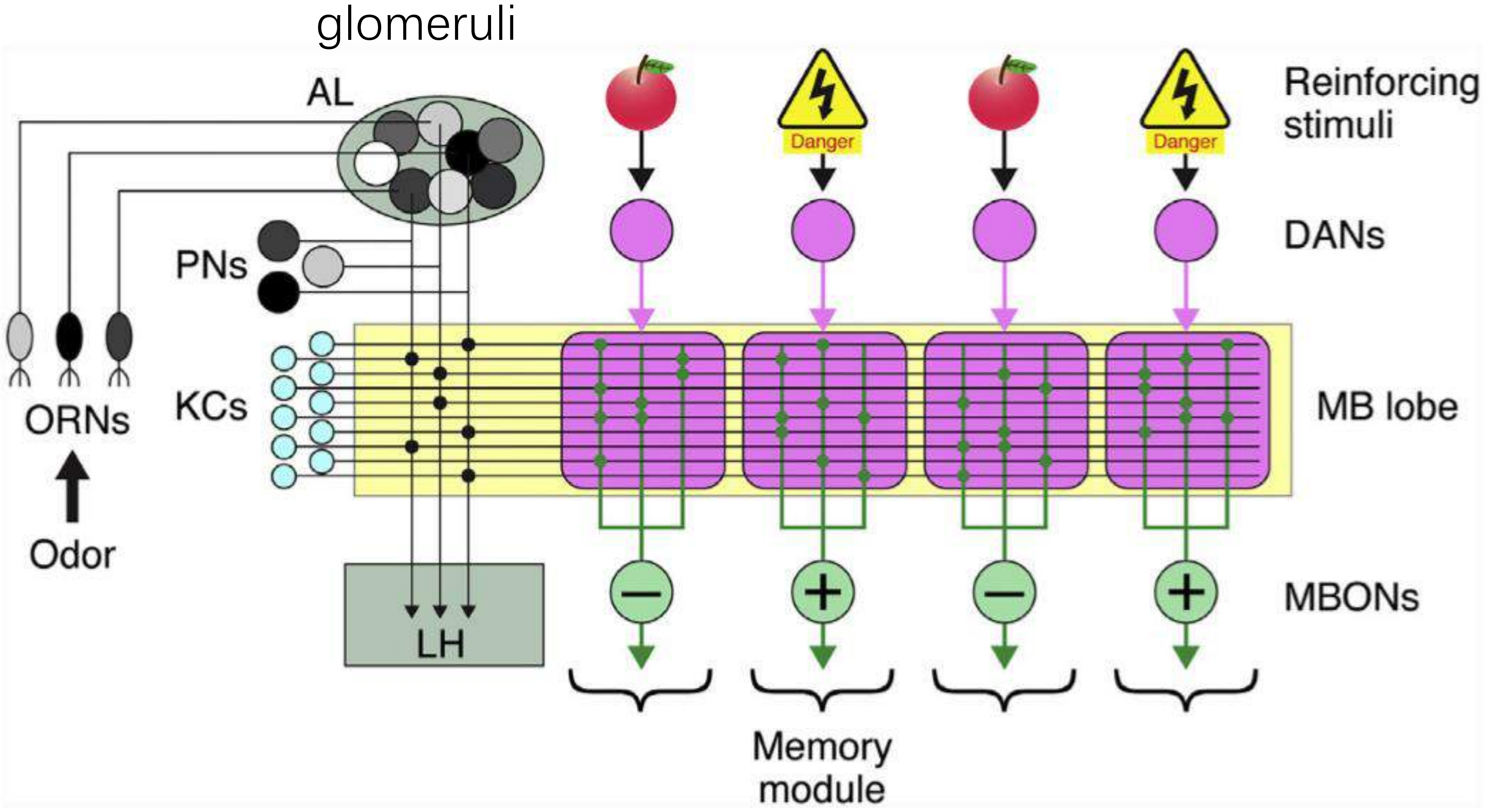
Paola Cognigni. Curr Opin Neurobiol. 2018

Active forgetting of odor memory in *Drosophila*



Berry JA. Prog Brain Res. 2014

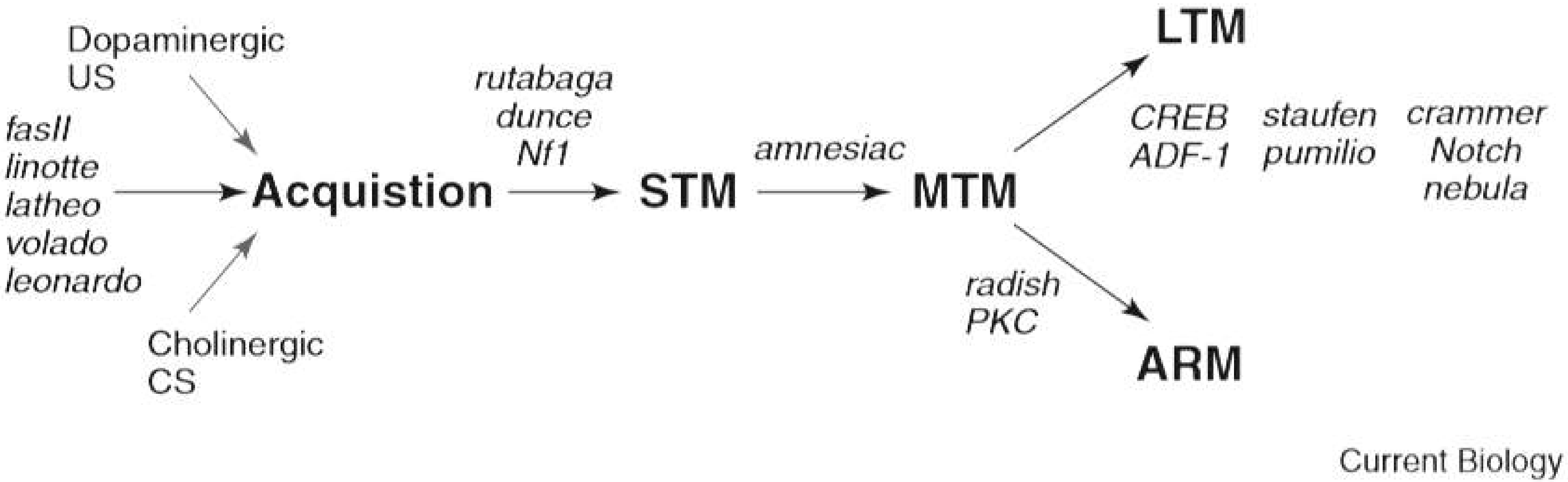
Schematic of the olfactory circuit in *Drosophila*



Toshihide Hige. Neurosci Res. 2018

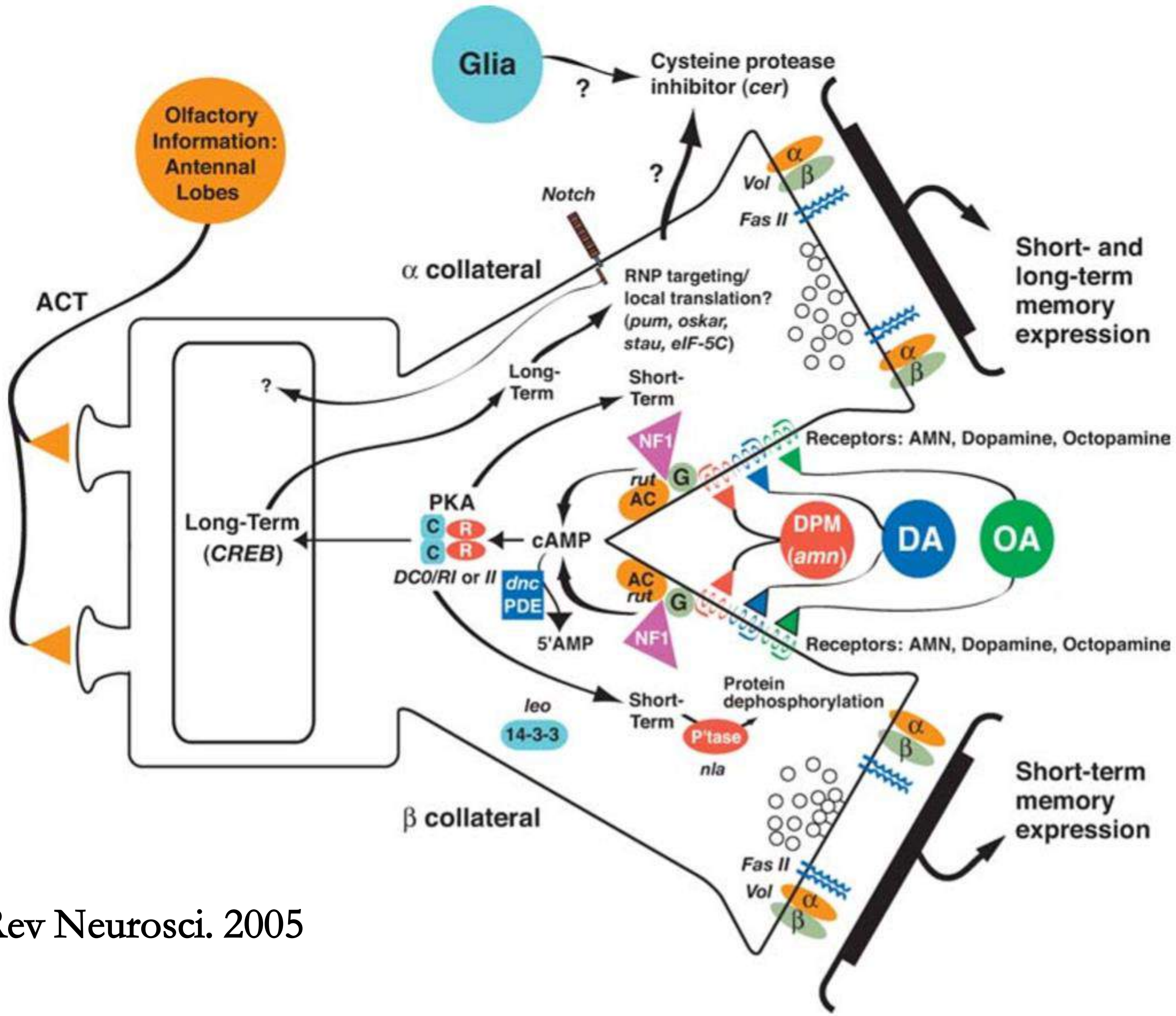
3 Molecular model for olfactory memory formation

Dissection of biochemical pathways



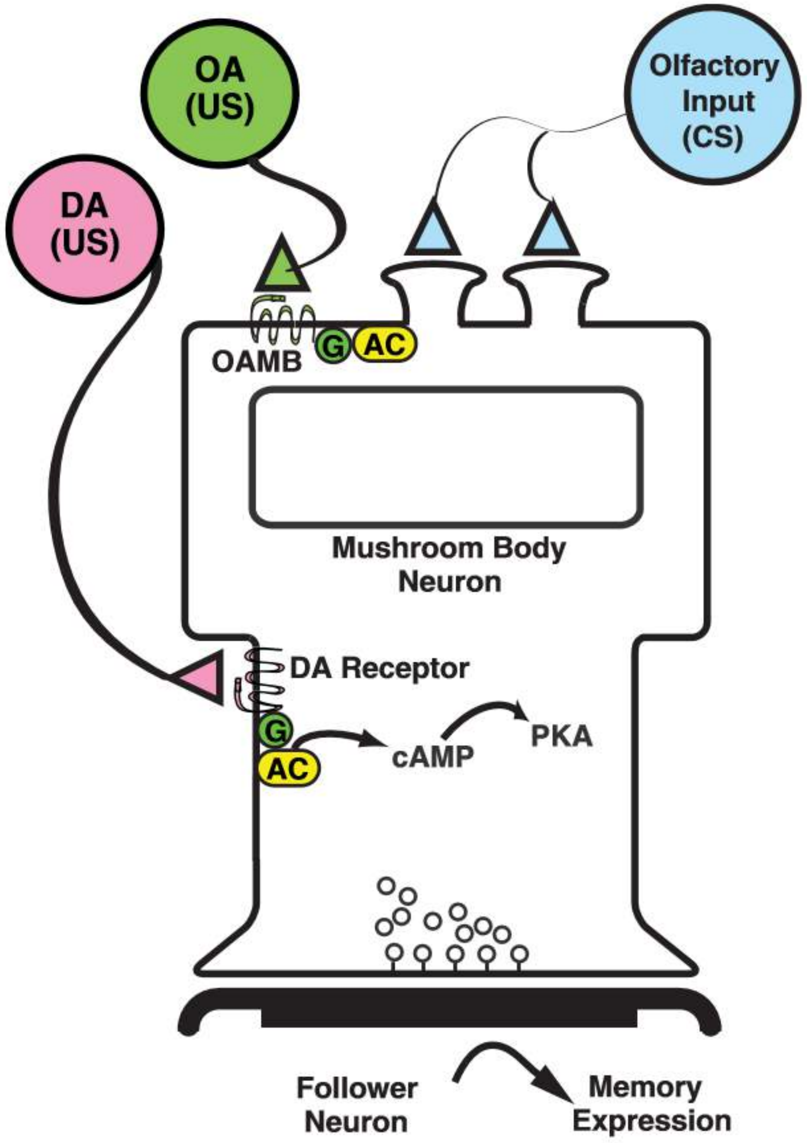
Carla Margulies. Current Biology. 2005

Current molecular model for olfactory memory formation with a focus on the role of the MB neurons



Davis RL. Annu Rev Neurosci. 2005

Original neural circuit model for CS and US integration



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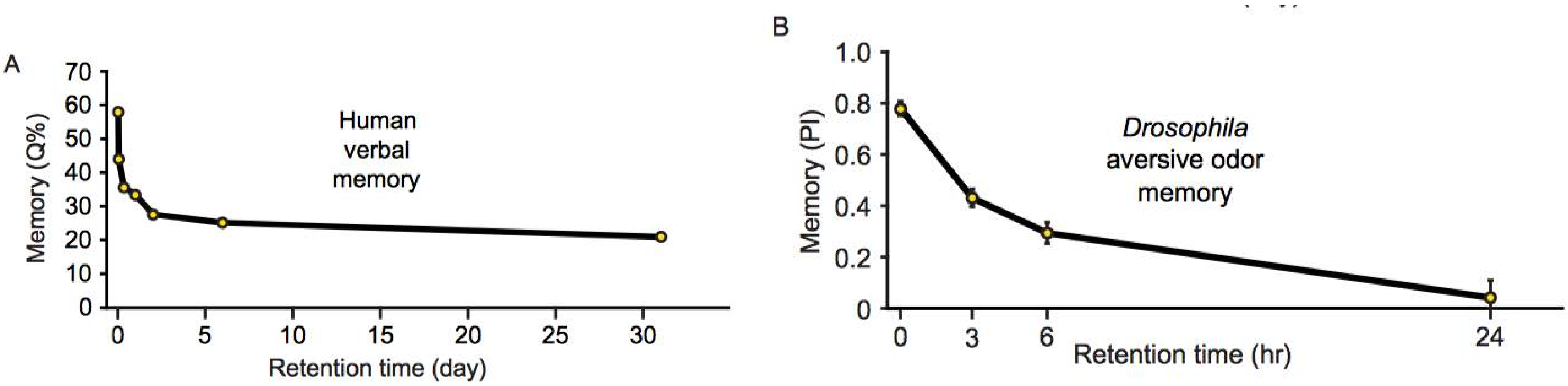
Forgetting and sleep-dependent memory retention in *Drosophila*

Sun Mengshi

Decay theory: memory is forgotten simply by the dissipation of memory over time.

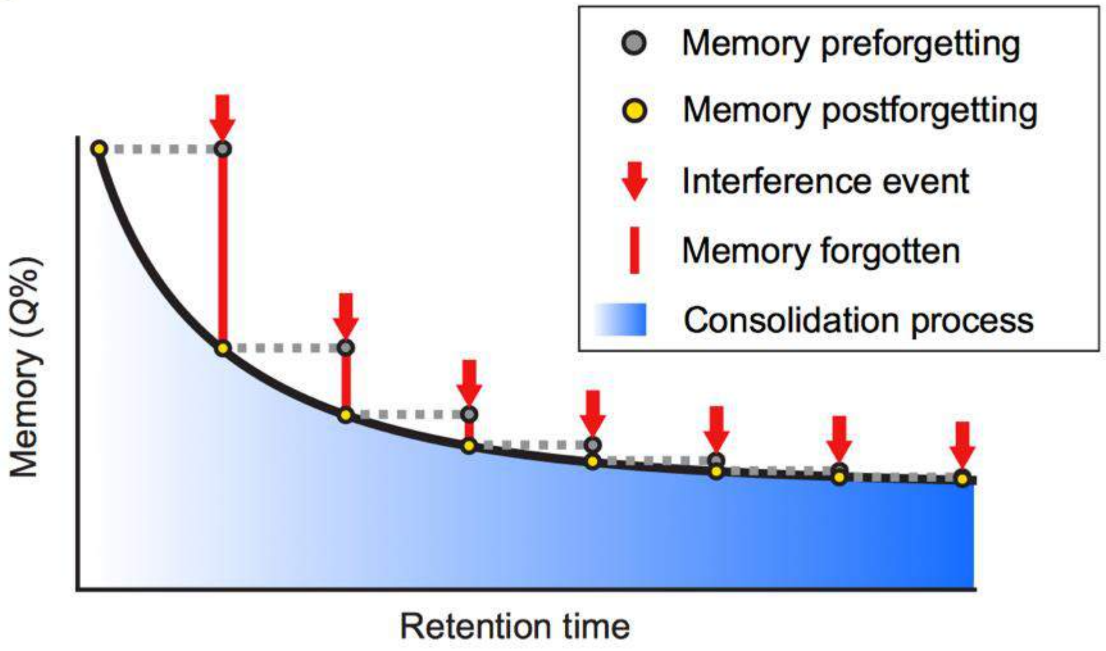


John McGeoch stated "In time iron, when unused, may rust, but oxidation, not time, is responsible".(1932)

Interference models of forgetting:

brain activity causes forgetting by interfering with memory storage or recall.

C



- Proactive interference: Events occurring prior to learning
- Retroactive interference: Events occurring after learning

Consolidation model of memory storage:

Memories are initially labile or easily disruptable, but transition, via consolidation, into more stable and resistant form.

- Cellular and molecular mechanisms of forgetting

  Forgetting is regulated by Rac and the cytoskeleton in the MBs

- Neural mechanisms of forgetting

  Dopamine participates in the regulation of forgetting

- Sleep-dependent memory retention

  Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgettin.

钟毅 博士

教授

1978-1982年，清华大学工程物理系　　学士

1982-1984年，清华大学生物科学与技术系　硕士

1985-1991年，美国Iowa大学生物科学学系　博士

1991-1992年，美国Iowa大学生物科学学系　博士后

1992-1995年，美国冷泉港实验室　　助理研究员

1992-2001年，美国冷泉港实验室　　副教授

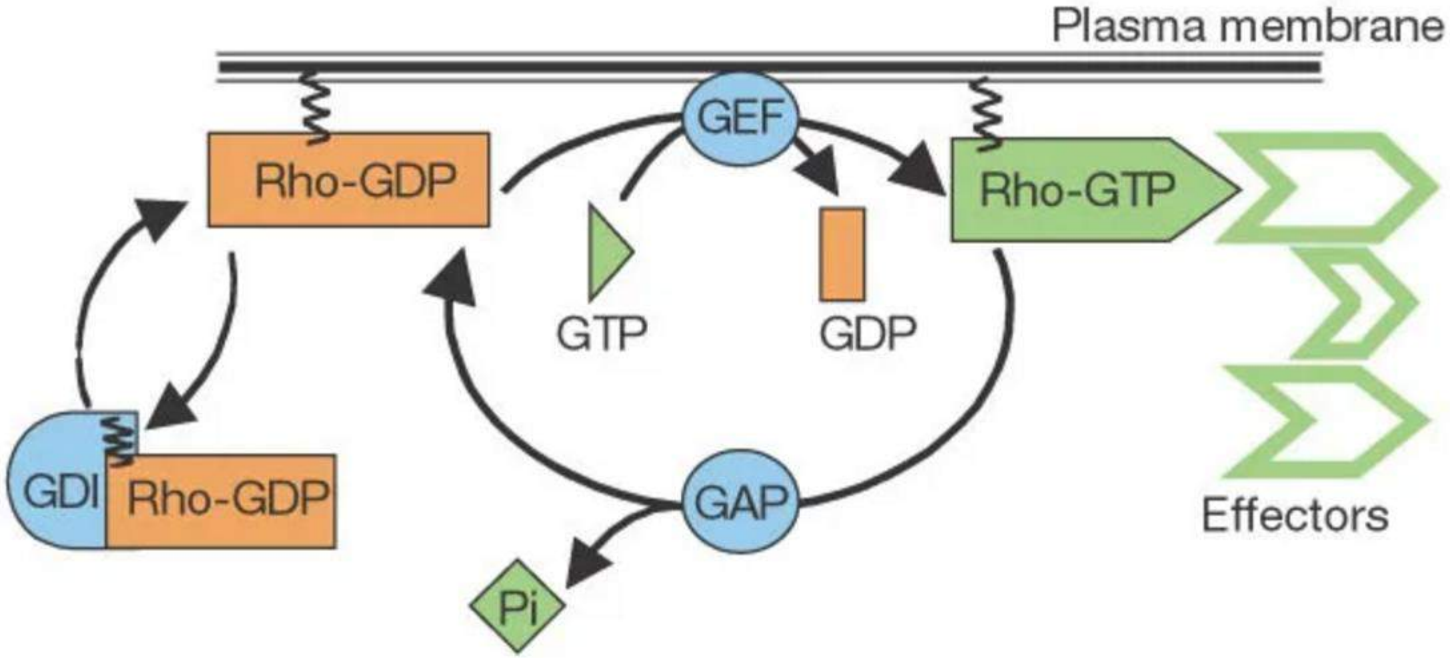
2001-2015年，美国冷泉港实验室教授，清华大学生命科学学院兼职教授

2015年至今，清华大学生命科学学院教授

Forgetting Is Regulated through Rac Activity in *Drosophila*

Yichun Shuai • Binyan Lu • Ying Hu • Lianzhang Wang • Kan Sun • Yi Zhong

The Rho GTPase cycle.



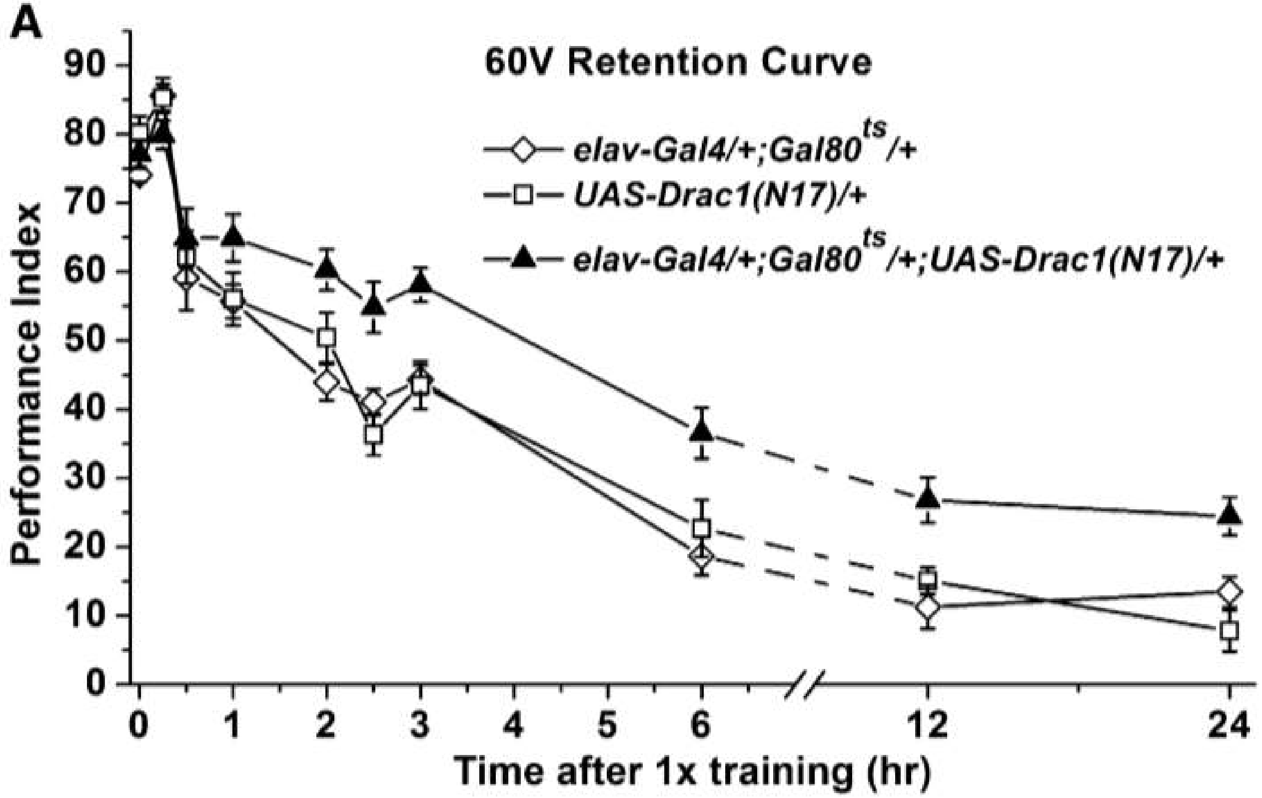
They cycle between an active (GTP-bound) and an inactive (GDP-bound) conformation. In the active state, they interact with one of over 60 target proteins (effectors).

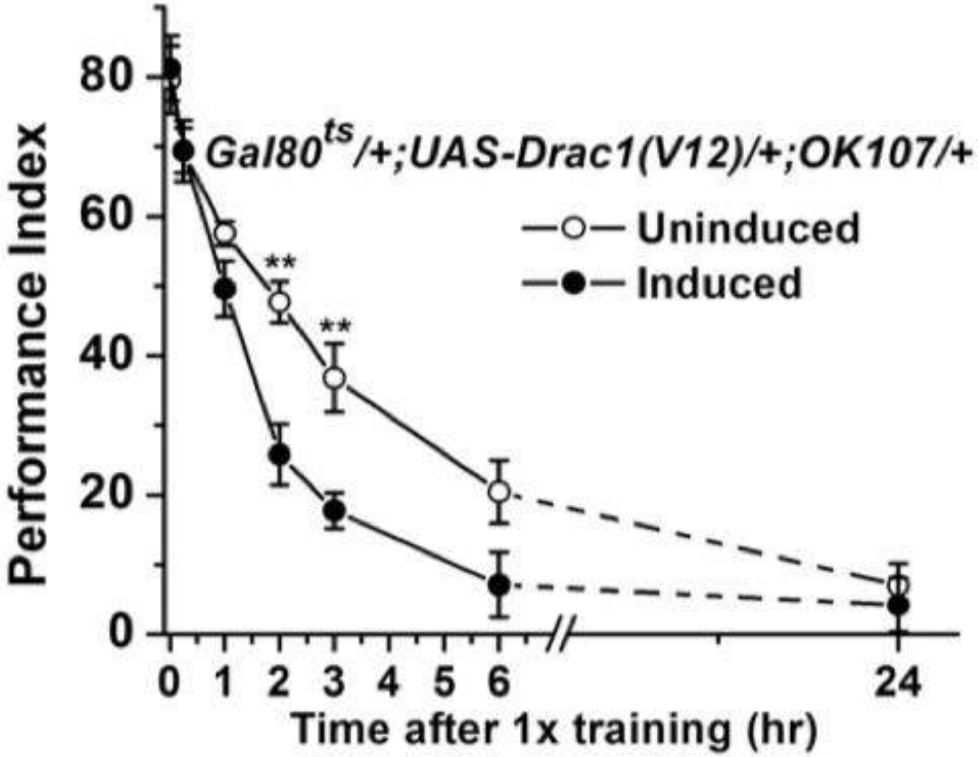
Shuai, Y. et al. 2010.

Bidirectional regulation of memory decay by Rac in the mushroom body

block Rac activity

increase Rac activity

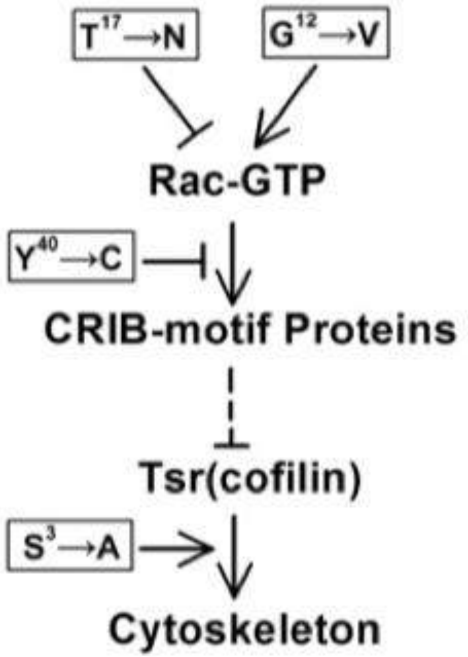


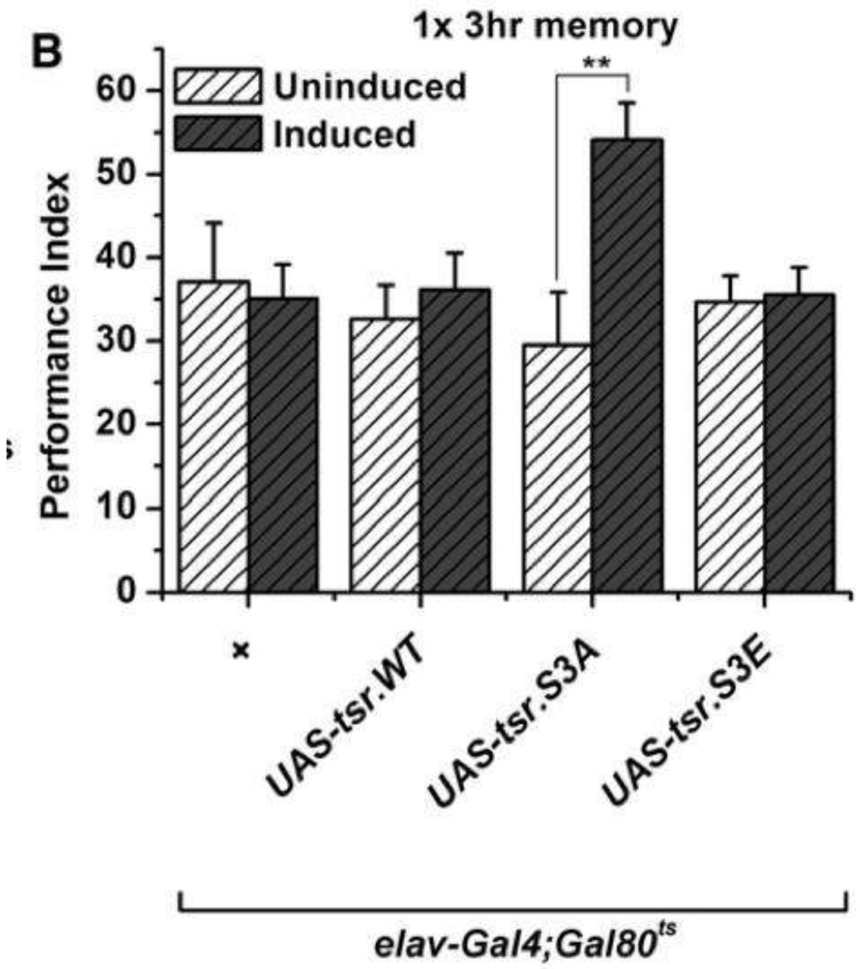


uas-Drac1(N17):
Expresses dominant negative Rac1 under UAS control.

uas-Drac(V12):
Expresses constitutively active Rac1 under UAS control.

Rac can signal through cofilin to regulate actin cytoskeleton remodeling.

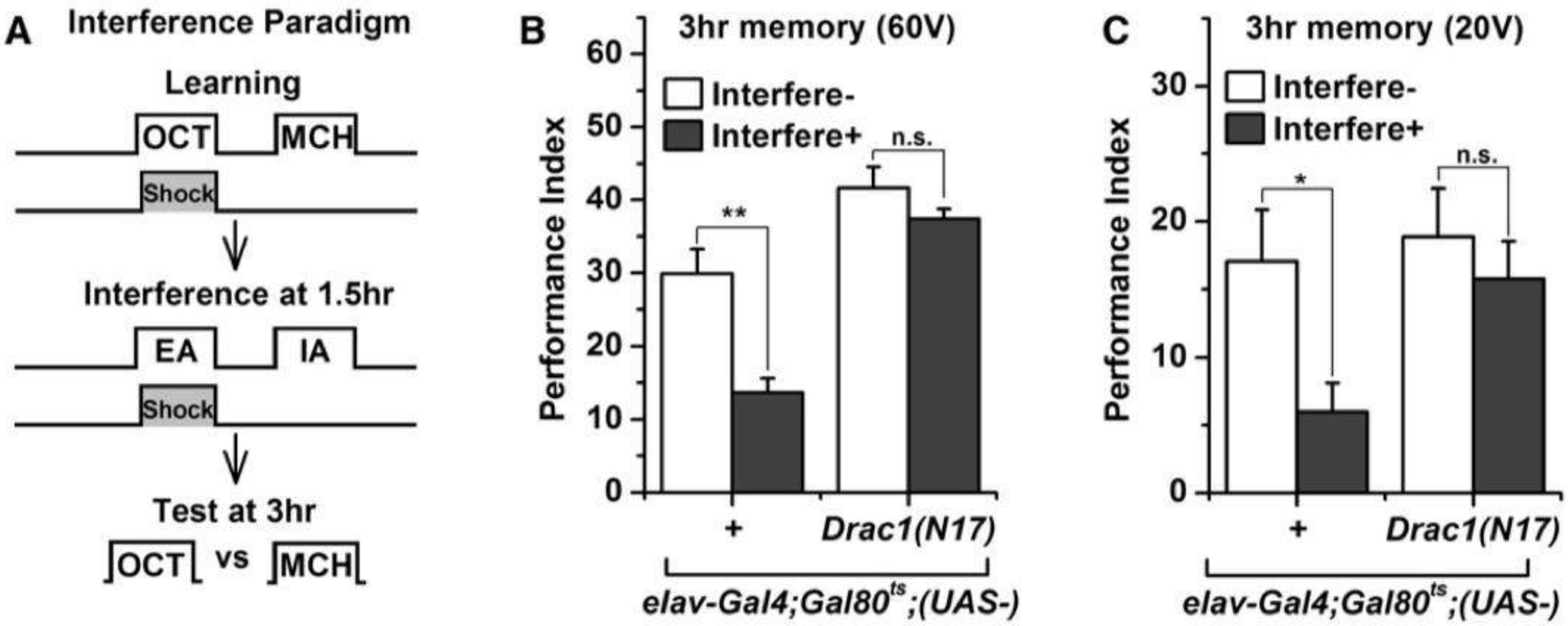




Tsr.S3A being persistently active
Tsr.S3E being inactive

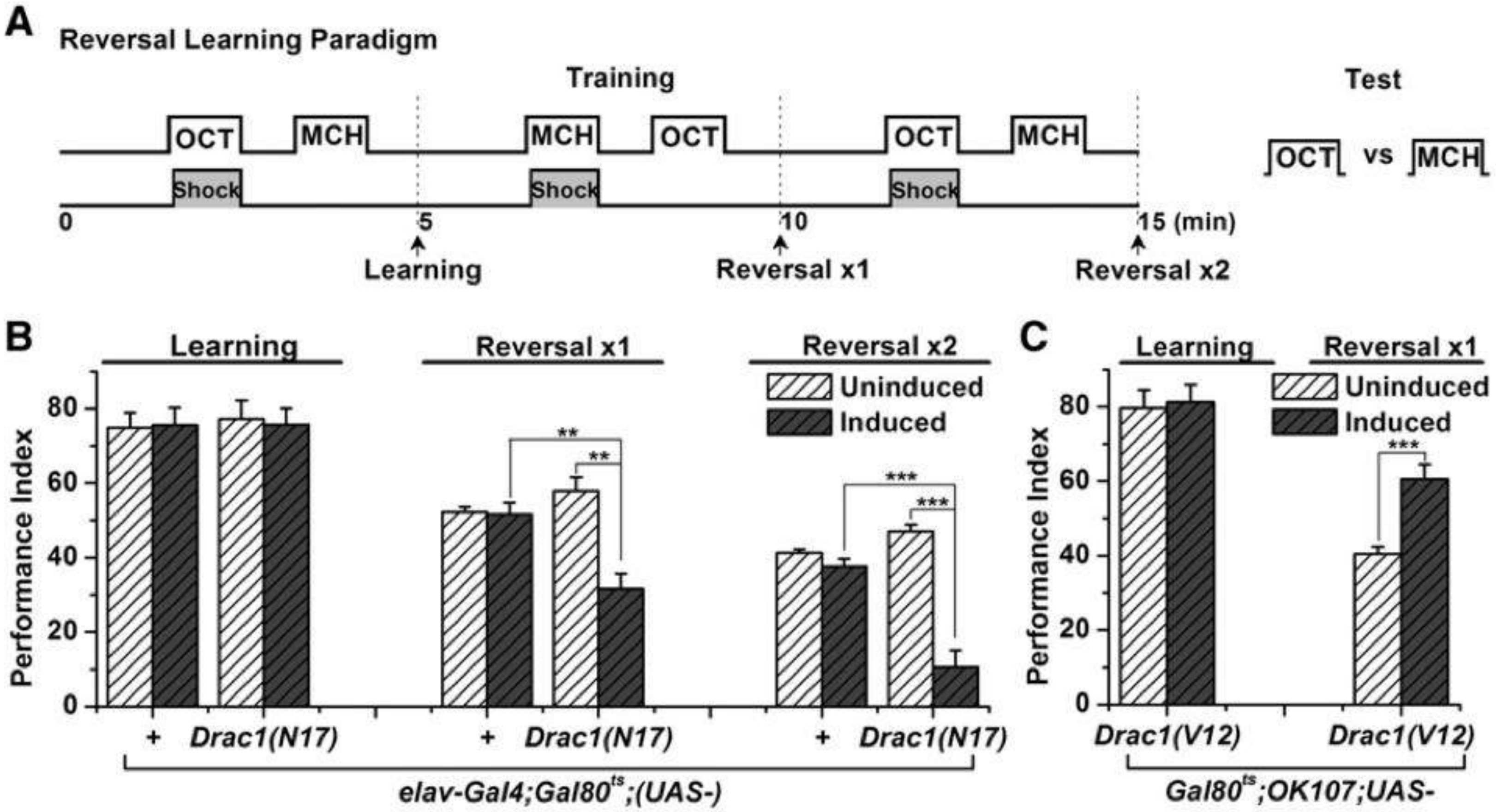
the actin-depolymerizing activity of cofilin has been shown to be important for synaptic plasticity and activity-dependent modification of spine morphology.

Suppression of interference-induced memory loss in Drac1(N17)-expressing flies



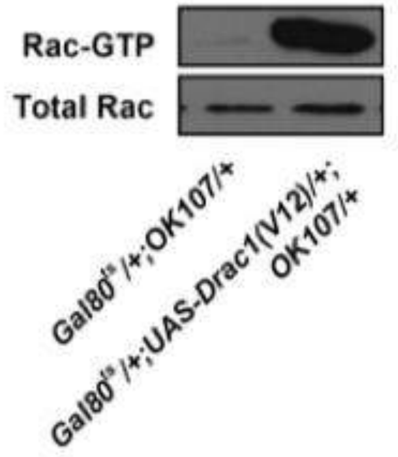
uas-Drac1(N17):
Expresses dominant negative Rac1 under UAS control.

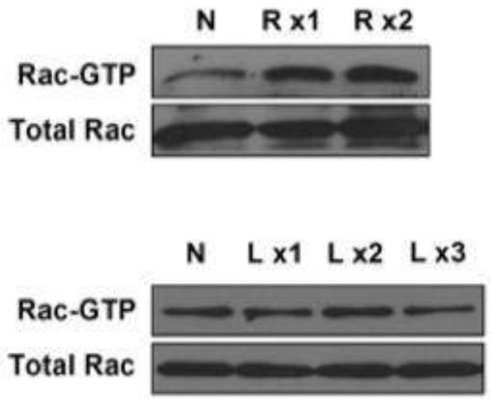
interference-induced forgetting

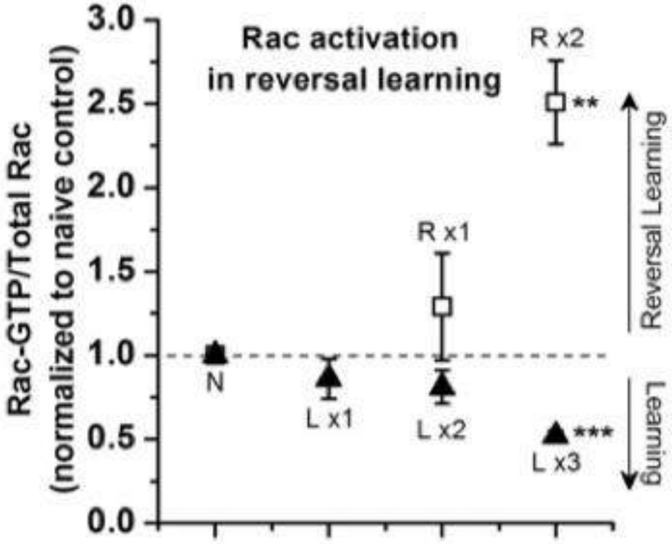


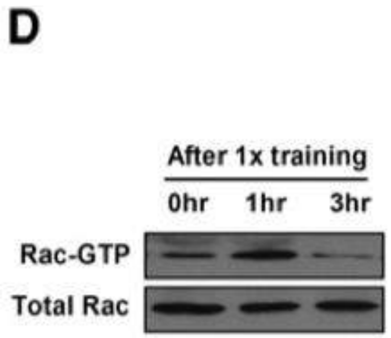
If Rac activity is blocked, this retroactive interference-based forgetting is completely inhibited.

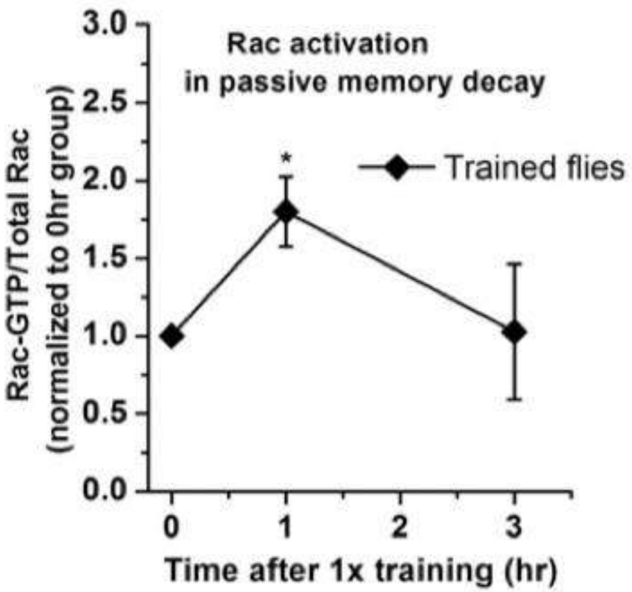
Endogenous Rac activation correlates with forgetting.











Learning itself activates Rac and increases the rate of forgetting postacquisition

Report

Current Biology

Hippocampal Activation of Rac1 Regulates the Forgetting of Object Recognition Memory

Highlights

- In mice, hippocampal Rac1 activity regulates natural decay of object memory
- Interference-induced forgetting is also regulated by hippocampal Rac1 activity
- Manipulation of Rac1 activity affects long-term potentiation stability

Authors

Yunlong Liu, Shuwen Du, Li Lv, ..., Yikai Tang, Lianzhang Wang, Yi Zhong

Correspondence

zhongyi@tsinghua.edu.cn

In Brief

Y. Liu et al. discovered a forgetting

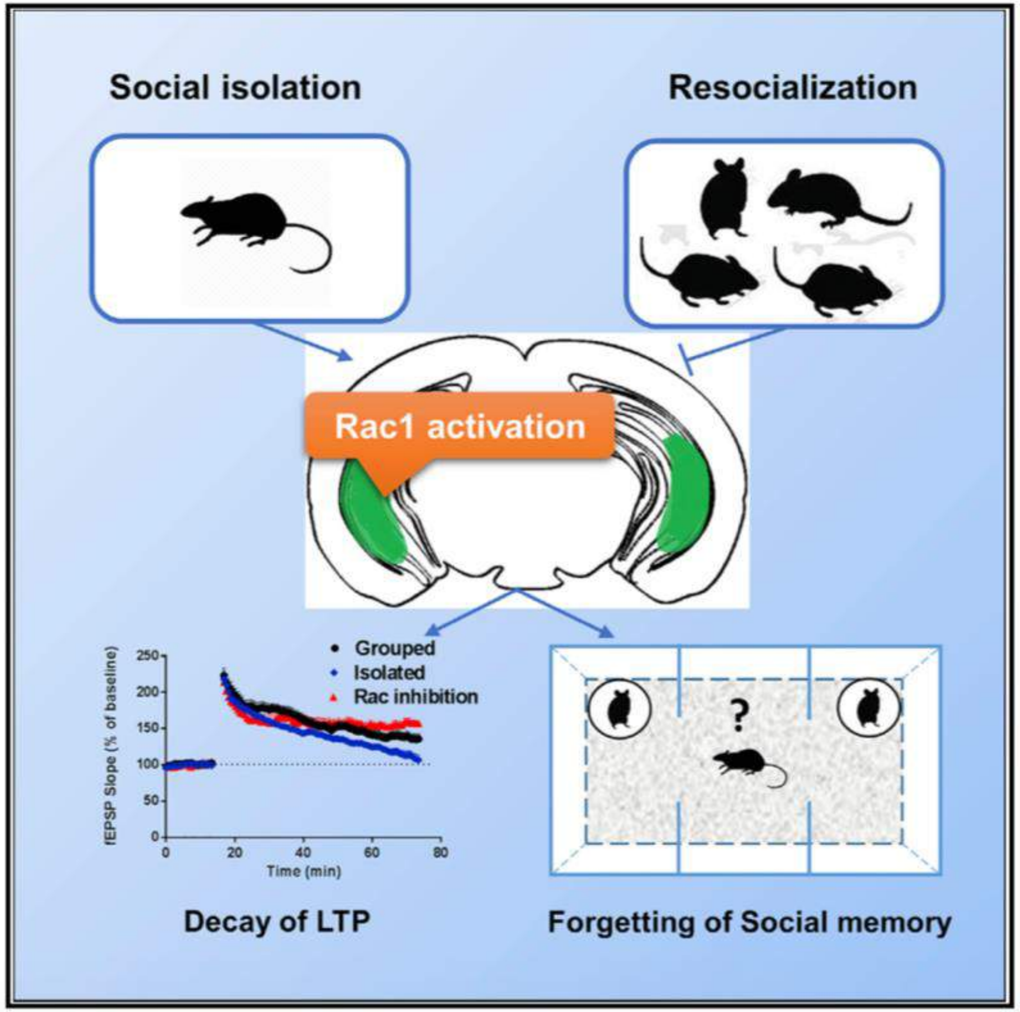
Liu, Y. et al. 2016.

Cell Reports

Report

Social Isolation Induces Rac1-Dependent Forgetting of Social Memory

Graphical Abstract



Authors

Yunlong Liu, Li Lv, Lianzhang Wang, Yi Zhong

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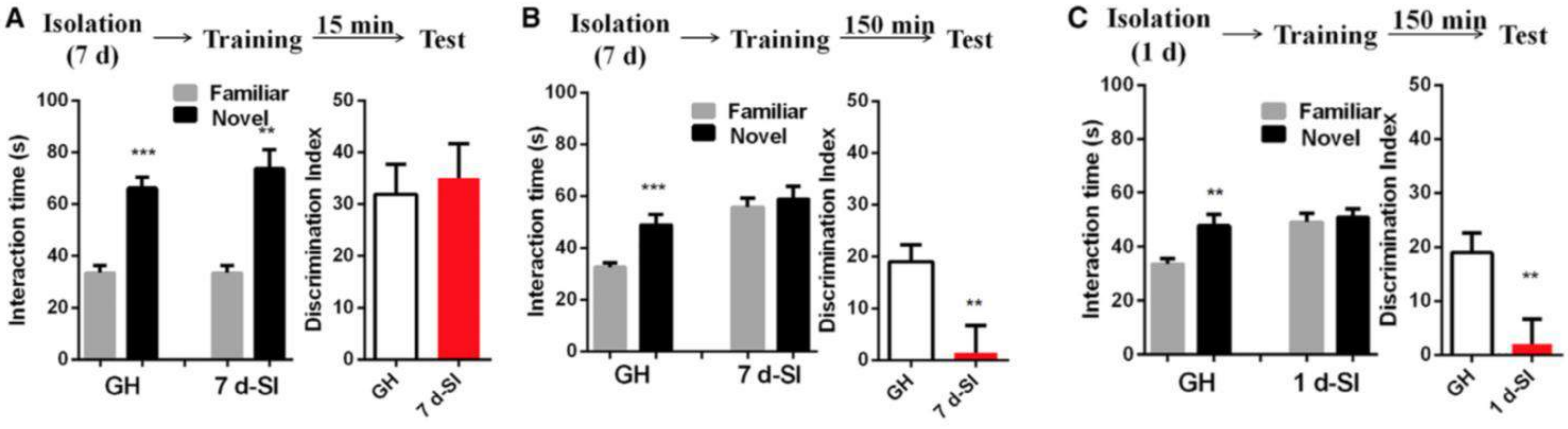
In Brief

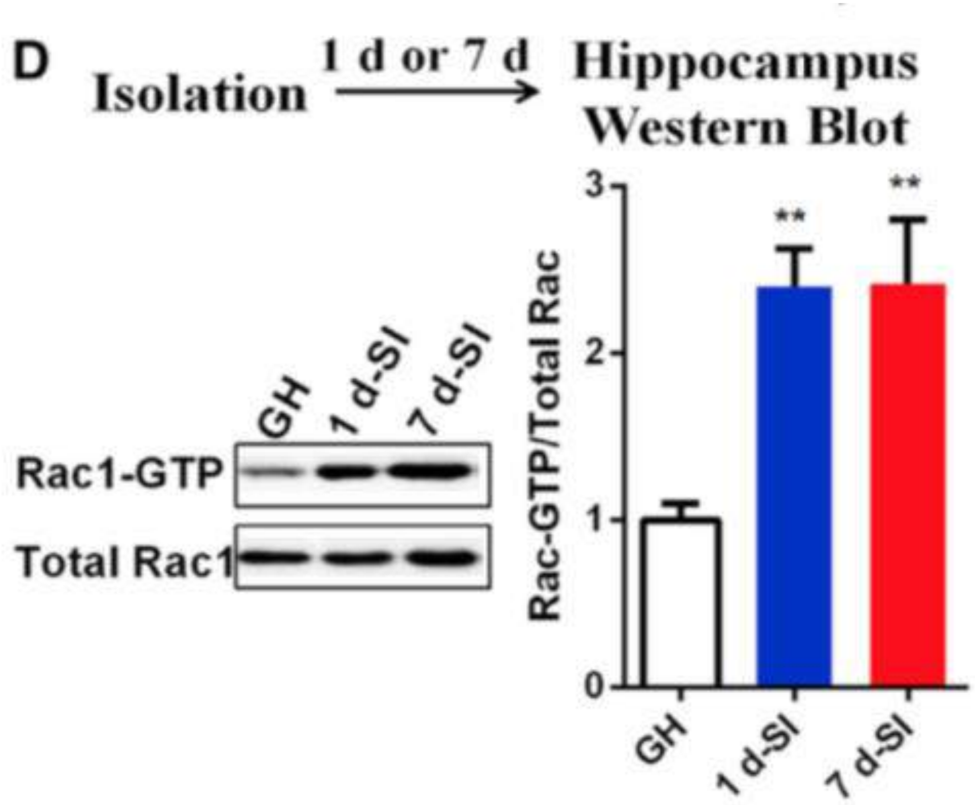
Liu et al. identify a Rac1-dependent forgetting pathway that mediates isolation-induced memory impairment. Such findings underscore the importance of maintained social interactions on cognitive function, which may have implications for autism and Alzheimer's disease.

Liu, Y. et al. 2018.

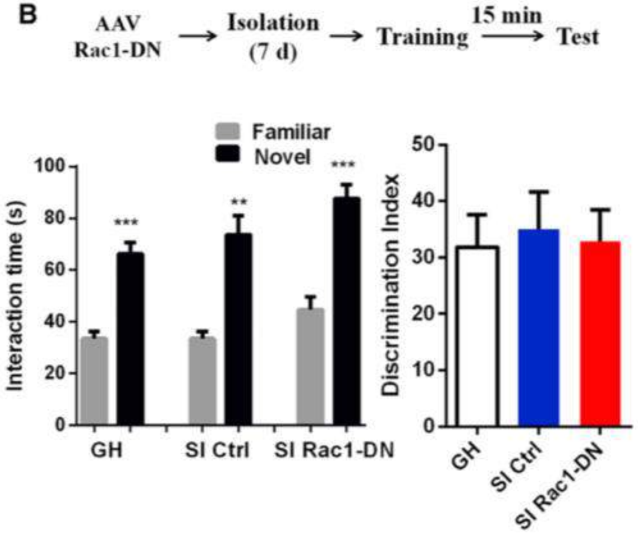
Isolation leads to a phenotype of accelerated forgetting.



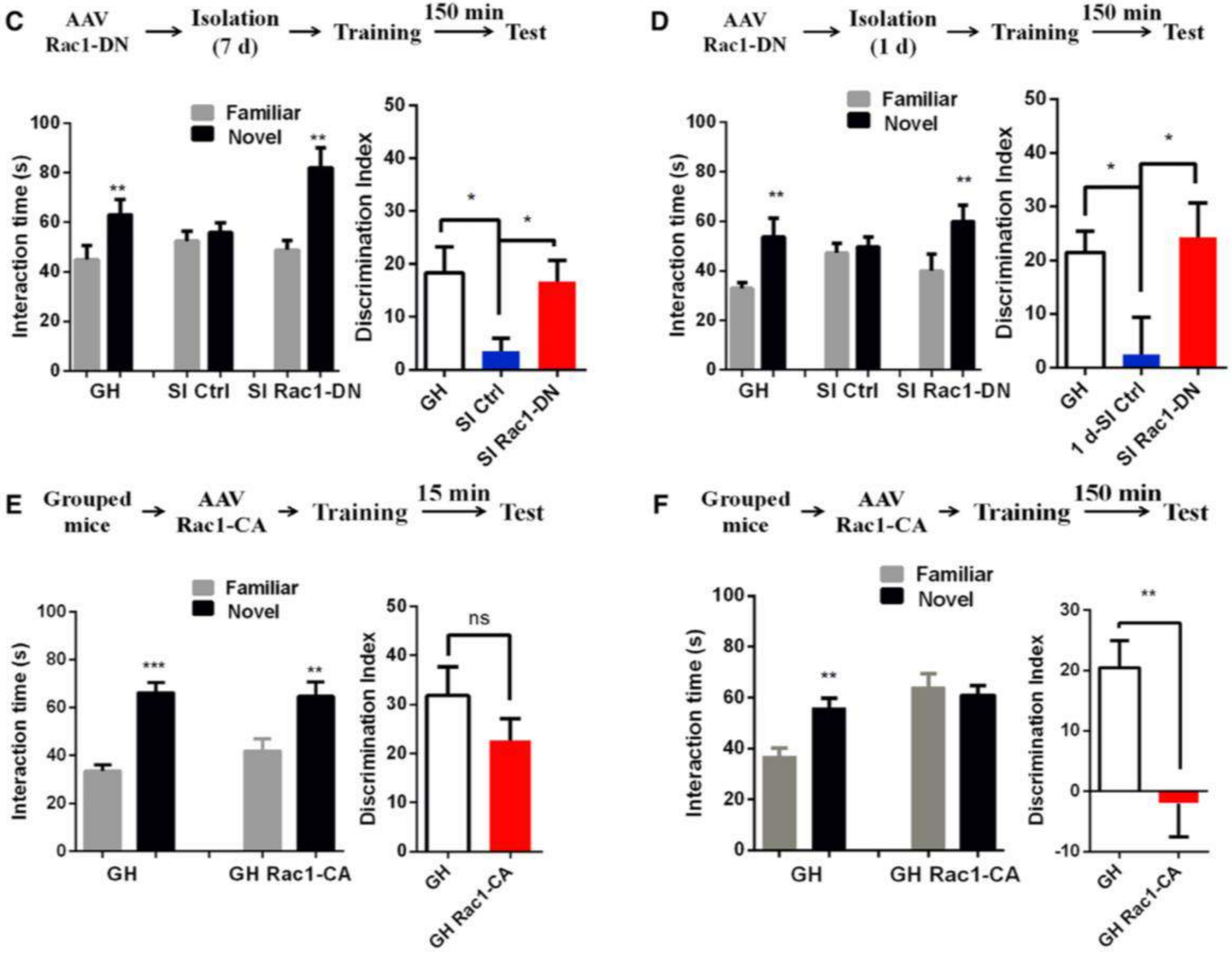
Isolation-induced impairment of social recognition memory is correlated with hippocampal Rac1 activity.



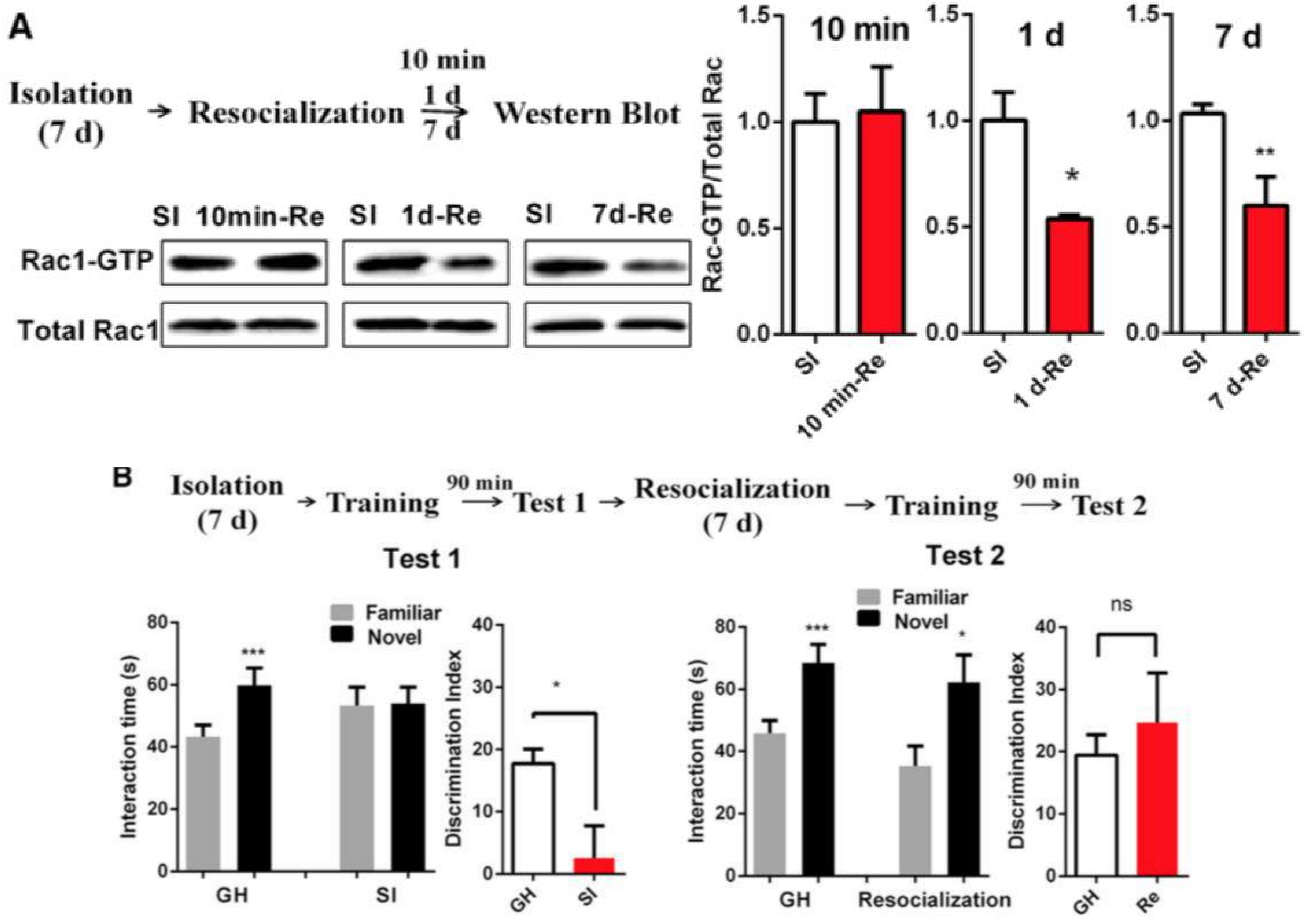
Manipulation of Rac1 activity affects the retention, but not the acquisition, of social memory.



acquisition

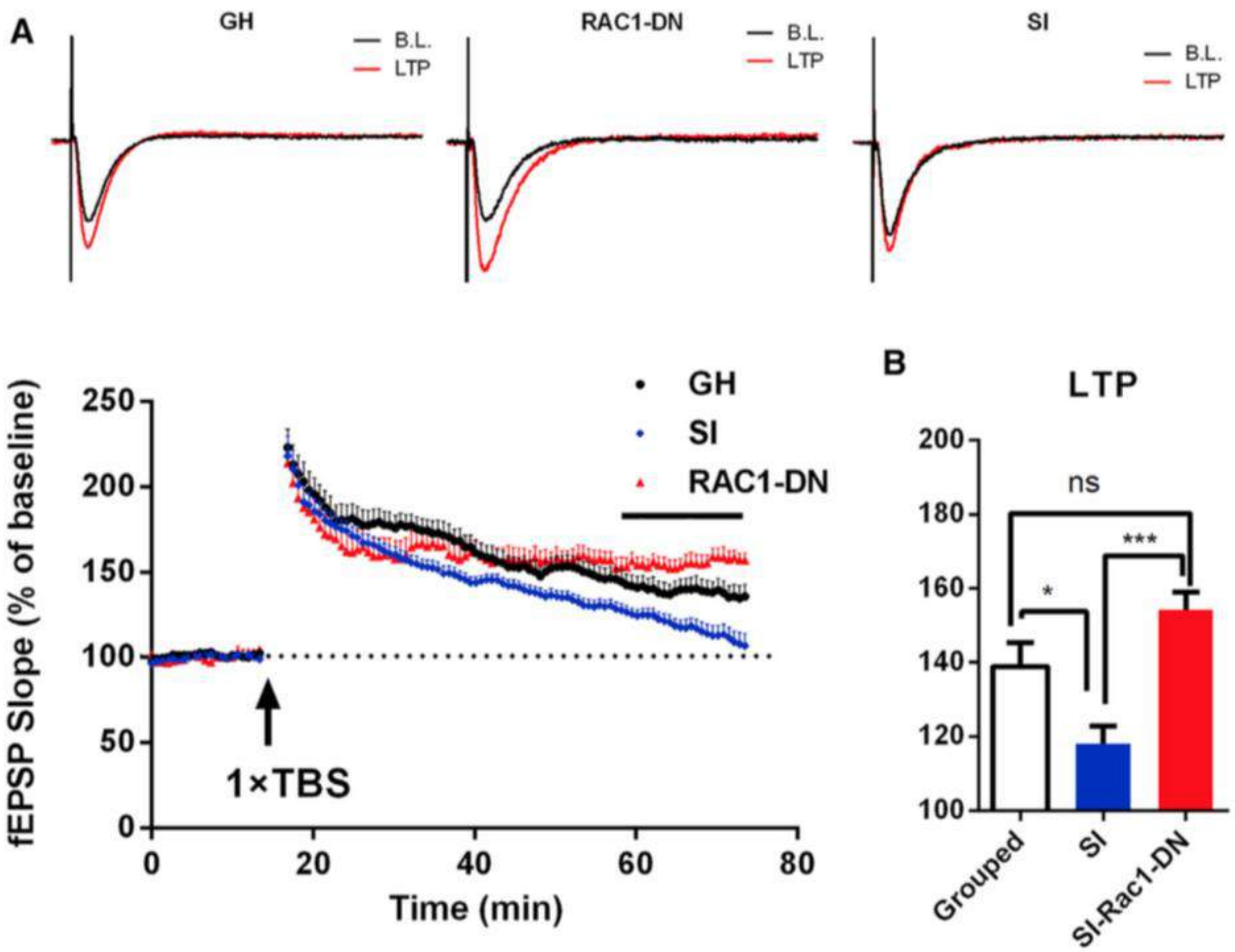


Effects of social isolation on Rac1 activity and social memory are reversed by resocialization.



Social interacting may protect memories from being forgotten by inhibiting Rac1-dependent forgetting

Inhibiting Rac1 activity suppressed accelerated decay of LTP in isolated mice.



- Cellular and molecular mechanisms of forgetting

  Forgetting is regulated by Rac and the cytoskeleton in the MBs

- Neural mechanisms of forgetting

  Dopamine participates in the regulation of forgetting

- Sleep-dependent memory retention

  Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgettin.

Jacob Berry

Postdoctoral Associate
Email: jaberry@scripps.edu

Jacob graduated in 2002 with a Bachelor's degree in Computation Physics from the University of Texas at Austin. After working for two years in breast cancer research at Baylor College of Medicine and MD Anderson Cancer Center, he entered the Developmental Biology Program at BCM and started his PhD research on learning and memory in the Davis lab. Jacob recently obtained his PhD and is currently a postdoctoral fellow studying dopamine neurons and their role in learning and forgetting using a combination of in vivo functional imaging and behavioral assays.

Ron Davis

Cell PRESS

Neuron
Article

Dopamine Is Required for Learning and Forgetting in *Drosophila*

Jacob A. Berry,[1,2] Isaac Cervantes-Sandoval,[1] Eric P. Nicholas,[1] and Ronald L. Davis[1,*]
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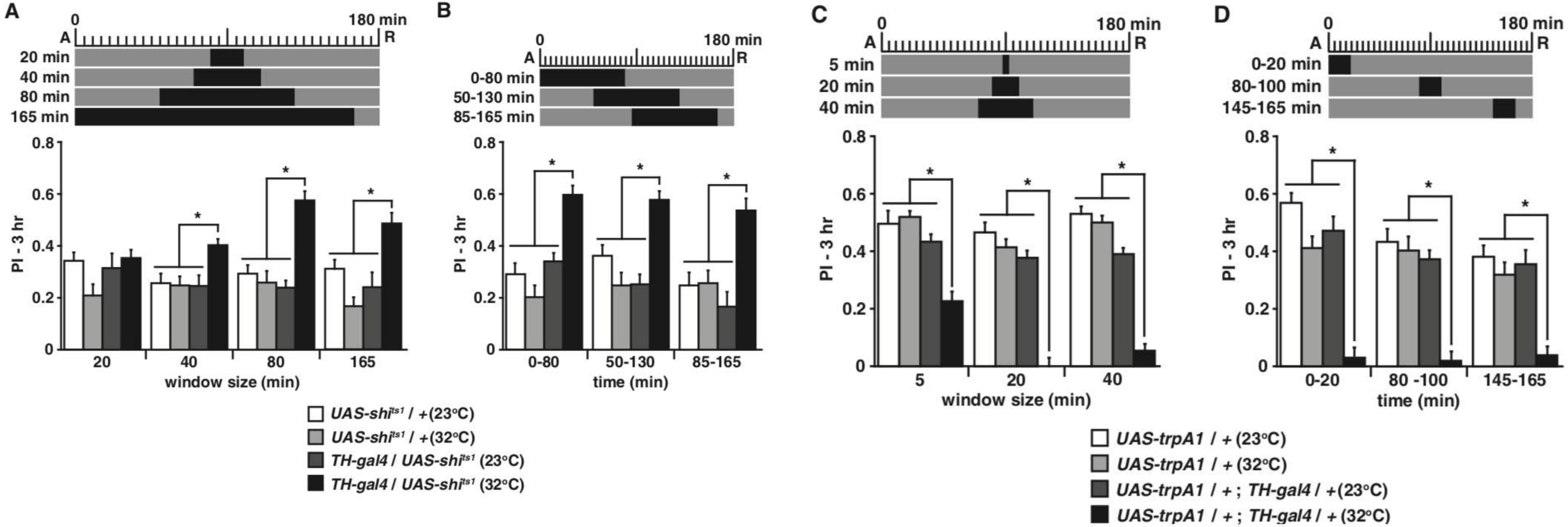
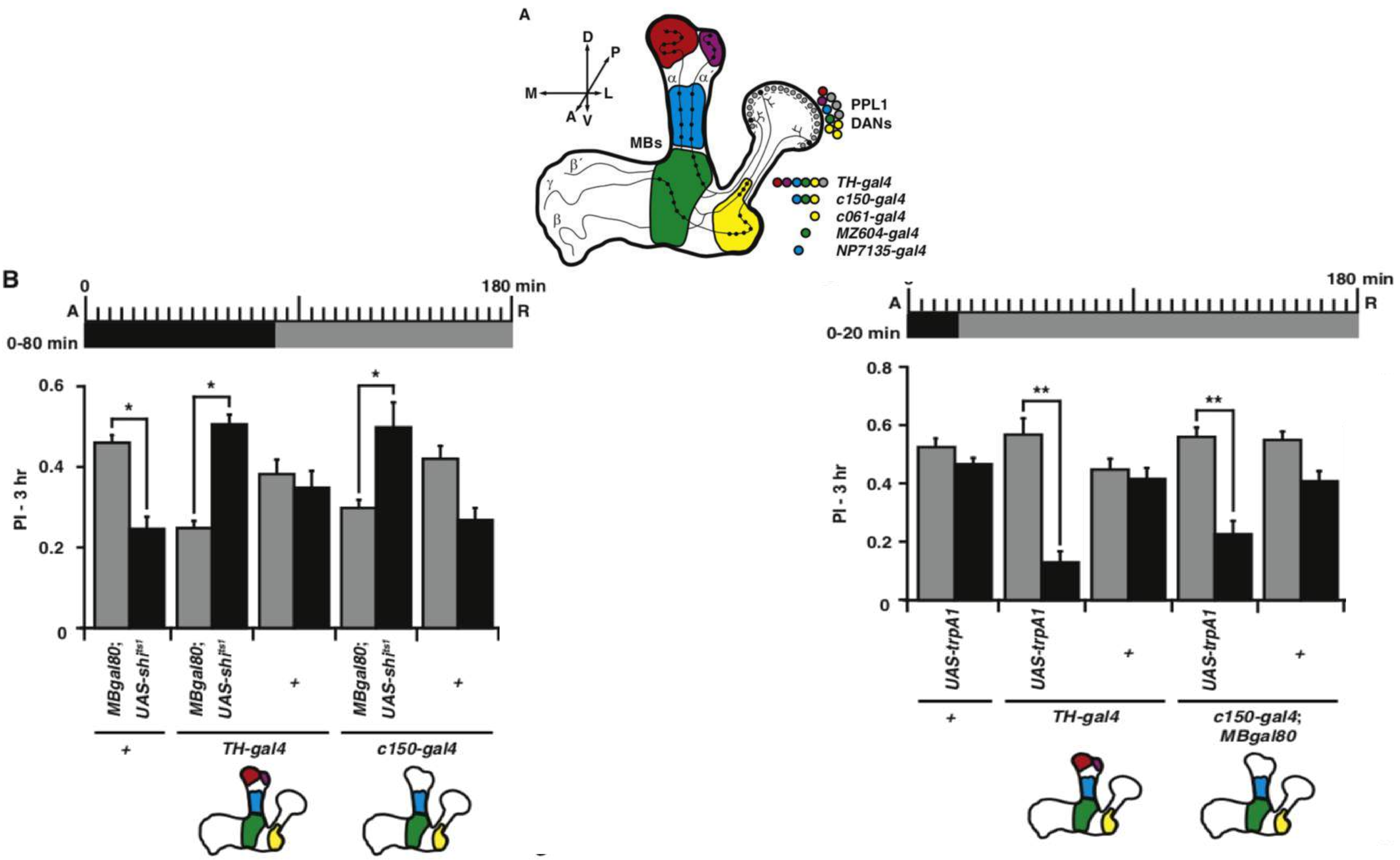
[2]Program in Developmental Biology, Baylor College of Medicine, Houston, TX 77030, USA
*Correspondence: rdavis@scripps.edu
DOI 10.1016/j.neuron.2012.04.007

Berry, J. et al. 2012.

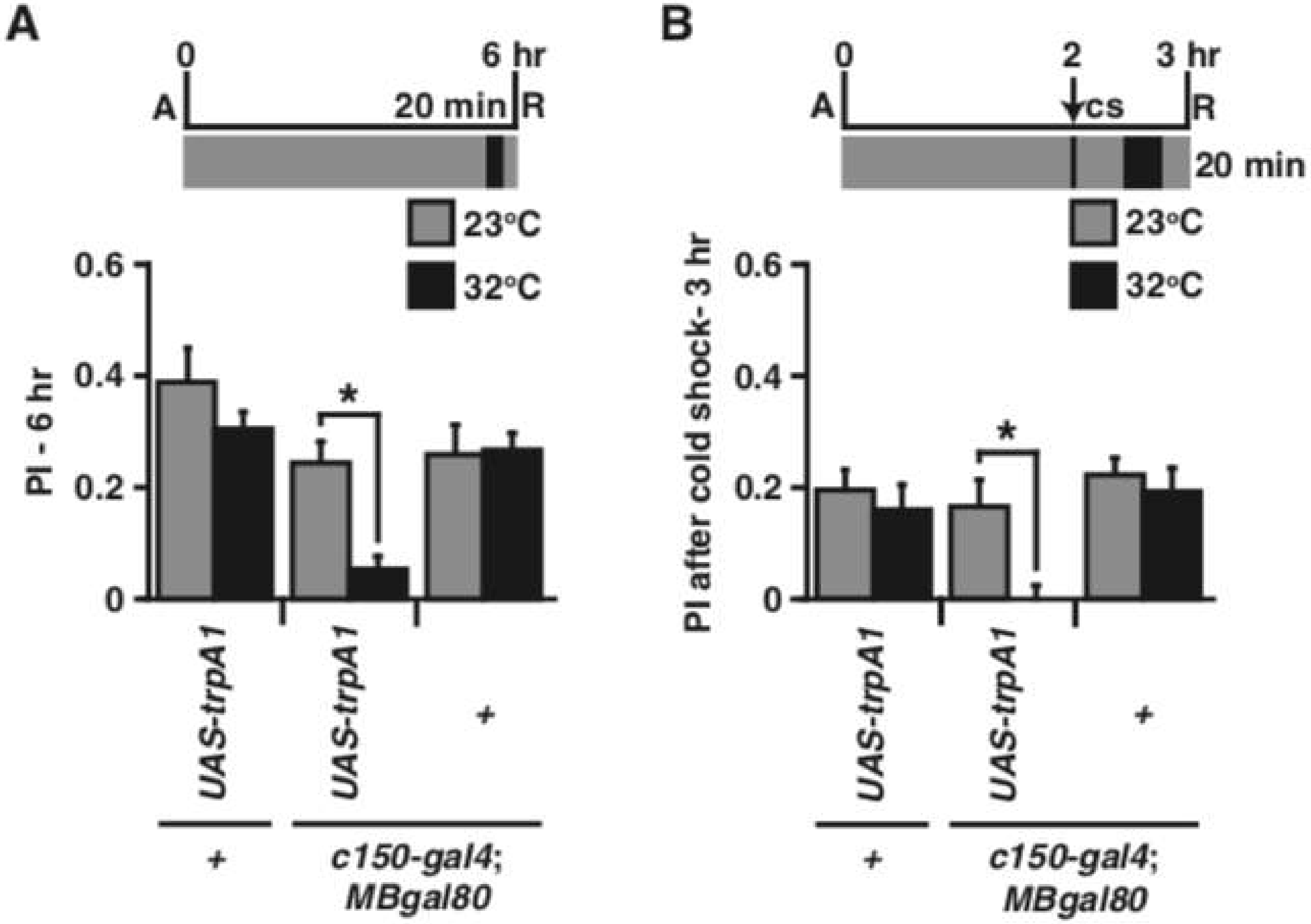
DAN activity after learning inhibits memory consolidation and/or promotes forgetting.





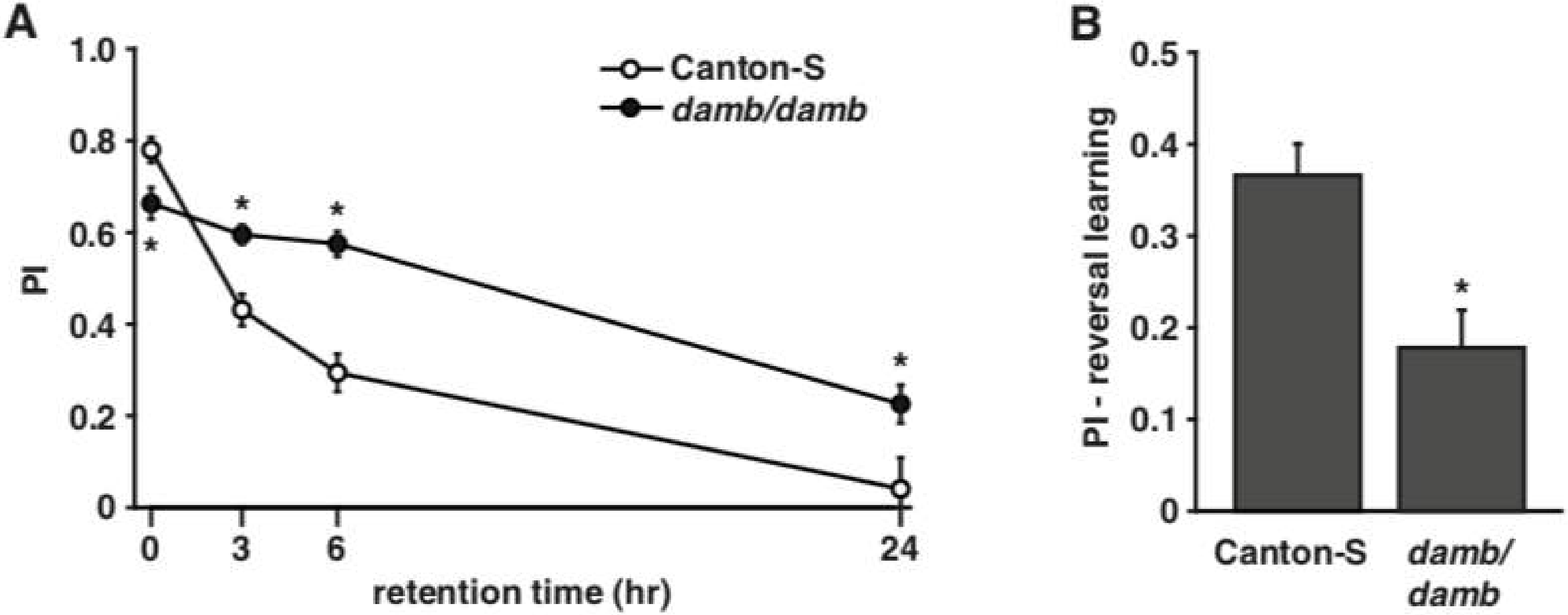
A
D
P
M
L
A
V
MBs
PPL1
DANs
TH-gal4
c150-gal4
c061-gal4
MZ604-gal4
NP7135-gal4
B
0
180 min
A
R
0-80 min
0-20 min
PI - 3 hr
0.6
0.4
0.2
0
0.8
MBgal80;
UAS-shi^ts1
+
TH-gal4
c150-gal4
UAS-trpA1
c150-gal4;
MBgal80
*
**

Stimulation of c150-gal4 DANs induces forgetting of consolidated memories

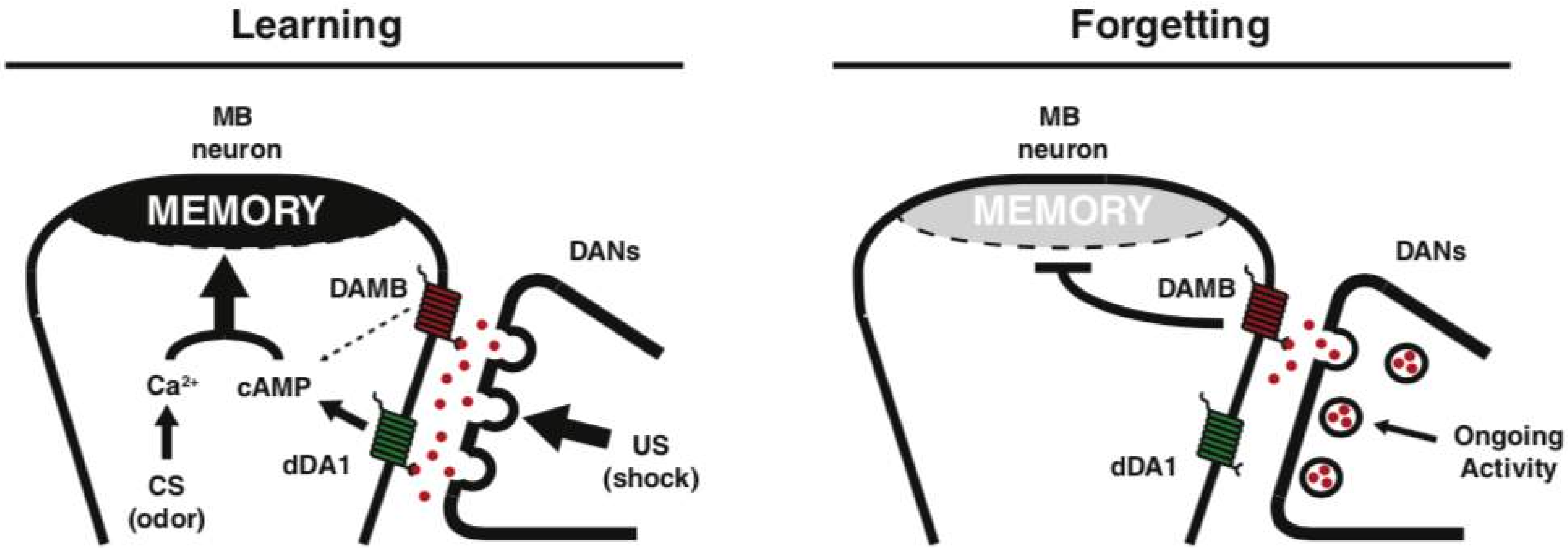


cold shock :
to eliminate remaining labile memory

Dopamine receptor DAMB is required for forgetting



Model of dopamine-mediated learning and forgetting.



Neuron

Article

Scribble Scaffolds a Signalosome for Active Forgetting

Highlights

- *Scribble* is a *Drosophila* memory suppressor gene
- The gene is expressed and functions in mushroom body and dopaminergic neurons
- It is necessary for normal active forgetting
- It regulates memory loss by scaffolding a forgetting signalosome

Authors

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Molee Chakraborty,
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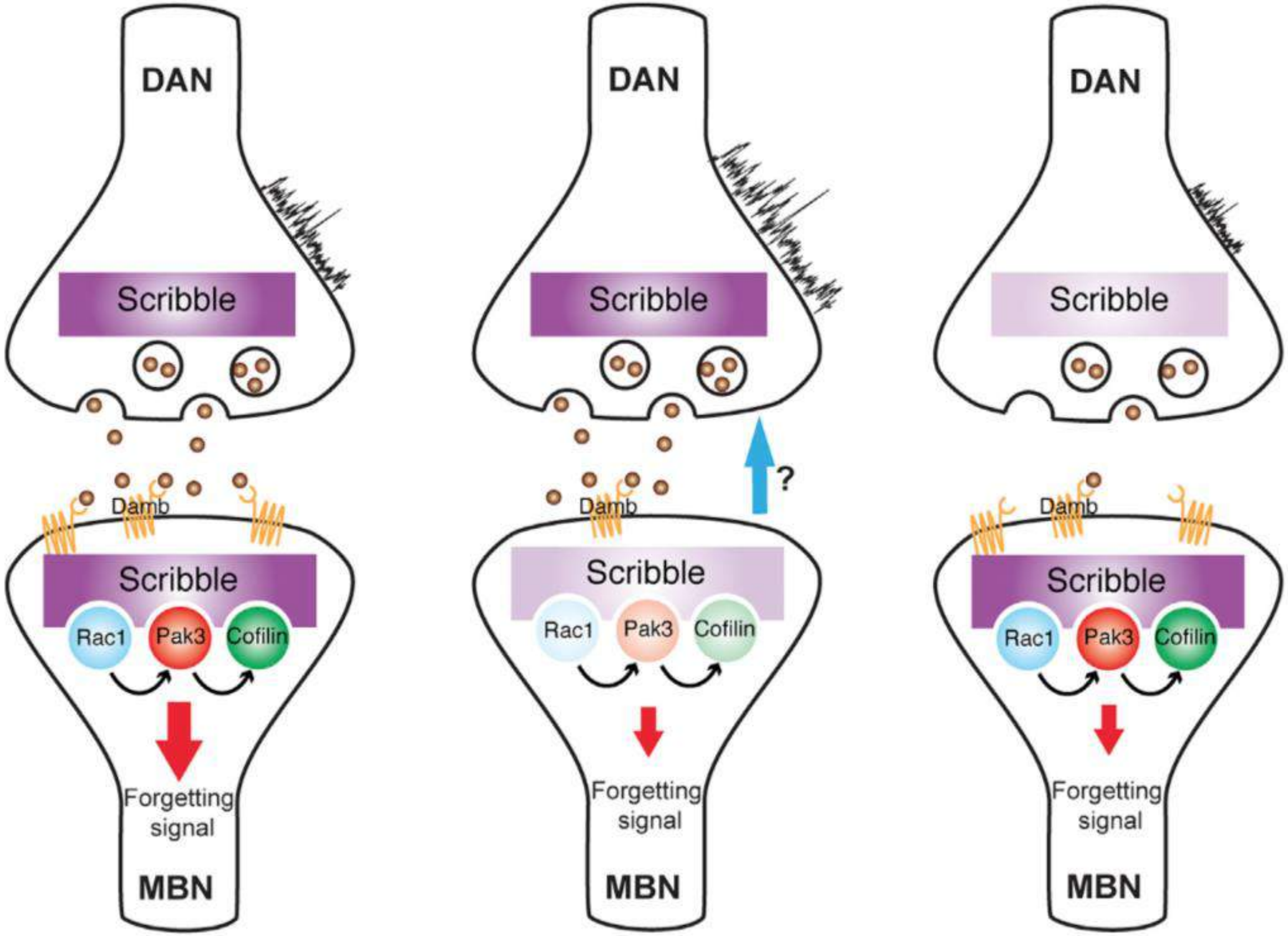
In Brief

Cervantes-Sandoval, I. et al. 2016



Dopamine→ Dopamine Receptor

→Scribble→Rac→Cofilin.

- Cellular and molecular mechanisms of forgetting

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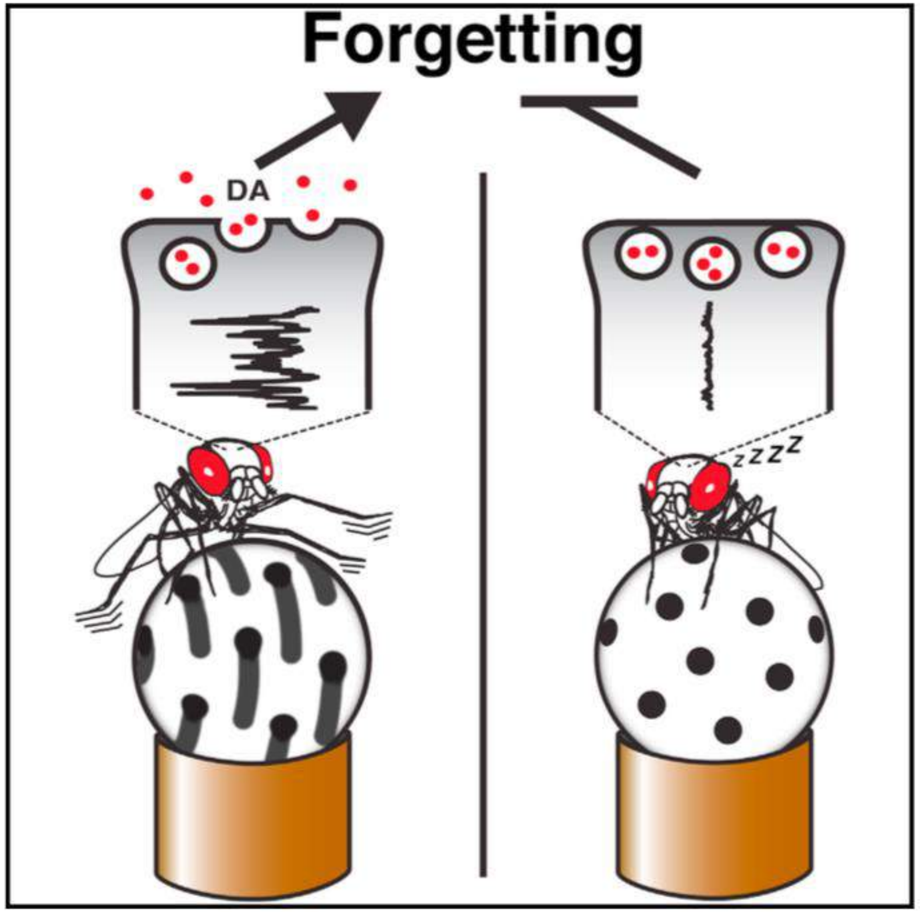
  Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgetting.

Cell

Article

Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgetting

Graphical Abstract



Authors

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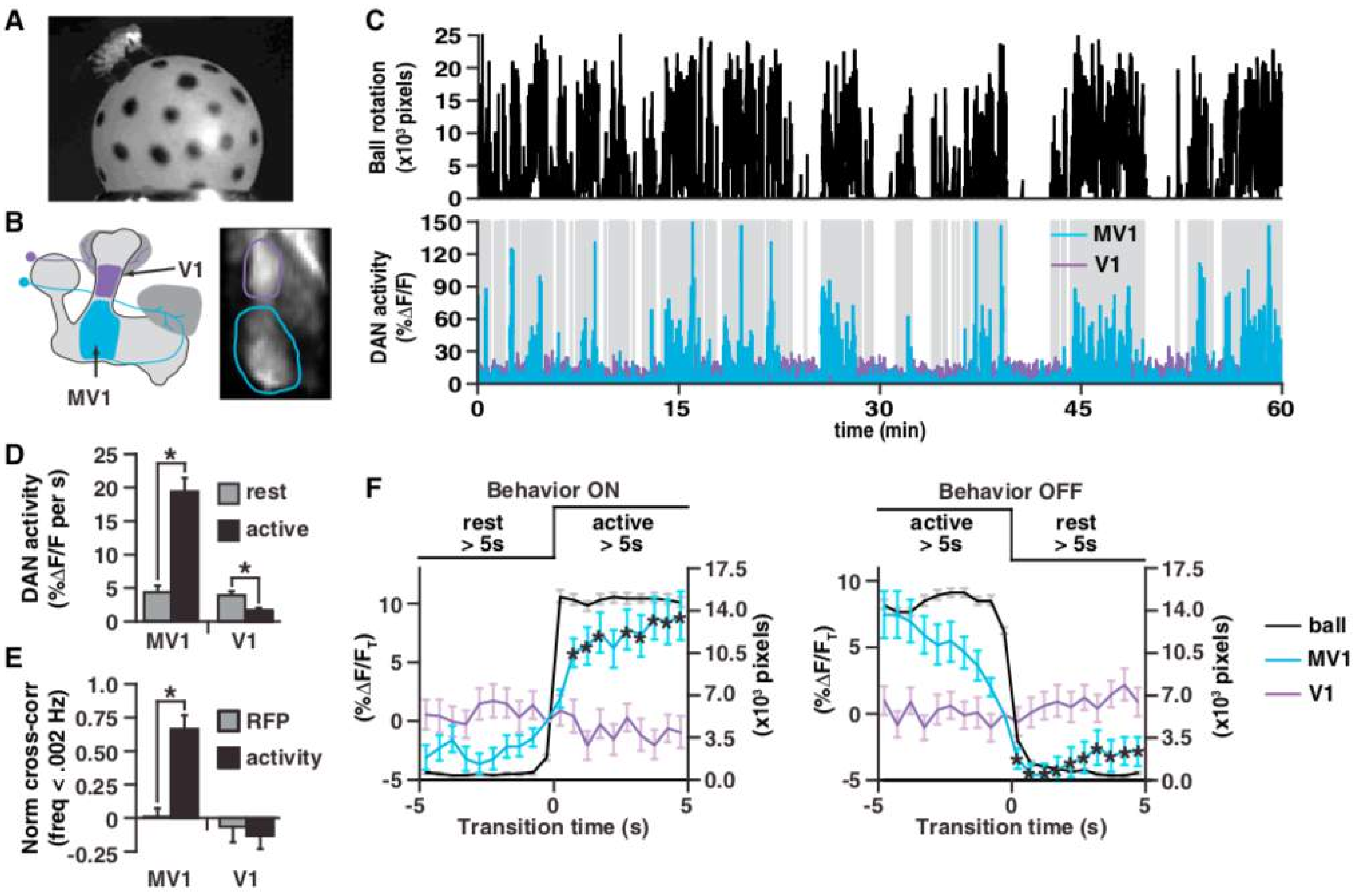
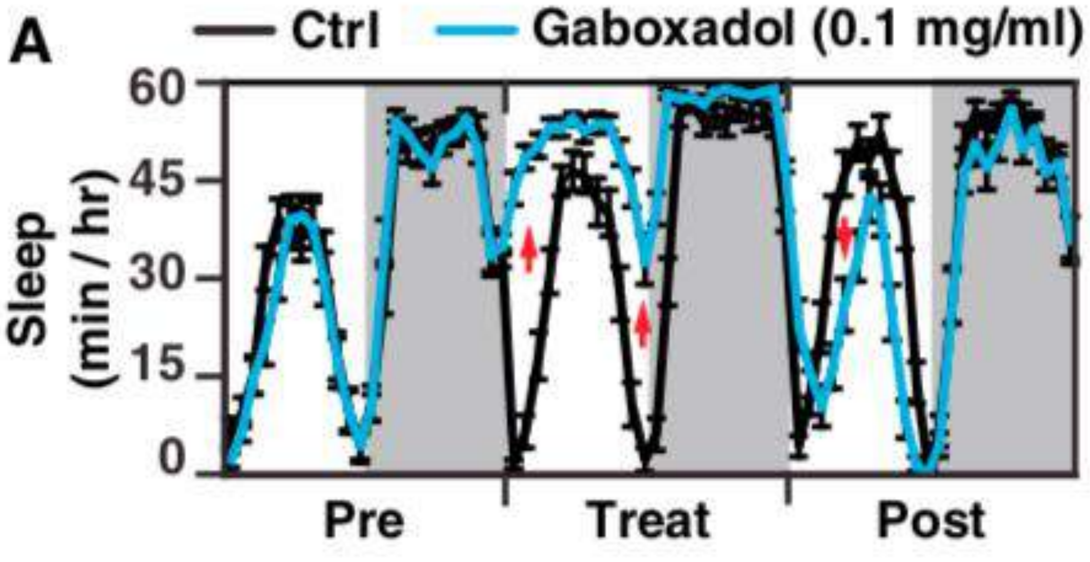
In Brief

Sleep is generally thought to stabilize new memories, but early psychology studies suggest that it prevents new learning from interfering with old memories. This study shows that sleep suppresses the activity of dopamine neurons that promote active forgetting of olfactory memories in flies, providing integration between neuroscience and psychology research.

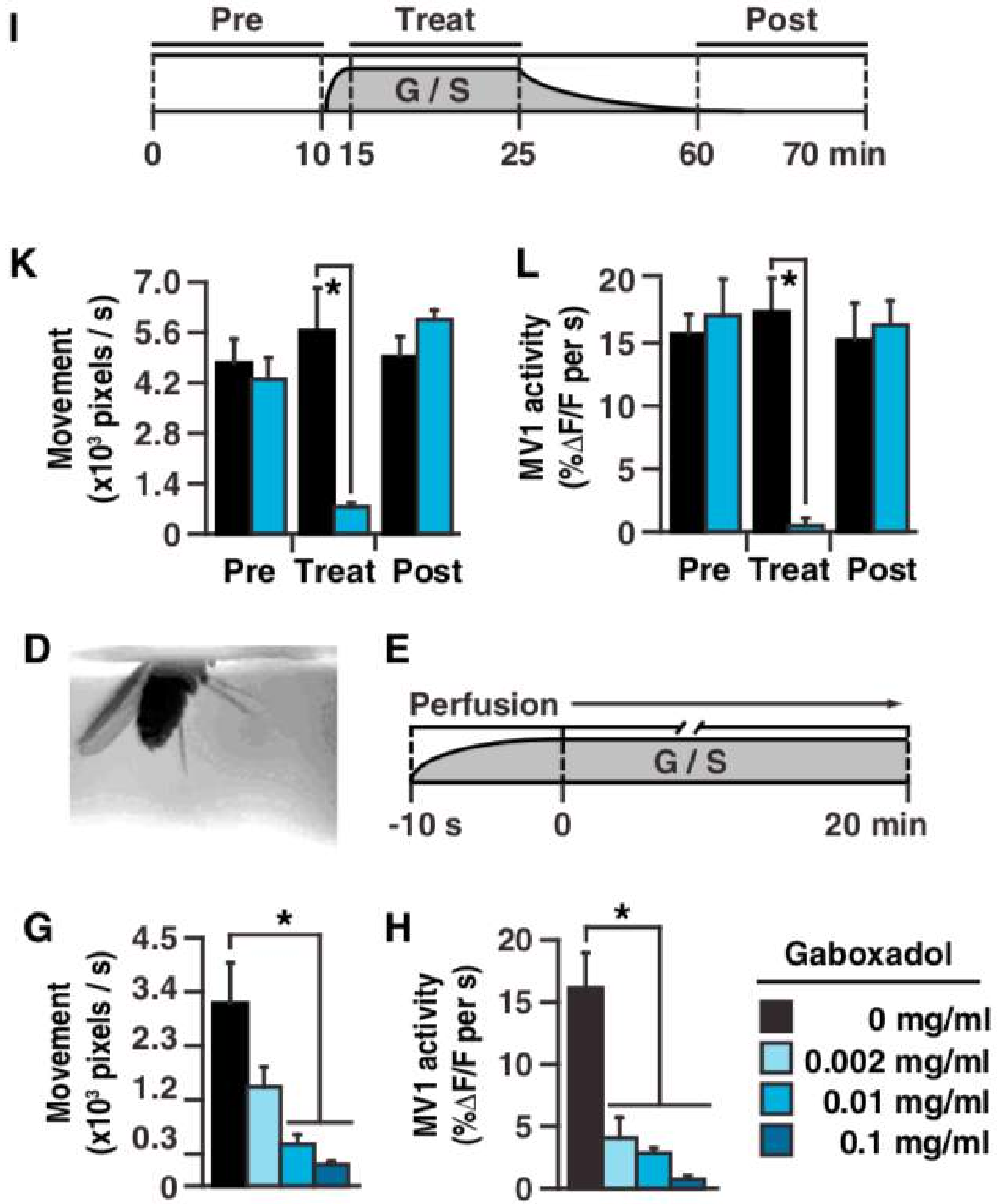
Ongoing dopamine neuron activity is regulated by behavioral state.



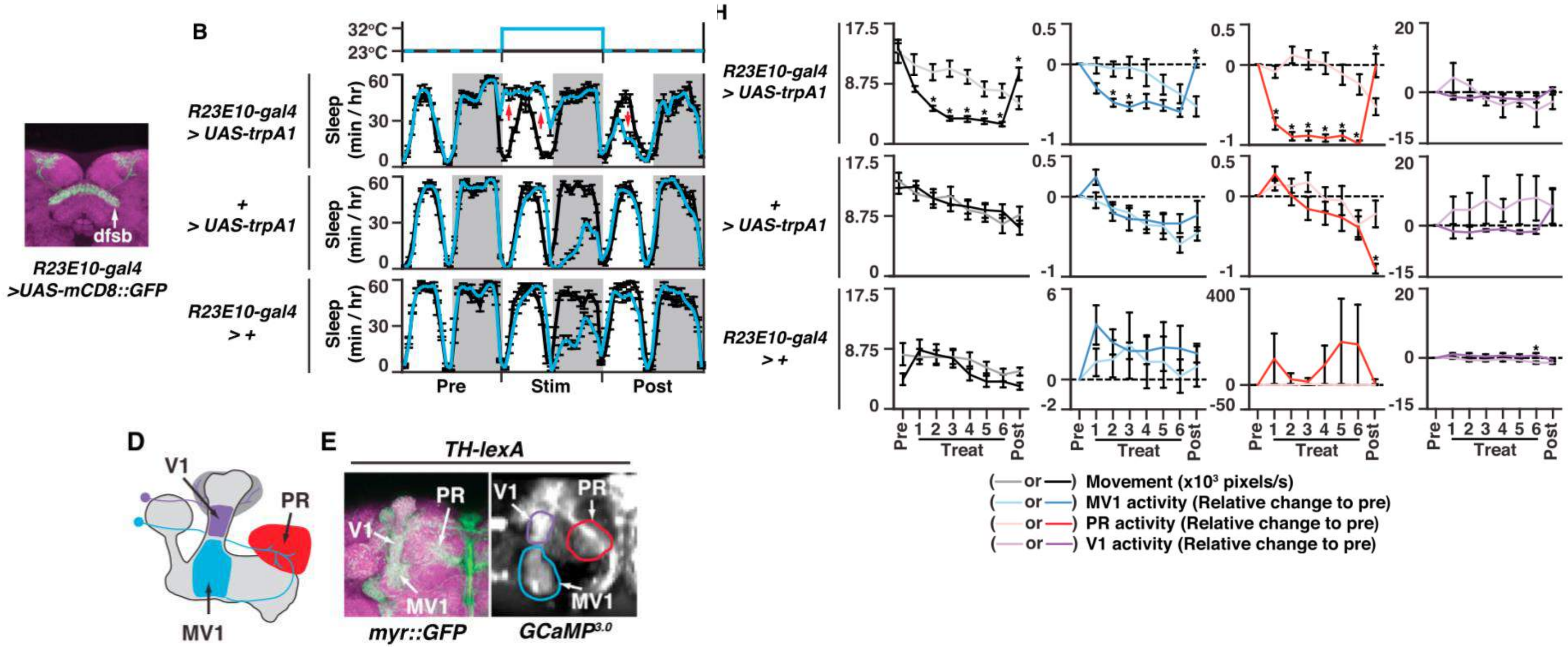
Increased sleep drive dramatically reduces the ongoing activity of DANs involved in forgetting.



Gaboxadol

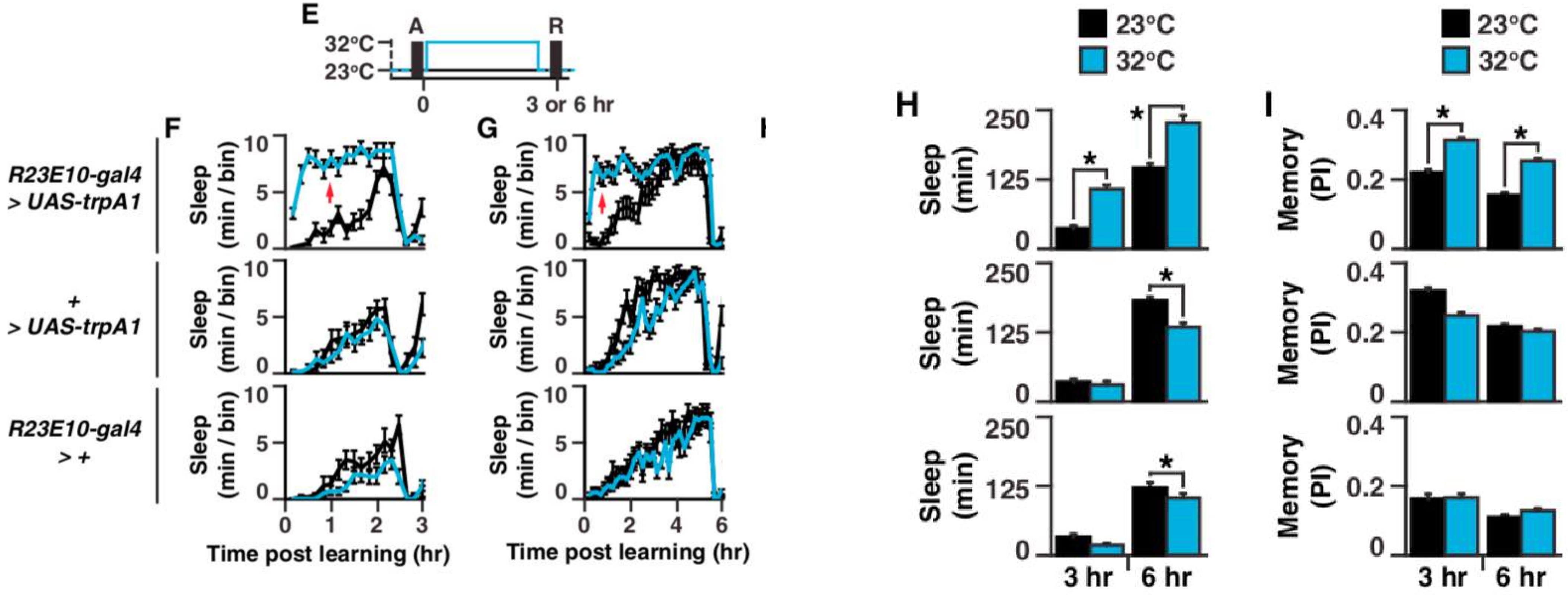


Increased sleep drive dramatically reduces the ongoing activity of DANs involved in forgetting.

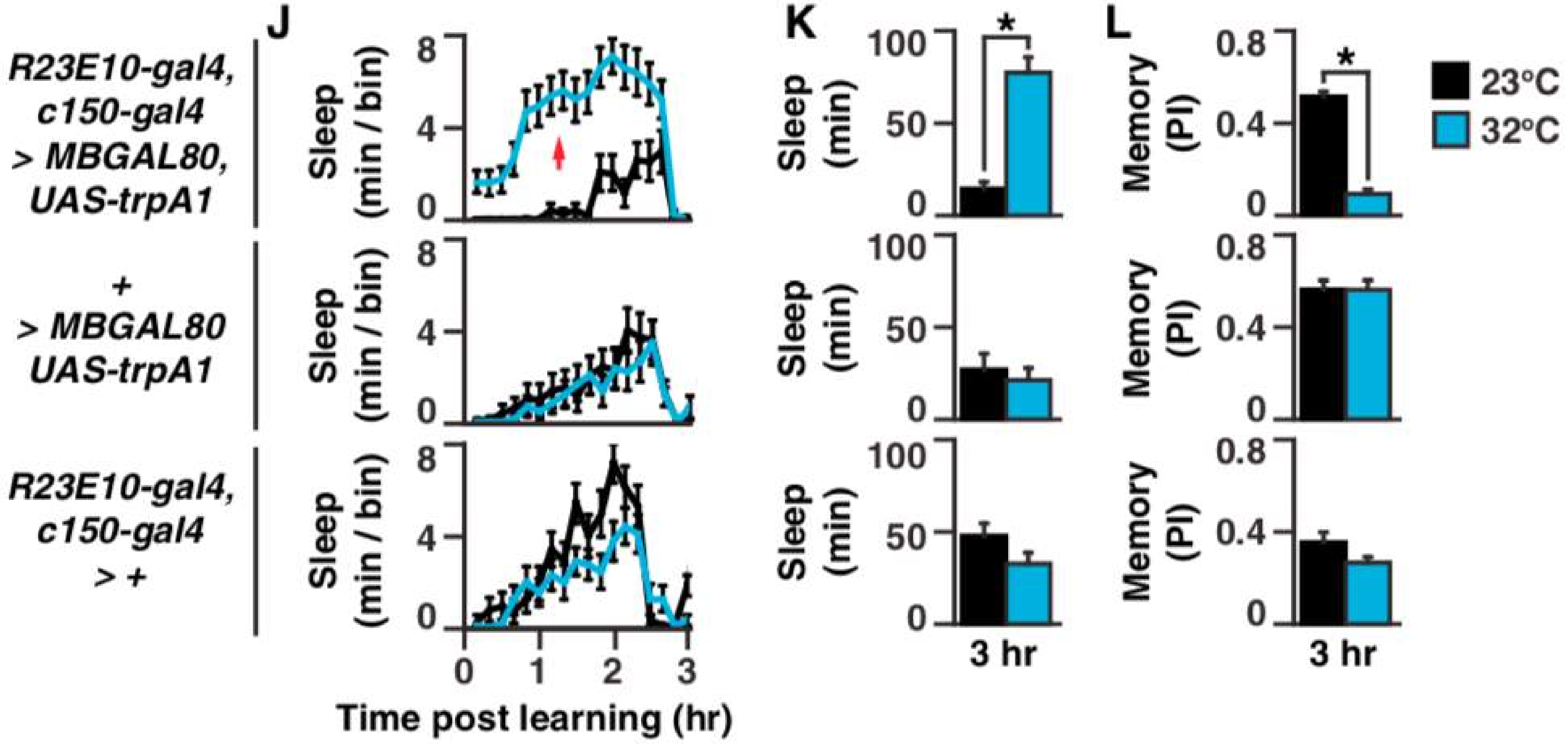


light: 23°C; dark: 34°C

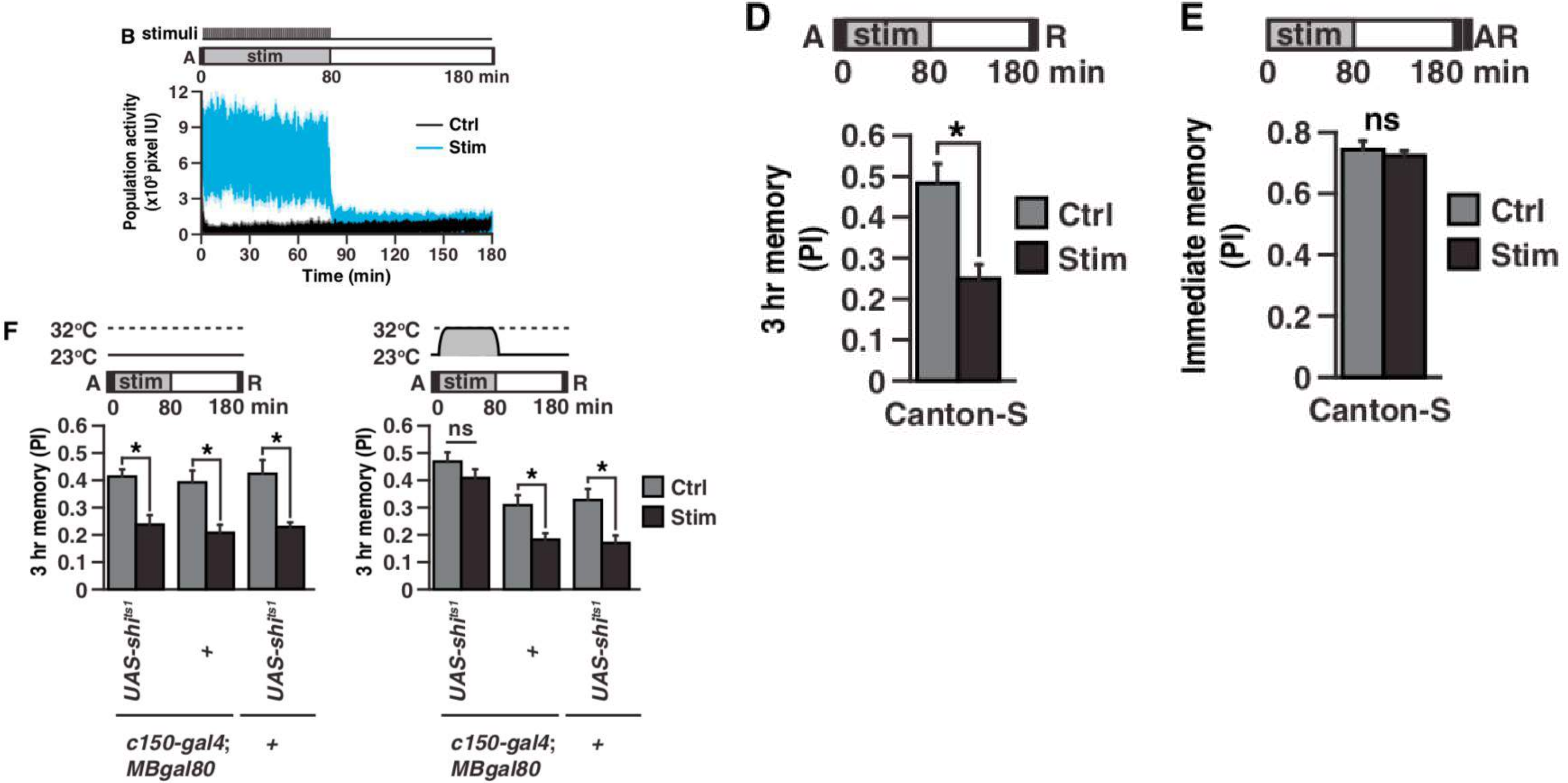
Increased sleep and reduced arousal after learning reduces DAN-mediated forgetting.



DAN-mediated forgetting is downstream of sleep networks.



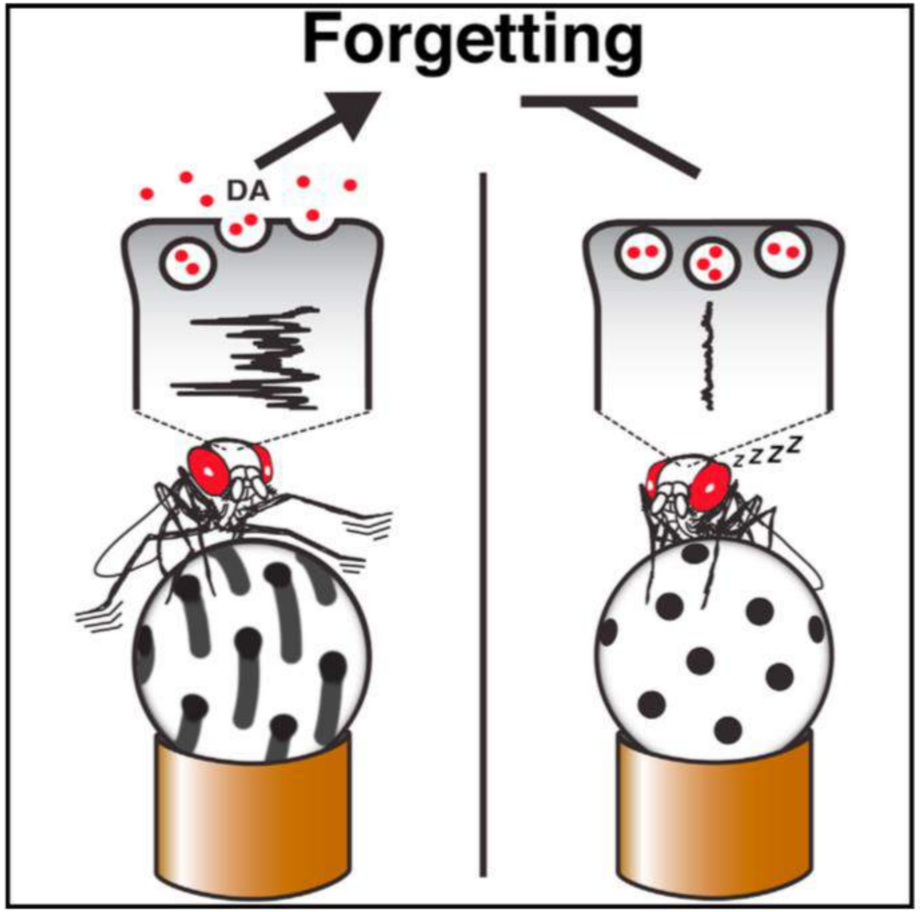
Mechanical stimuli increase population activity after learning and induce forgetting through the DAN forgetting pathway



Cell

Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgetting

Graphical Abstract



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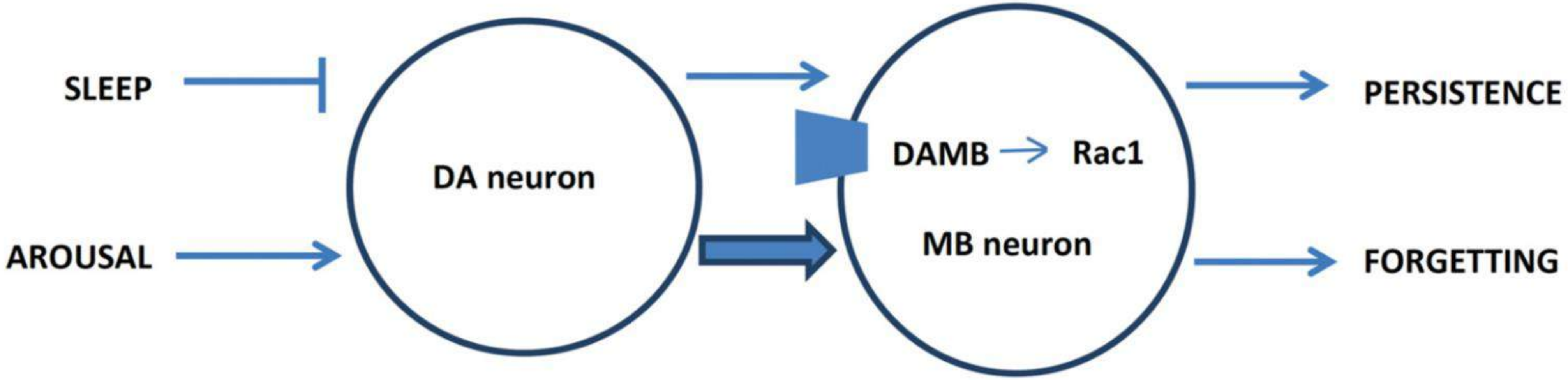
In Brief

Sleep is generally thought to stabilize new memories, but early psychology studies suggest that it prevents new learning from interfering with old memories. This study shows that sleep suppresses the activity of dopamine neurons that promote active forgetting of olfactory memories in flies, providing integration between neuroscience and psychology research.

Forgetting is an active, biologically regulated process.

Aversive and appetitive memories. Timescale in hours after training.



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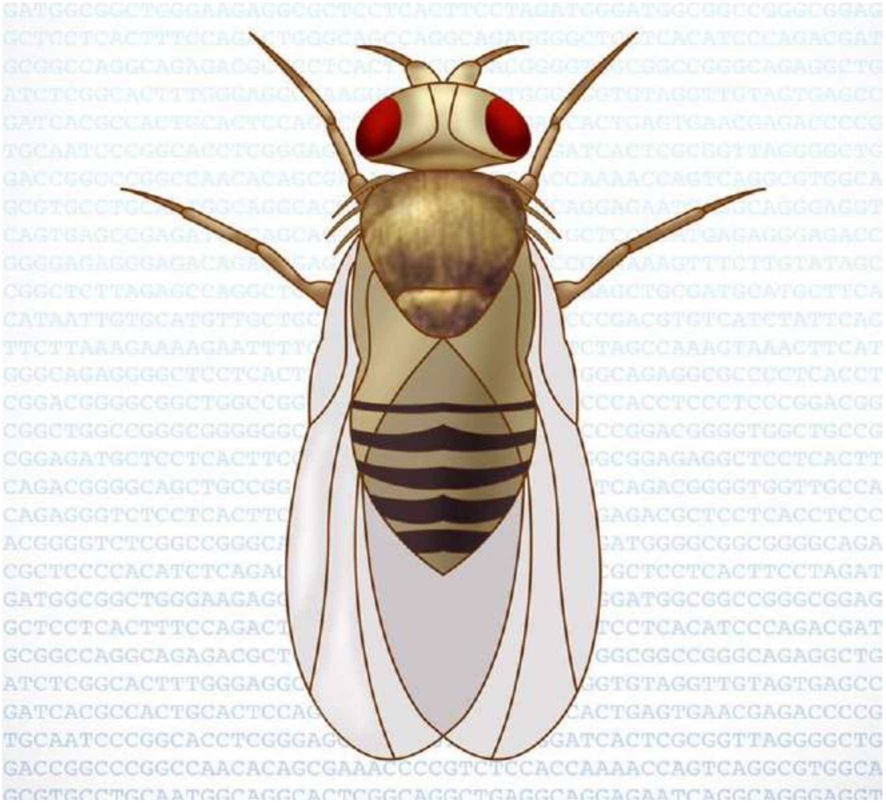
[2] Liu, Y. et al. 2016. Hippocampal Activation of Rac1 Regulates the Forgetting of Object Recognition Memory. Current Biology. 26, 17 (2016), 2351–2357.

[3] Liu, Y. et al. 2018. Social Isolation Induces Rac1-Dependent Forgetting of Social Memory.Cell Reports. 25, 2 (2018), 288–295.e3.

[4] Berry, J. et al. 2012. Dopamine Is Required for Learning and Forgetting in *Drosophila*. Neuron. 74, 3 (2012), 530–542.

[5] Cervantes-Sandoval, I. et al. 2016. Scribble Scaffolds a Signalosome for Active Forgetting.Neuron. 90, 6 (2016), 1230–1242.

[6] Berry, J. et al. 2015. Sleep Facilitates Memory by Blocking Dopamine Neuron-Mediated Forgetting. Cell. 161, 7 (2015), 1656–1667.



THANKS