The research route of David Anderson on social behavior

赵环

蒋昕钰

朱寰

2020-11-12

David Anderson

For the first 20+ years of his career, Anderson's research focused on the biology of neural crest stem cells. Beginning in the early part of the last decade, Anderson gradually switched his research focus from neural development to the study of neural circuits underlying innate behaviors that are associated with emotional states.

- Establish the setup for social analysis
- Dissecting the brain circuit of social behavior
- How does social experience cast a shadow on other behaviors

Research route on Social behavior

> Nature. 2005 Jul 21;436(7049):395-400. doi: 10.1038/nature03859. Epub 2005 Jun 15.

Male-specific fruitless specifies the neural substrates of Drosophila courtship behaviour

Devanand S Manoli [1], Margit Foss, Adriana Villella, Barbara J Taylor, Jeffrey C Hall, Bruce S Baker

> Nat Neurosci. 2006 Dec;9(12):1469-71. doi: 10.1038/nn1809. Epub 2006 Nov 19.

fruitless regulates aggression and dominance in Drosophila

Eleftheria Vrontou [1], Steven P Nilsen, Ebru Demir, Edward A Kravitz, Barry J Dickson

> Curr Biol. 2008 Feb 12;18(3):159-67. doi: 10.1016/j.cub.2007.12.052. Epub 2008 Jan 31.

Octopamine in male aggression of Drosophila

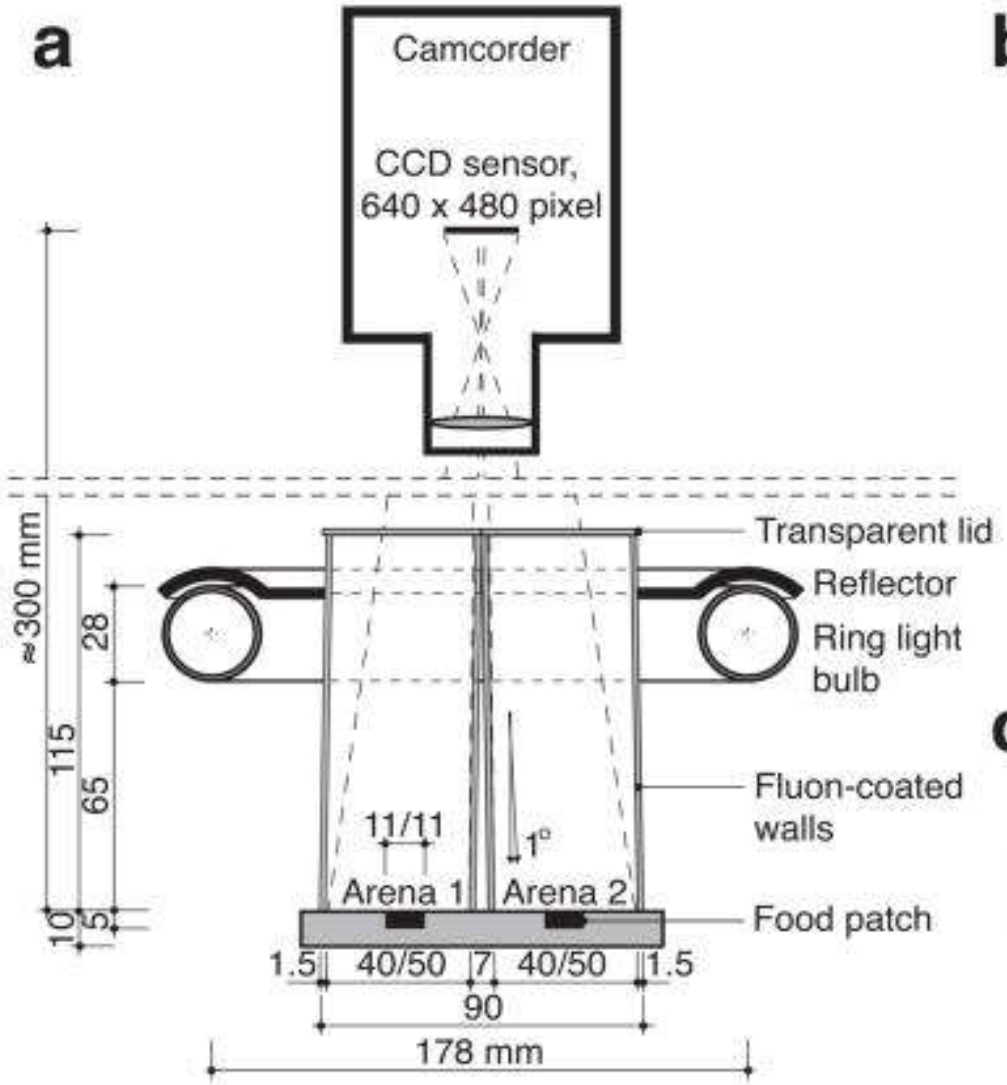
Susanne C Hoyer [1], Andreas Eckart, Anthony Herrel, Troy Zars, Susanne A Fischer, Shannon L Hardie, Martin Heisenberg

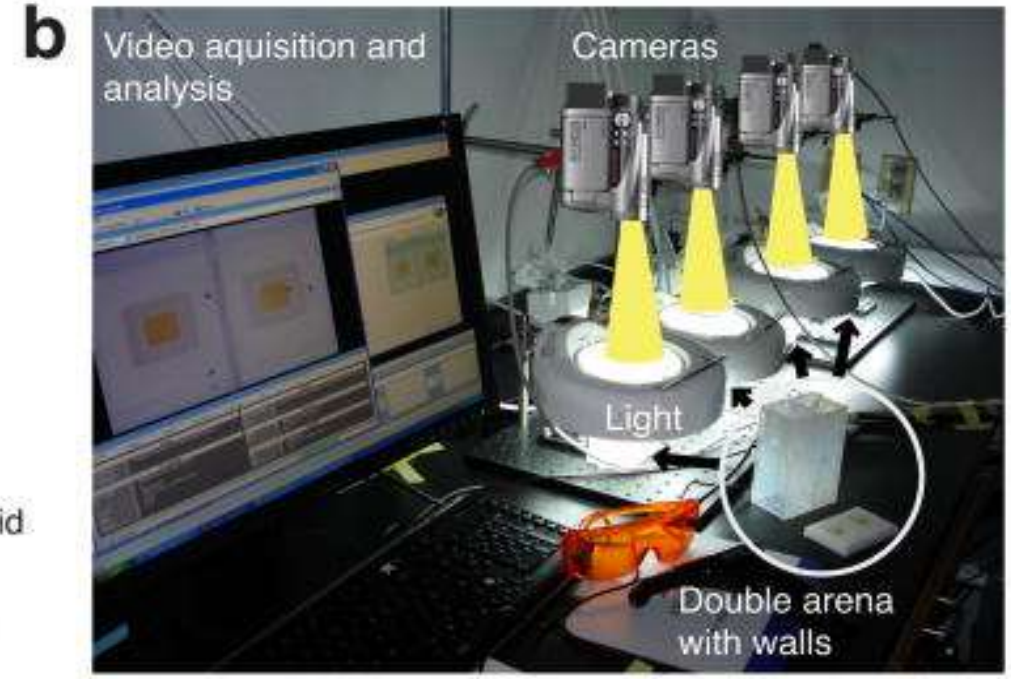
657-63. doi: 10.1073/pnas.0801327105.

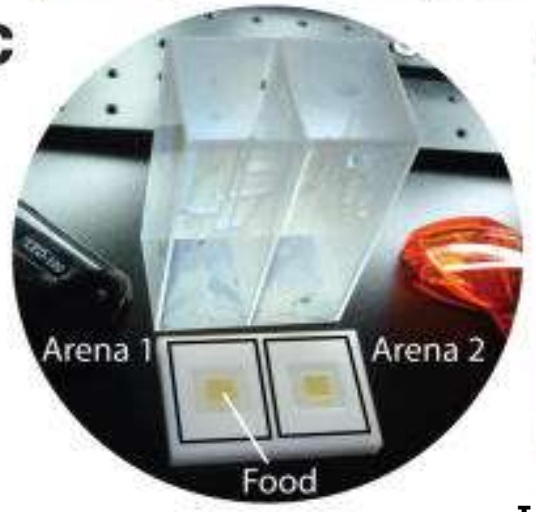
A common genetic target for environmental and heritable influences on aggressiveness in Drosophila

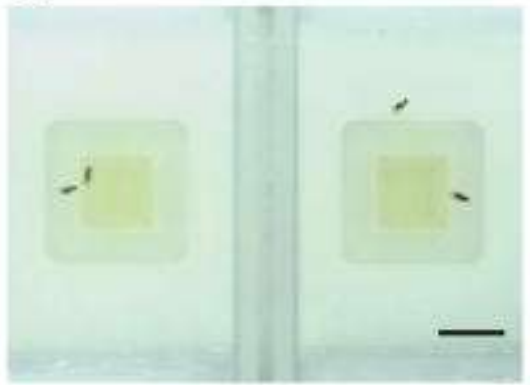
Liming Wang [1], Heiko Dankert, Pietro Perona, David J Anderson

Imaging setup for genetic screens in *Drosophila*



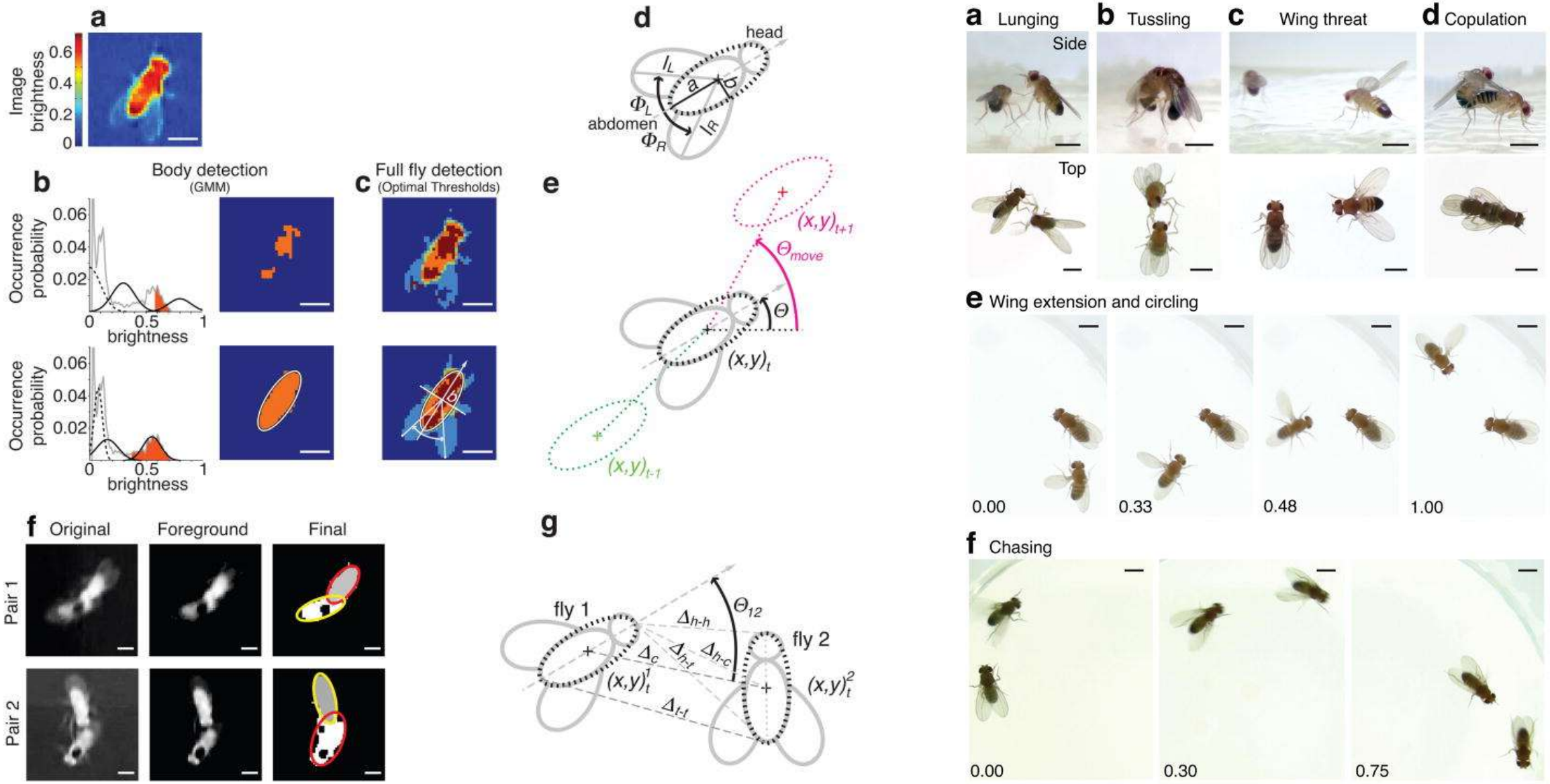






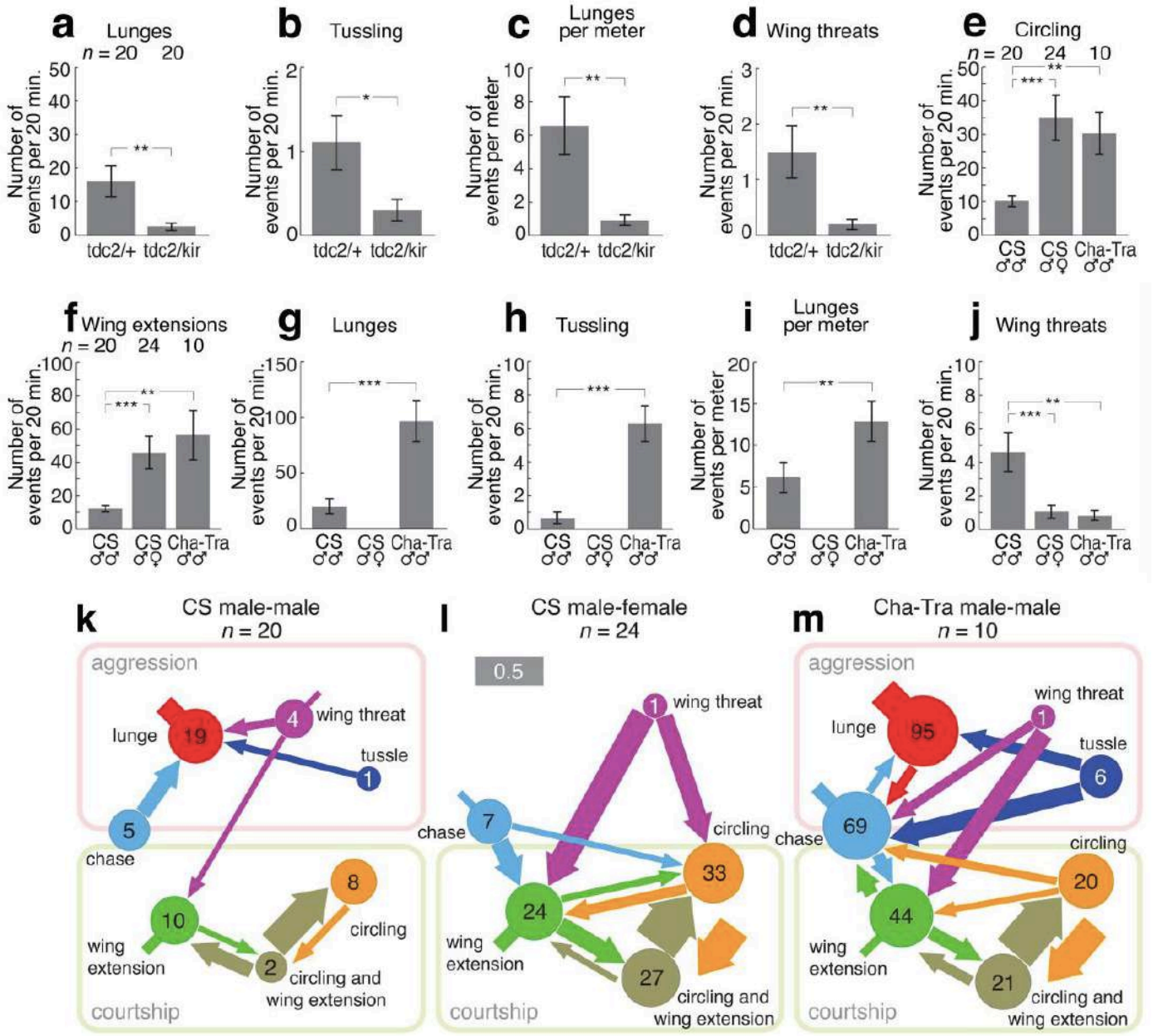
Heiko Dankert et al.2009

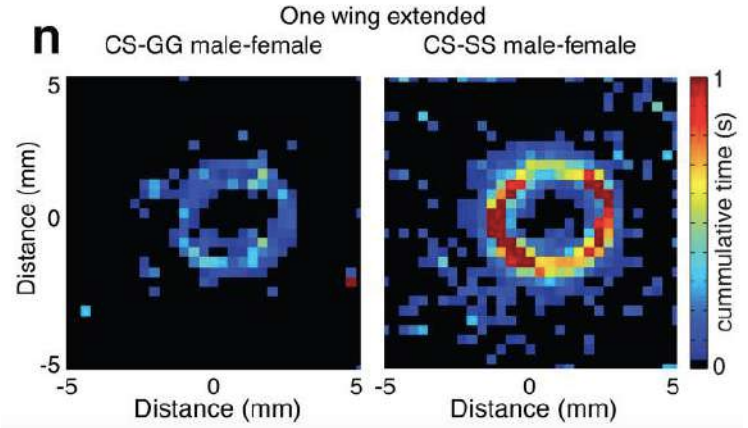
CADABRA software processing

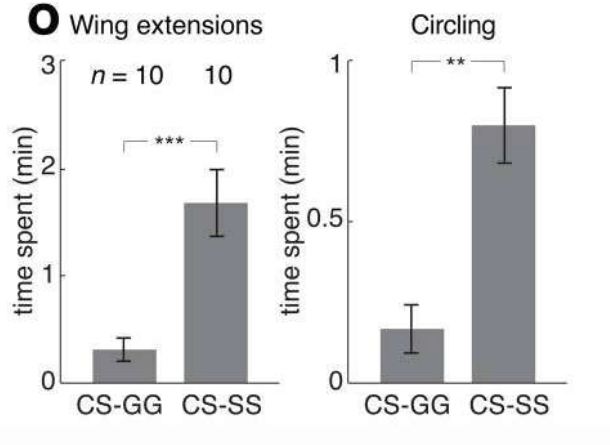


Heiko Dankert et al.2009

CADABRA software output



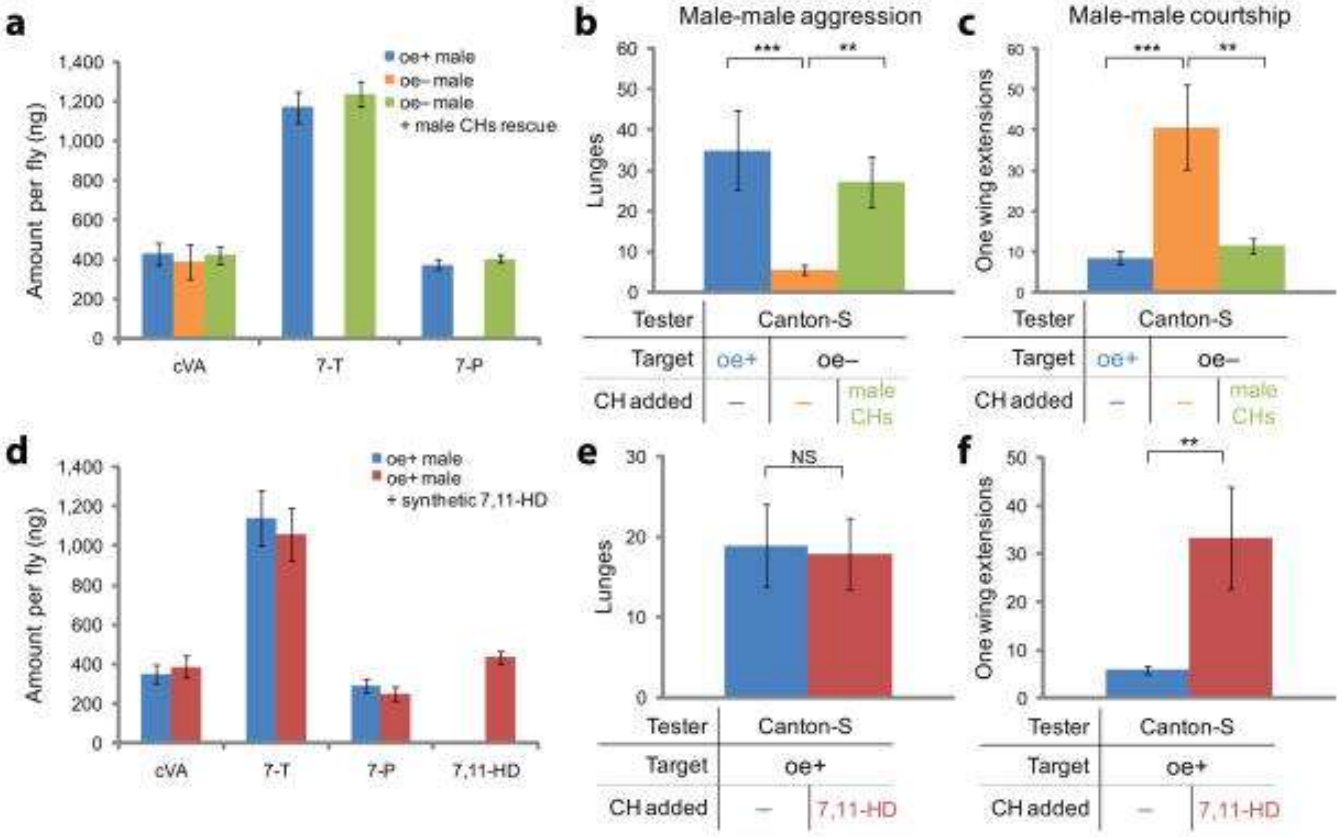




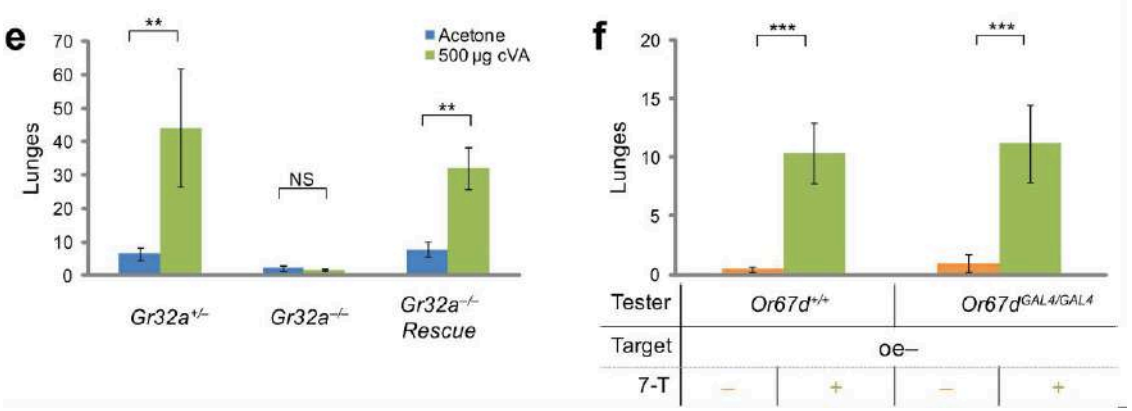
Heiko Dankert et al.2009

Hierarchical chemosensory regulation of male-male social interactions in *Drosophila*

Liming Wang,[1,*] Xiaoqing Han,[1,2] Jennifer Mehren,[3] Makoto Hiroi,[4] Jean-Christophe Billeter,[5] Tetsuya Miyamoto,[6] Hubert Amrein,[6] Joel D. Levine,[5] and David J. Anderson[1,2,*]



The reciprocal effects of CHs on male-male aggression vs. male-male courtship therefore reflect parallel, direct influences of such pheromones on these two social behaviors.



the aggression-promoting effect of cVA is dependent upon signaling through 7-T/Gr32a, but not vice versa, suggesting a hierarchical interaction between the gustatory and olfactory systems in regulating aggression

Genetics. 2017 Aug; 206(4): 1969–1984.
Published online 2017 May 26. doi: 10.1534/genetics.117.200642
PMCID: PMC5560801
PMID: 28550016

Genomic Analysis of Genotype-by-Social Environment Interaction for *Drosophila melanogaster* Aggressive Behavior

Palle Duun Rohde,[*††‡,1] Bryn Gaertner,[§**††] Kirsty Ward,[§**††] Peter Sørensen,[*] and Trudy F. C. Mackay[§**††]

Neuron. Author manuscript; available in PMC 2018 Aug 30.
Published in final edited form as:
Neuron. 2017 Aug 30; 95(5): 1112–1128.e7.
doi: 10.1016/j.neuron.2017.08.017
PMCID: PMC5588916
NIHMSID: NIHMS899874
PMID: 28858617

A circuit node that integrates convergent input from neuromodulatory and social behavior-promoting neurons to control aggression in *Drosophila*

Kiichi Watanabe,[1,2] Hui Chiu,[1,2] Barret D. Pfeiffer,[2,3,4] Allan Wong,[2,4] Eric D. Hoopfer,[1] Gerald M. Rubin,[4] and David J. Anderson[1,2,5,*]

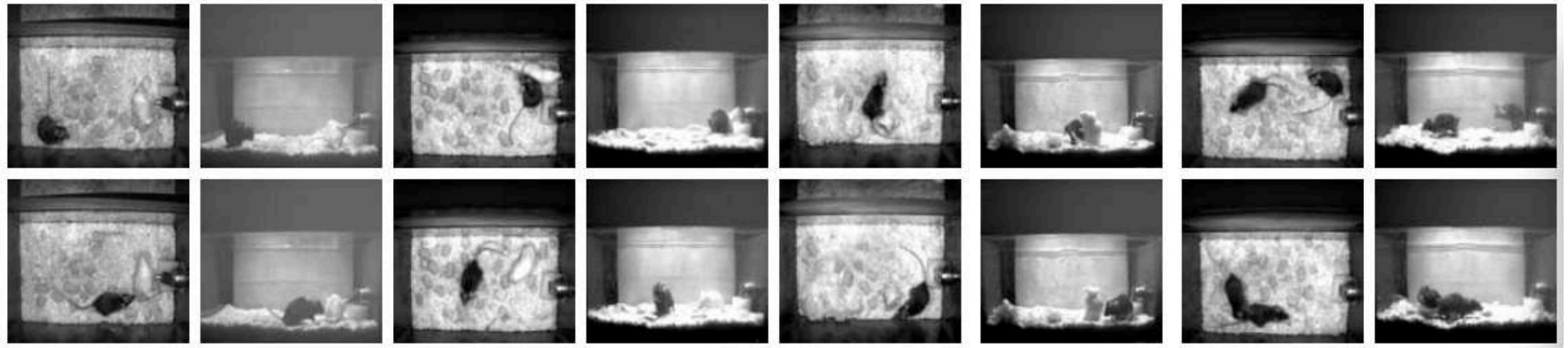
Mol Brain. 2019; 12: 1.
Published online 2019 Jan 3. doi: 10.1186/s13041-018-0417-0
PMCID: PMC6318936
PMID: 30606245

The *peacefulness* gene promotes aggression in *Drosophila*

Mahmoudreza Ramin,[1,2] Yueyang Li,[1] Wen-Tzu Chang,[1] Hunter Shaw,[1] and Yong Rao[✉1,2,3,4]

Social behavior recognition in continuous video

Xavier P. Burgos-Artizzu*, Piotr Dollár†, Dayu Lin+, David J. Anderson*, Pietro Perona*
*California Institute of Technology, †Microsoft Research, Redmond, +NYU Medical Center

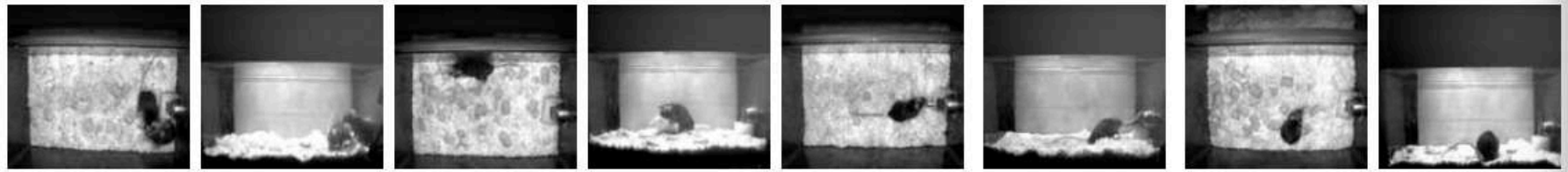


Approach intruder
p=3.4%, $\mu = 1.2, \sigma = 0.5$

Walk away from intruder
p=3.3%, $\mu = 1.6, \sigma = 0.6$

Circle around intruder
p=0.3%, $\mu = 2.4, \sigma = 2.5$

Chase intruder
p=1.0%, $\mu = 0.8, \sigma = 0.3$



Attacks intruder
(p=3.4%, $\mu = 2.3, \sigma = 17.4$

Copulation, courts intruder
p=4.2%, $\mu = 3.2, \sigma = 40.5$

Drink
p=0.3%, $\mu = 4.0, \sigma = 30.2$

Eat
p=1.6%, $\mu = 9.5, \sigma = 104$

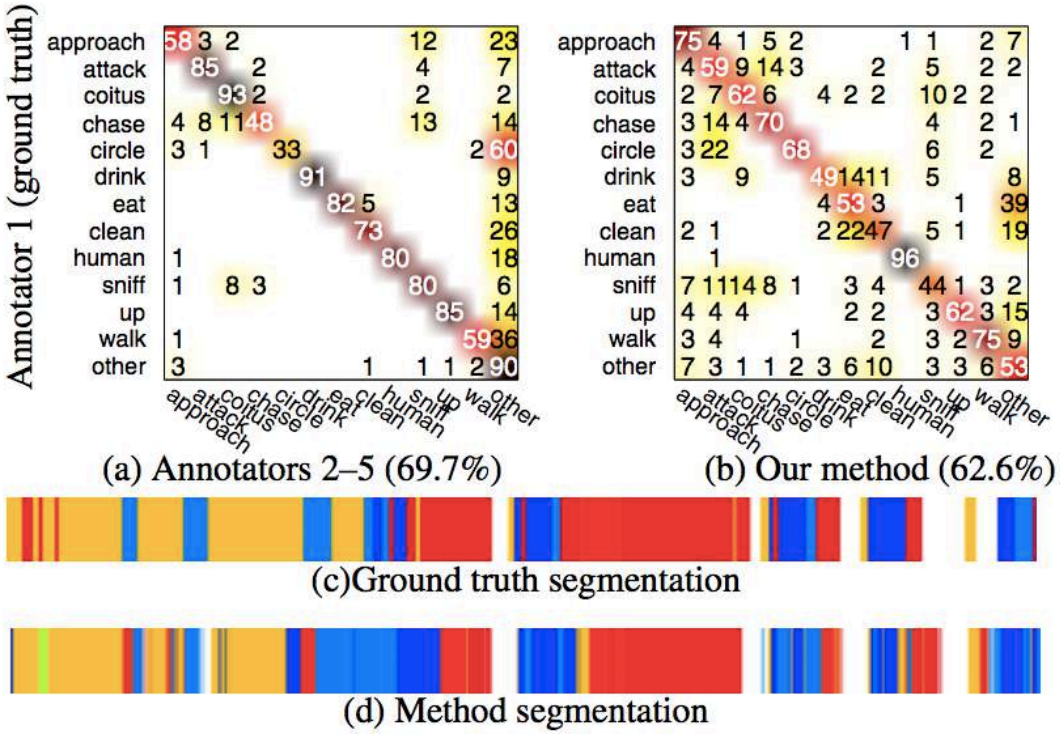
Clean, grooms itself
p=7.6%, $\mu = 2.6, \sigma = 25.4$

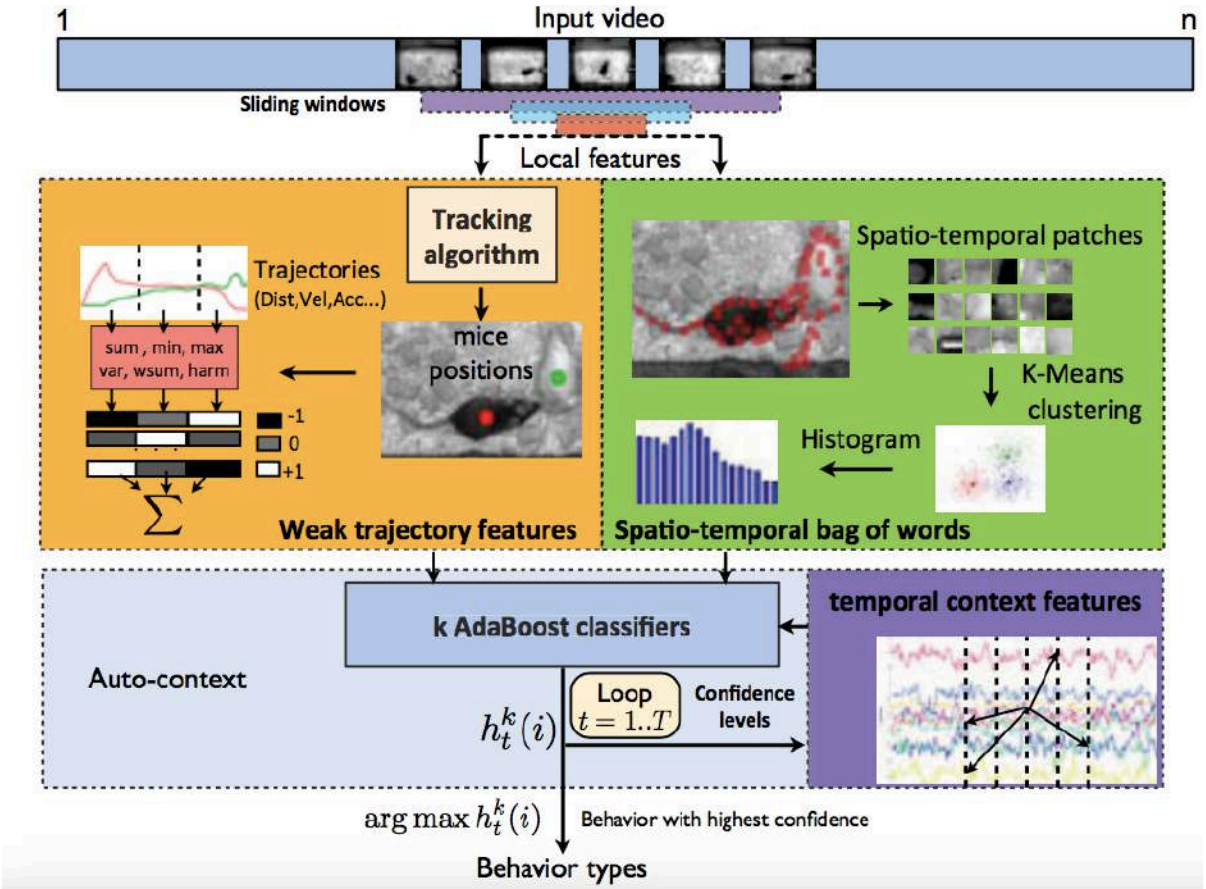
Human intervenes
p=1.2%, $\mu = 3.5, \sigma = 10.5$

Sniff any body part of intruder
p=14.4%, $\mu = 2.7, \sigma = 27.7$

Up Stands in its back legs
p=3.8%, $\mu = 2.1, \sigma = 12.0$

Comparison between ‘annotator1’ and the output of CRIM13





Xavier P. Burgos-Artizzu et al. 2012

Overview

Social and emotional neuroscience

Editorial overview

Ralph Adolphs and David Anderson

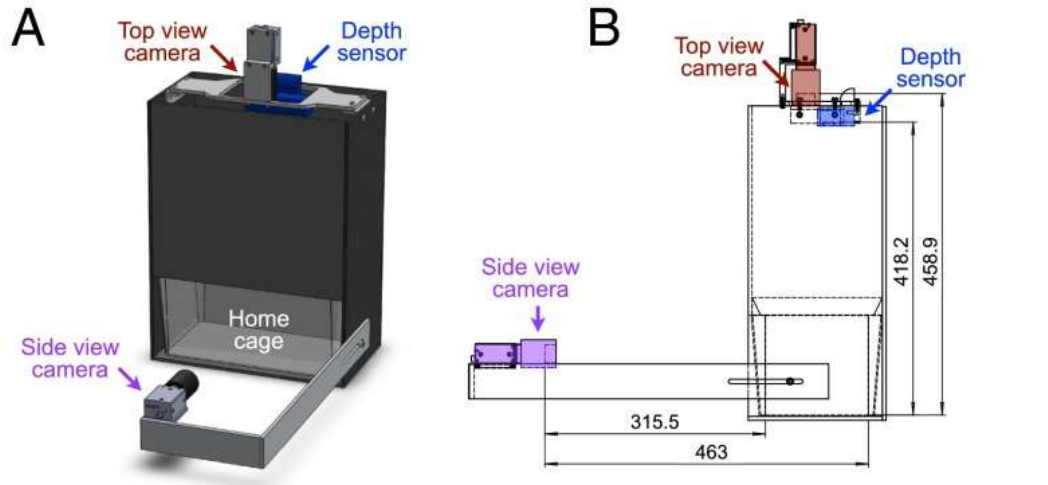
Current Opinion in Neurobiology 2013, **23**:291–293

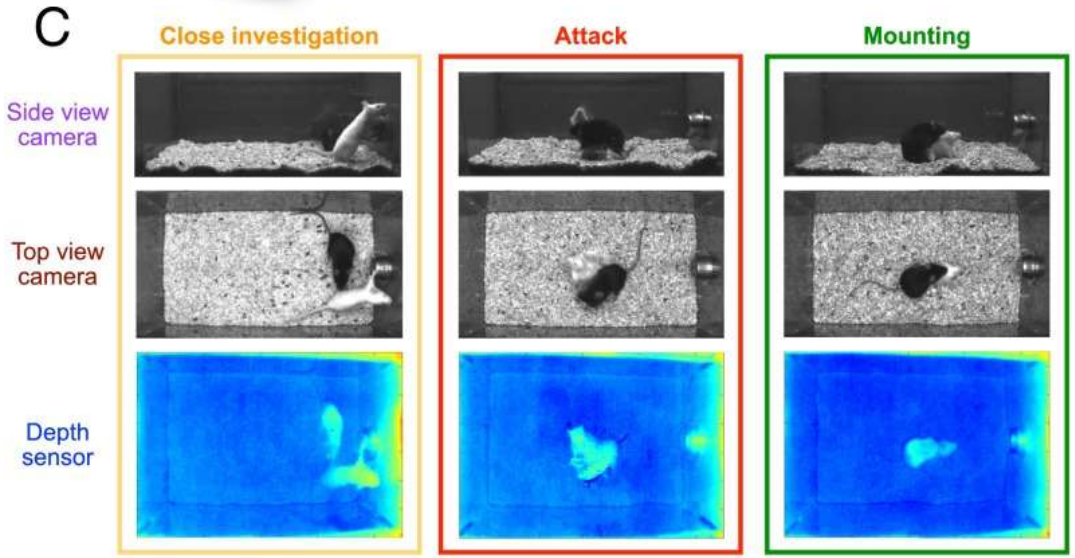
For a complete overview see the Issue

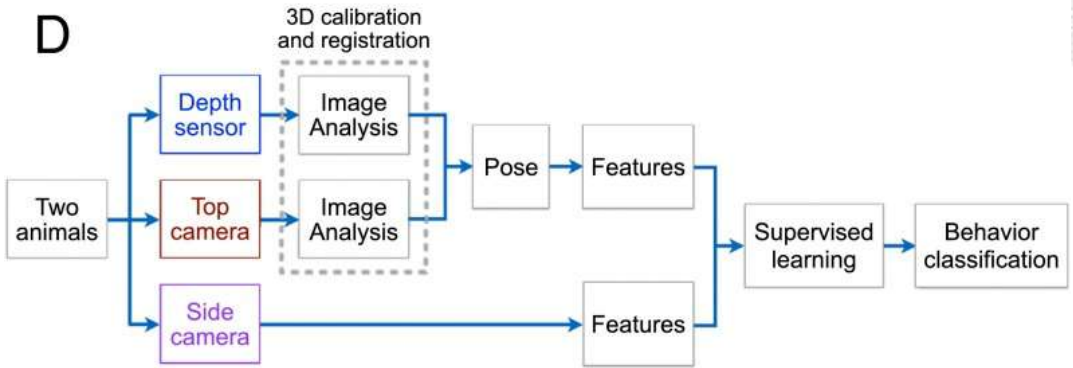
Available online 10th May 2013

http://dx.doi.org/10.1016/j.conb.2013.04.011

- Impairments in social behavior and emotion feature prominently in essentially every psychiatric disorder
- the different ecology of chimpanzees as compared to humans has resulted in broadly different styles of processing depth, related to differences in the need and ability for social communication.
- there are surprisingly common mechanisms shared between such high-level social influences on preference- based behavior, and more basic processes related to reward and punishment processing.







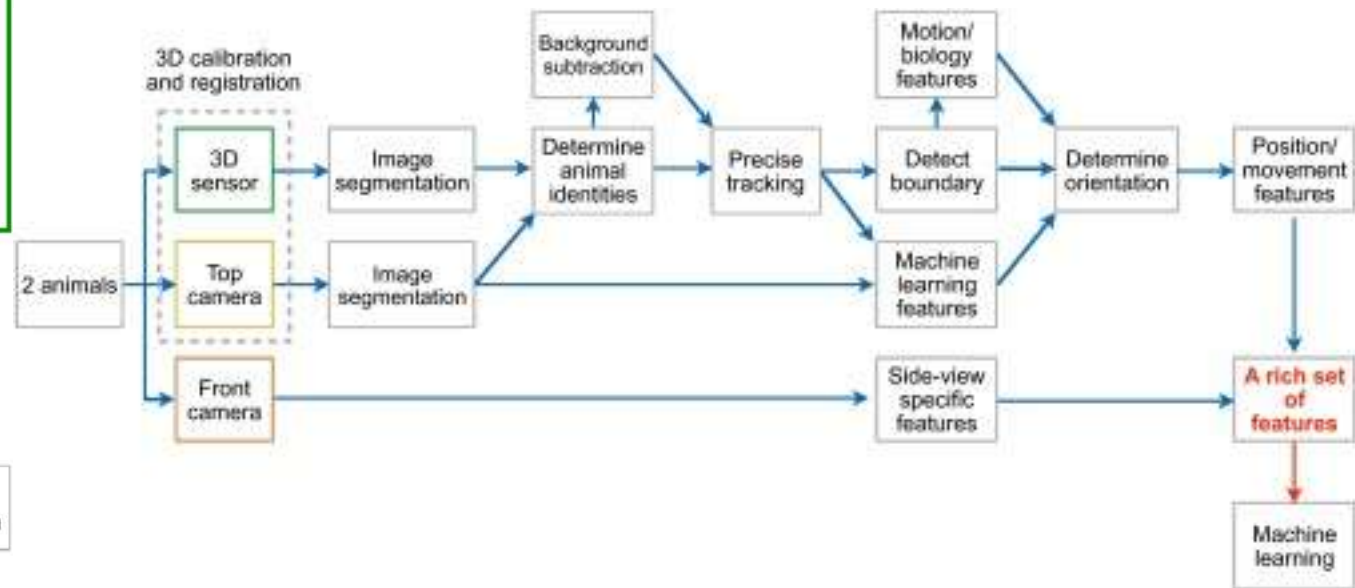
This Article | Info for Authors | Subscribe | About
PNAS
Proceedings of the National Academy of Sciences of the United States of America

Proc Natl Acad Sci U S A. 2015 Sep 22; 112(38): E5351–E5360.
Published online 2015 Sep 9. doi: 10.1073/pnas.1515982112
PNAS Plus
Neuroscience

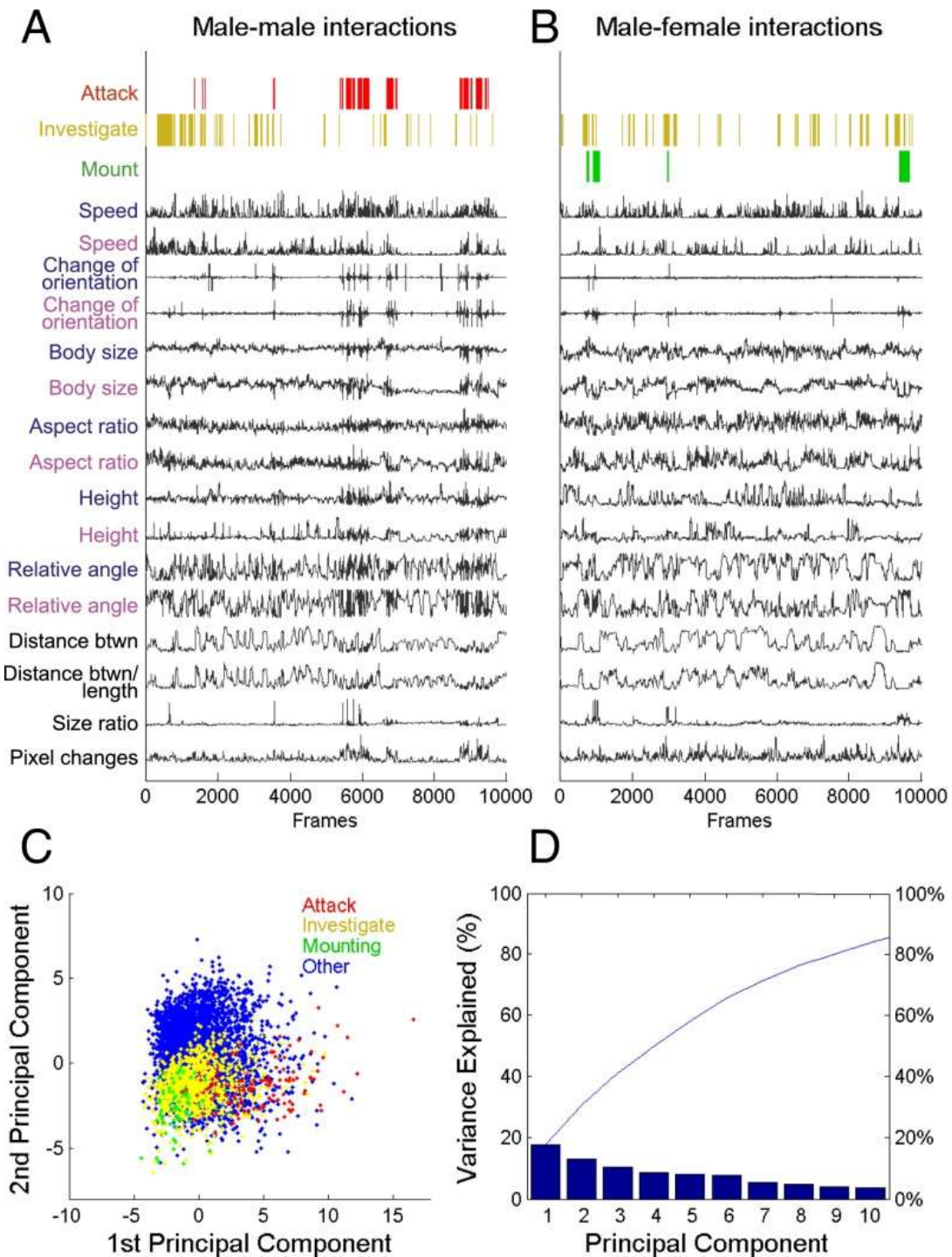
PMCID: PMC4586844
PMID: 26354123

Automated measurement of mouse social behaviors using depth sensing, video tracking, and machine learning

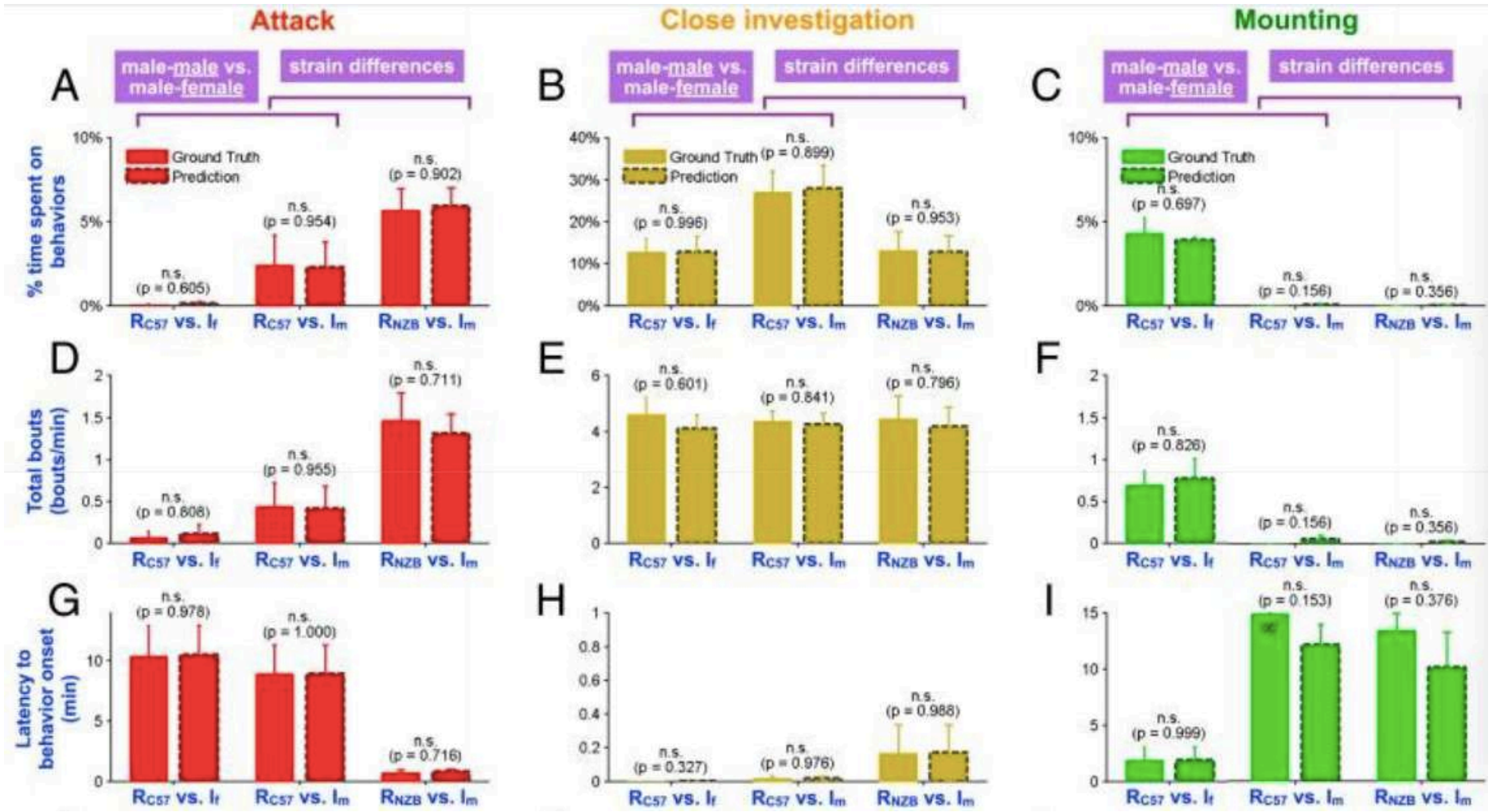
Weizhe Hong,[a,1] Ann Kennedy,[a] Xavier P. Burgos-Artizzu,[b] Moriel Zelikowsky,[a] Santiago G. Navonne,[b] Pietro Perona,[b,1] and David J. Anderson[a,1]



Feature extraction

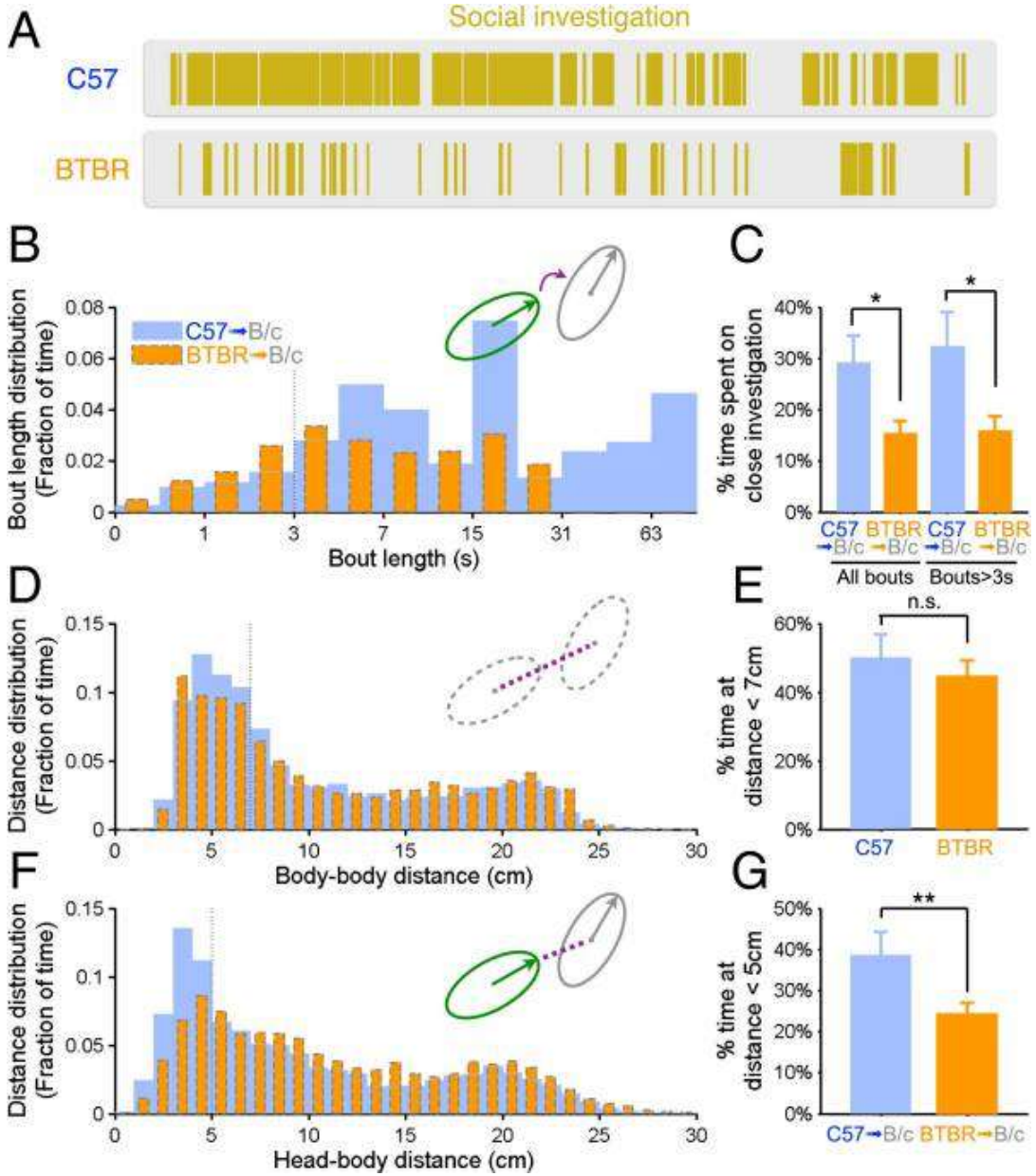


Genetic Influences on Social Behaviors.



Weizhe Hong et al. 2015

Detection of Social Deficits in an Autism Model.



Weizhe Hong et al. 2015

conclusions

- Establish two setups for automated analysis of fly and mice activity
- Put forward an overview perception about social and emotional neuroscience

Dissecting the brain circuit of social behavior

蒋昕钰

2020-11-12

Social interaction among conspecifics

- Aggressive encounter between two males
- Mating encounter between a male and a female

Asocial behaviors

- Self-grooming

How aggression circuits are organized in the brain

and their relationship to circuits for other instinctive social behaviours.

(Lin, Boyle et al. 2011) Nature

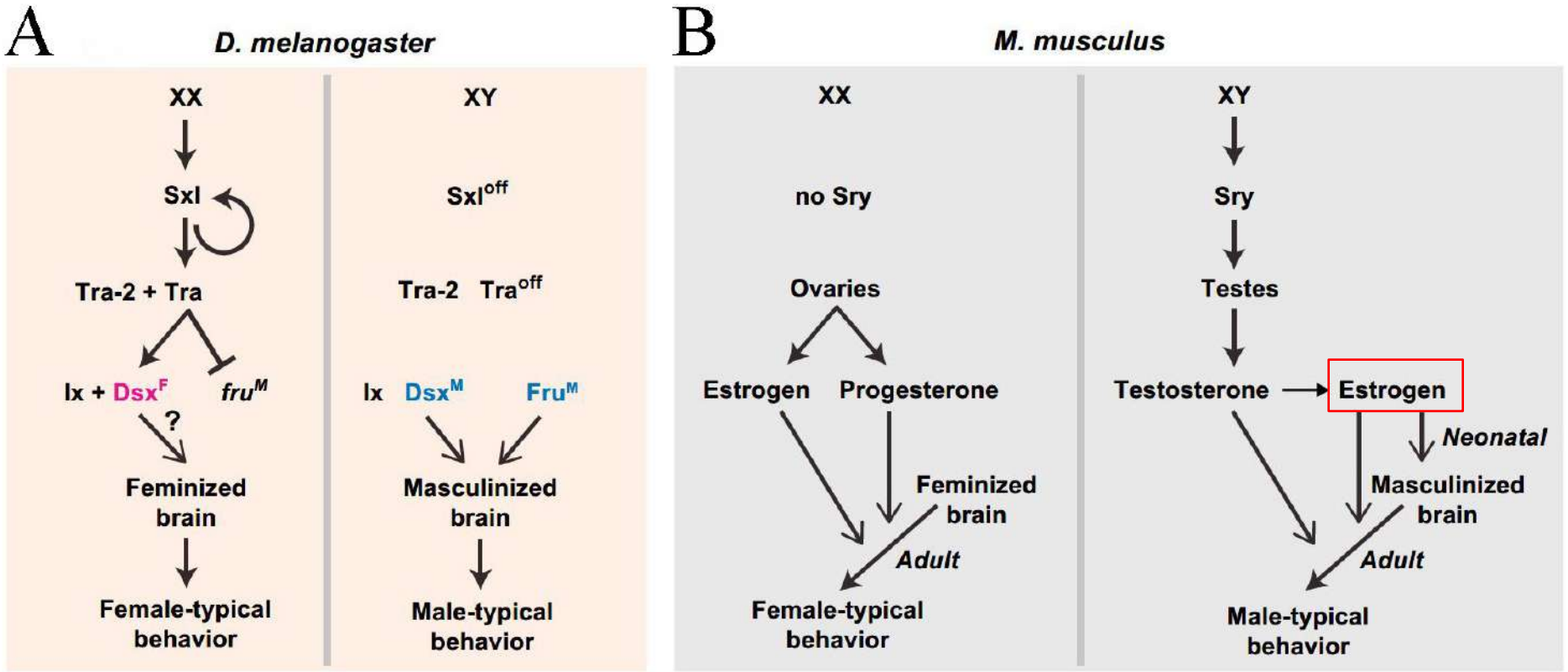
(Lee, Kim et al. 2014) Nature

(Hong, Kim et al. 2014) Cell

(Asahina, Watanabe et al. 2014) Cell

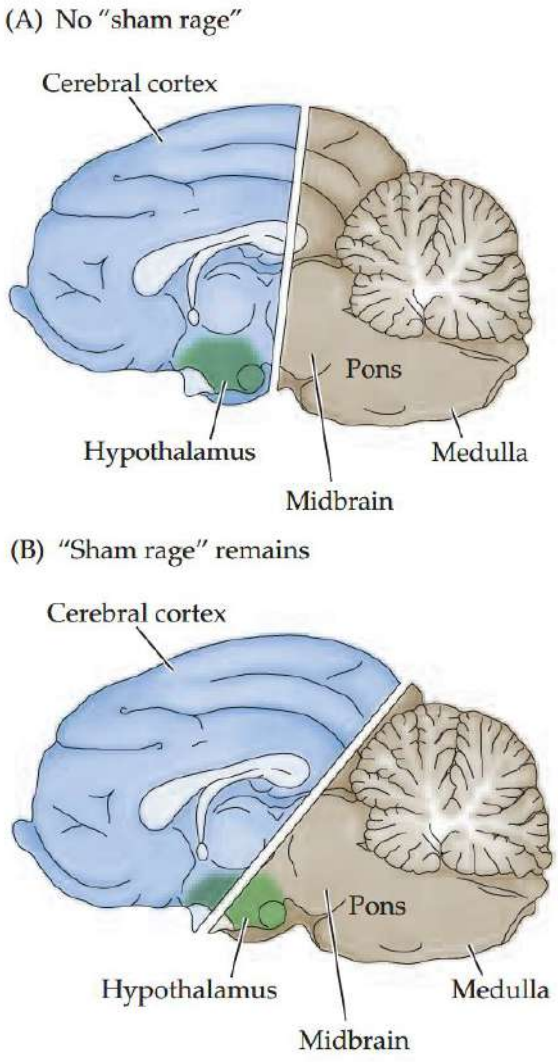
(Hoopfer, Jung et al. 2015) elife

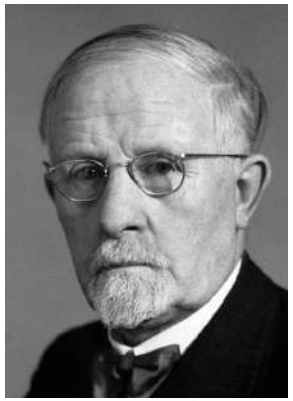
(Watanabe, Chiu et al. 2017) Neuron



The hypothalamus has been proven to be the center of attack behavior

Sham Rage（Bard, 1928）

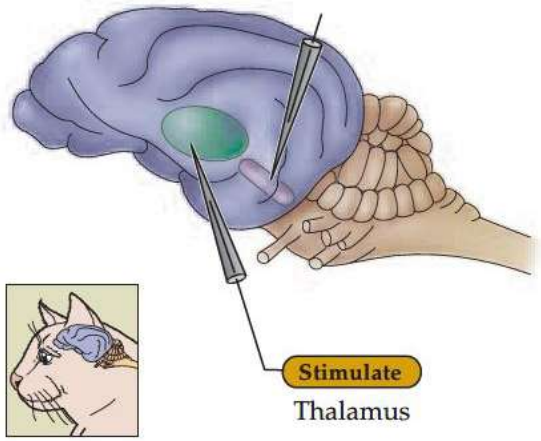




Swiss doctor Hess (1943)

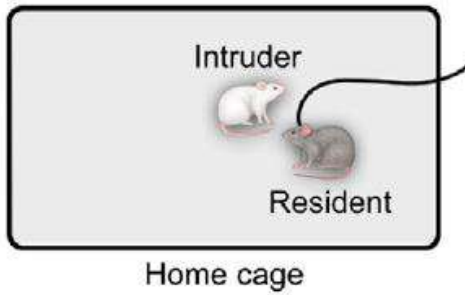
1949年诺贝尔生理或医学奖

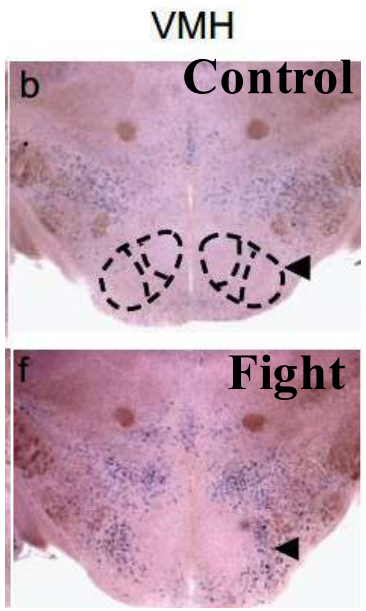
for his discovery of the functional organization of the interbrain [hypothalamus] as a coordinator of the activities of the internal organs



- activation of the neurons should be sufficient to trigger attack
- inhibition of these neurons should impair normal aggression
- these neurons should be active during aggressive encounters

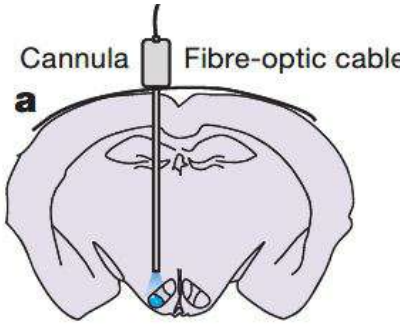
Ventromedial hypothalamus, ventrolateral subdivision is the inter-male aggression locus

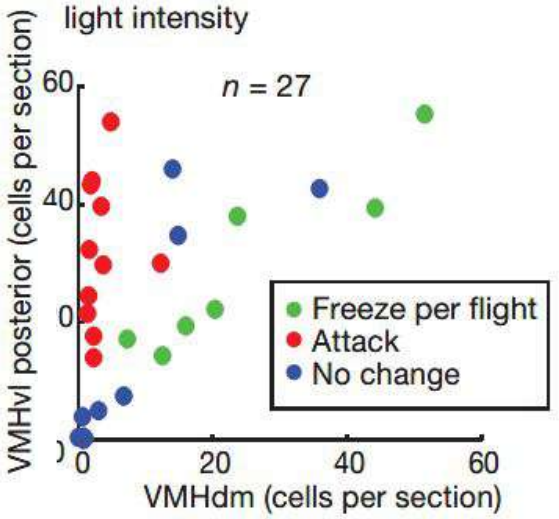




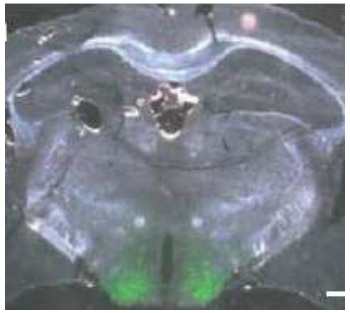
c-fos: a marker of neuronal excitation

Activation

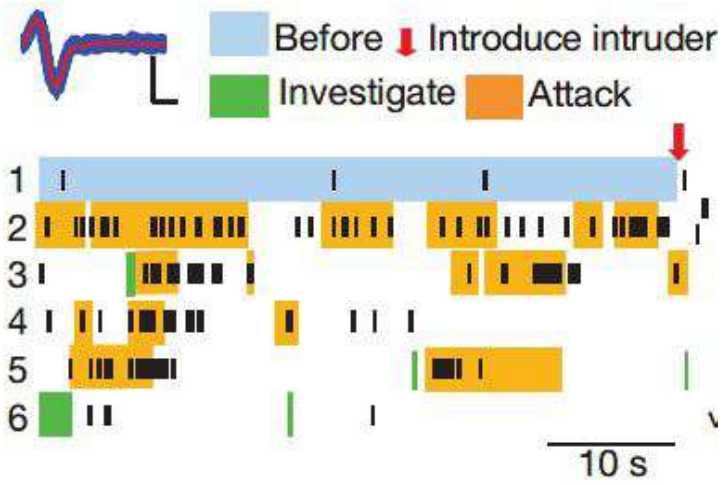


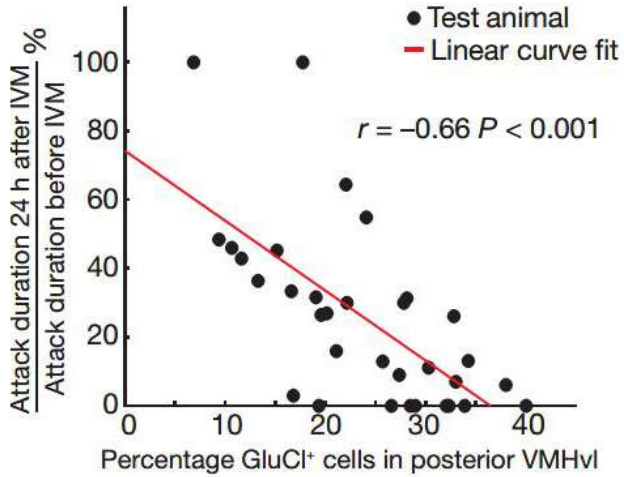


Inactivation



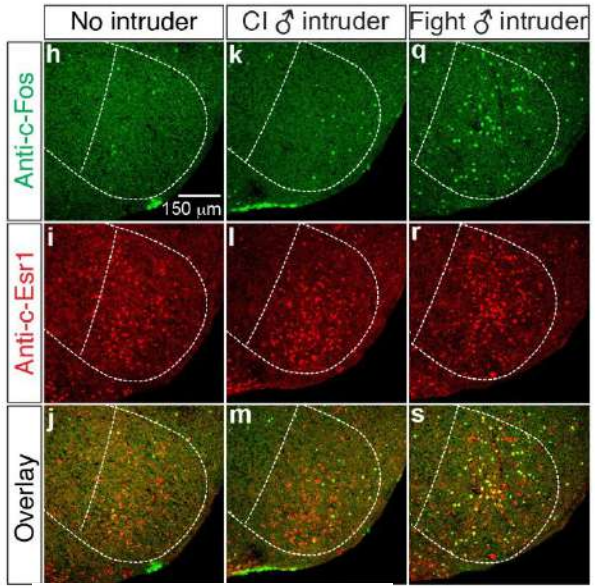
single-unit recordings

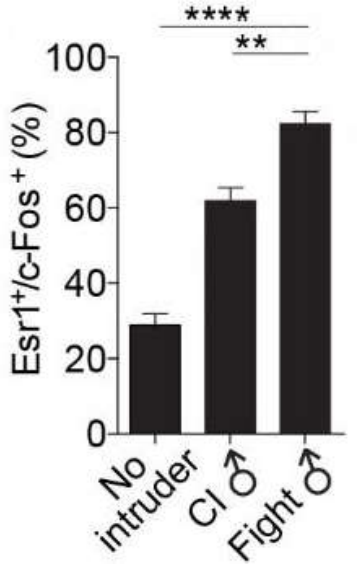




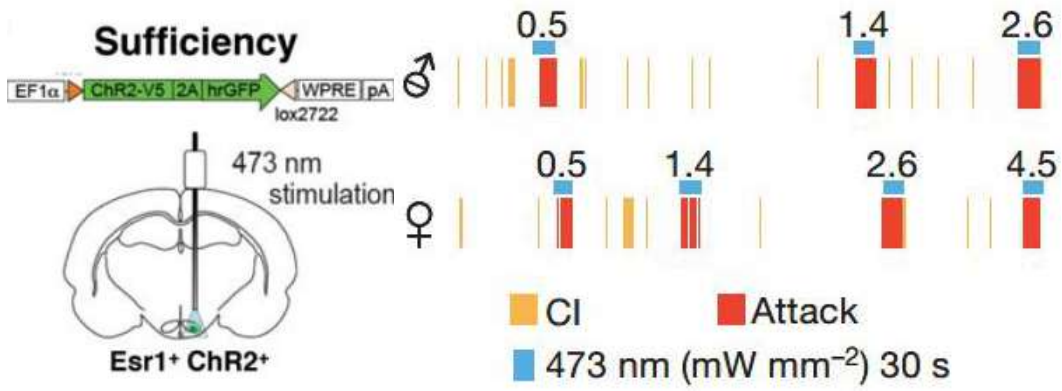
(Lin, Boyle et al. 2011)

VMHvl Esr1^{+} neurons are necessary and sufficient for investigative phase of a social encounter, as well as for attack

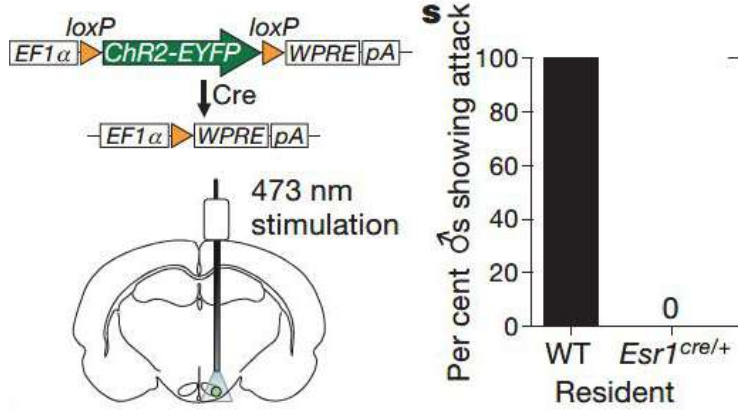




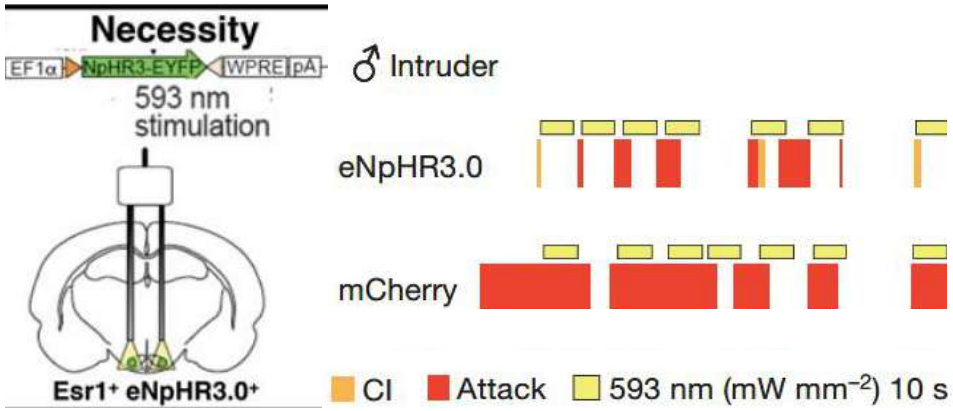
Esr1^{+} neurons Activation



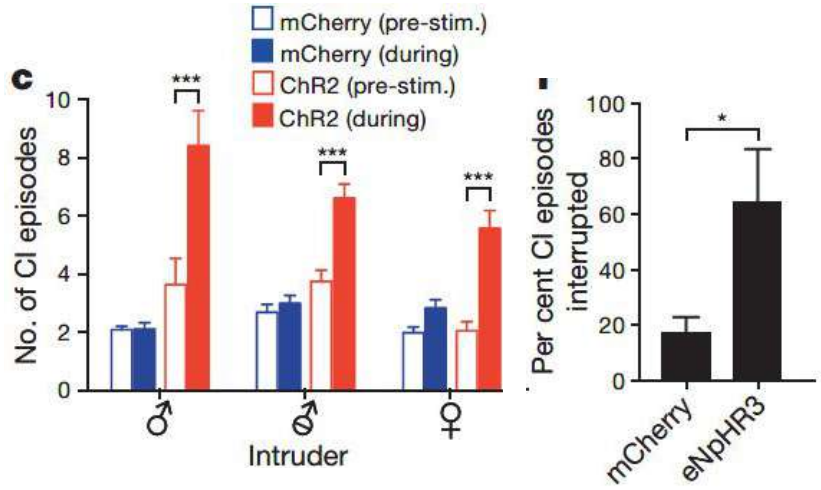
Esr1^{-} neurons Activation



Esr1^{+} neurons Inactivation

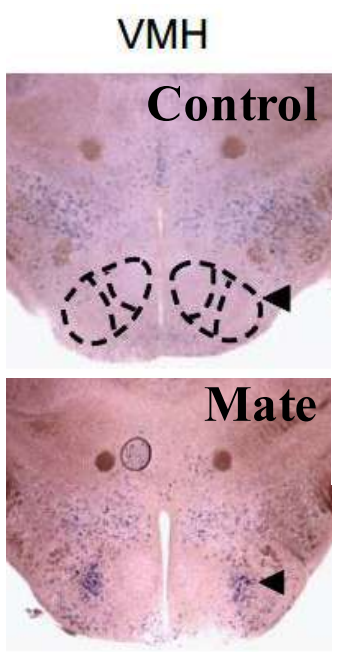


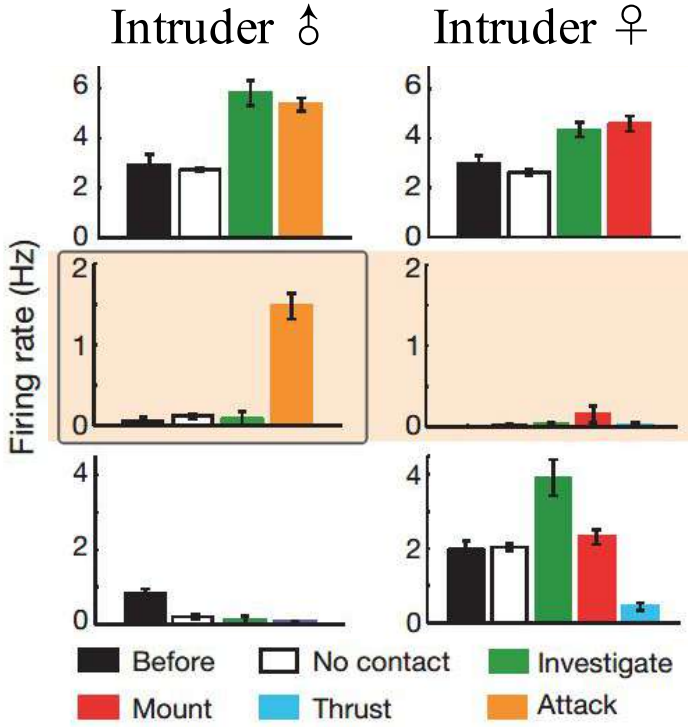
Close Investigation

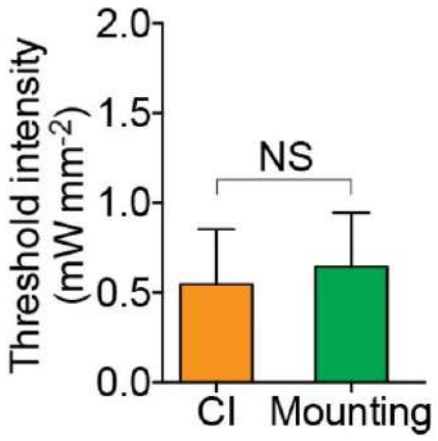


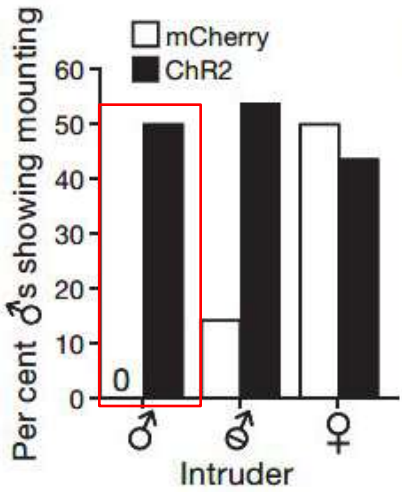
(Lee, Kim et al. 2014)

Scalable control of mate and attack by VMHvl Esr1^{+} neurons

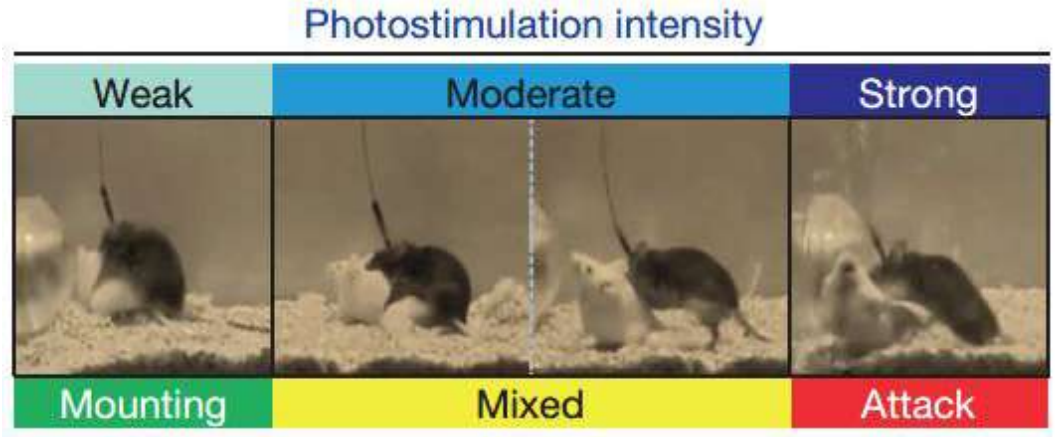


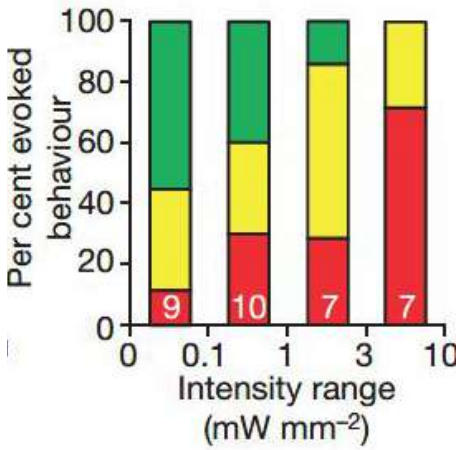




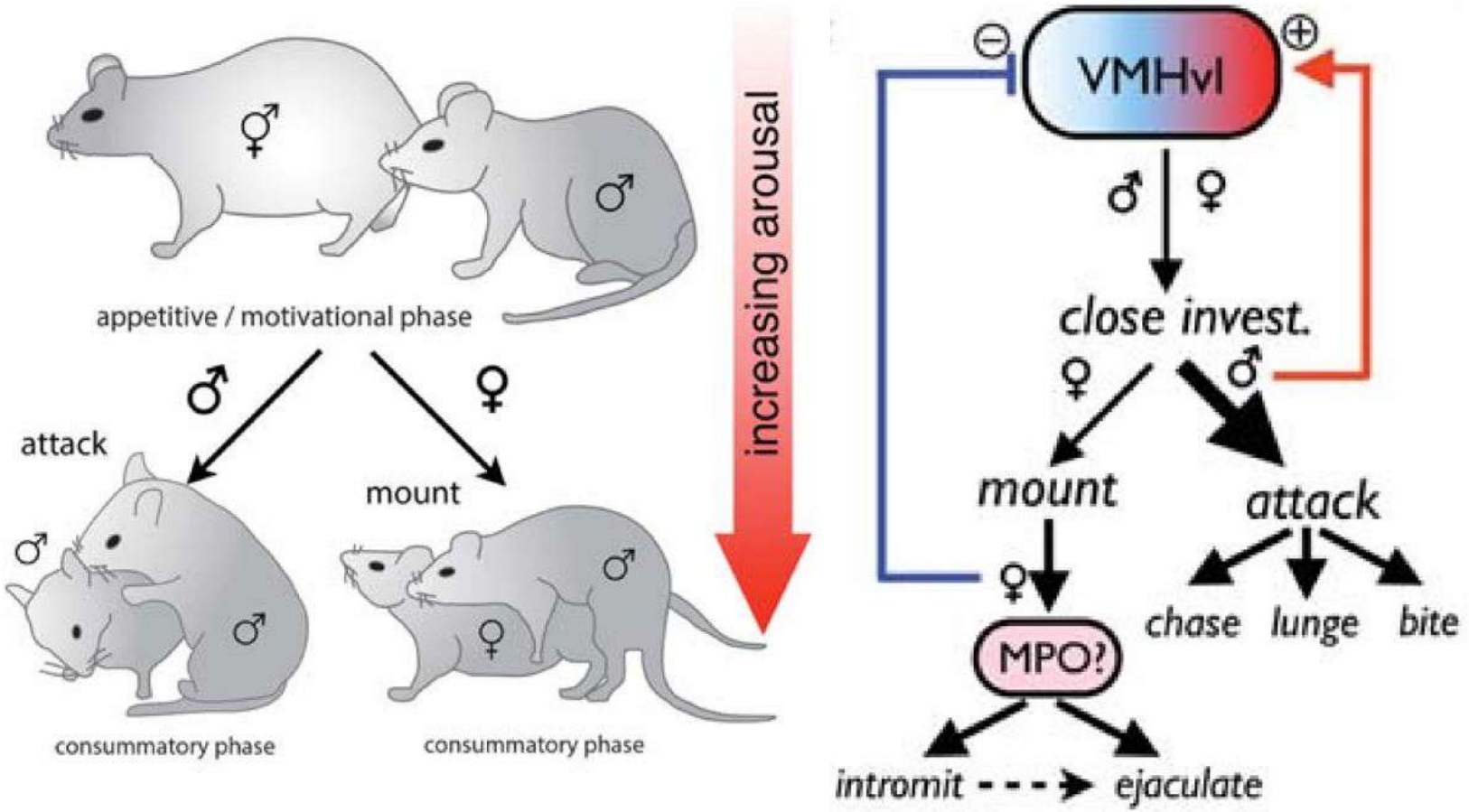


optogenetic inhibition did not interrupt ongoing male–female mounting



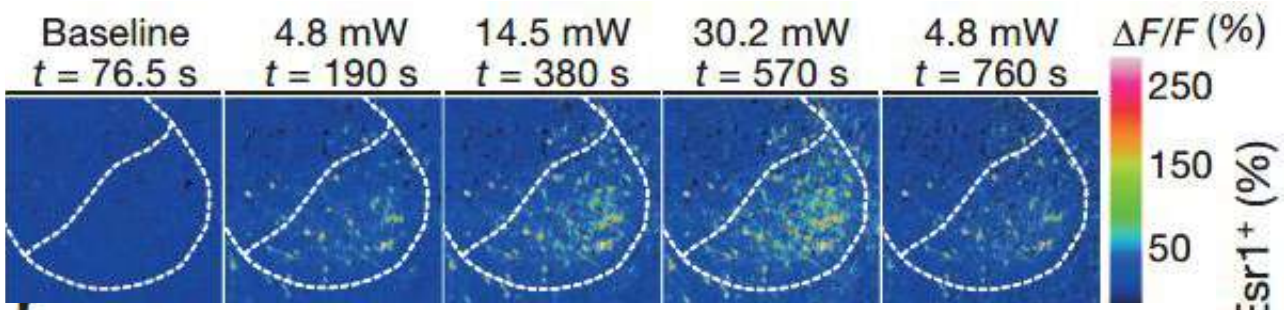


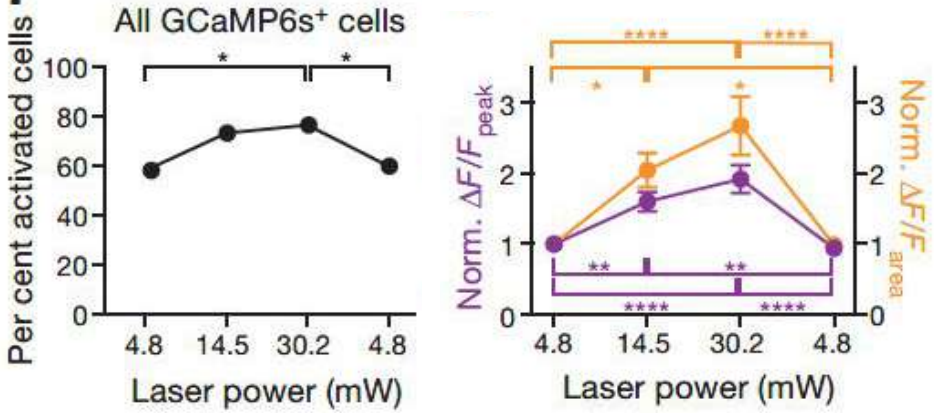
VMHvl control the progression of a social encounter from its appetitive through its consummatory phases, in a scalable manner

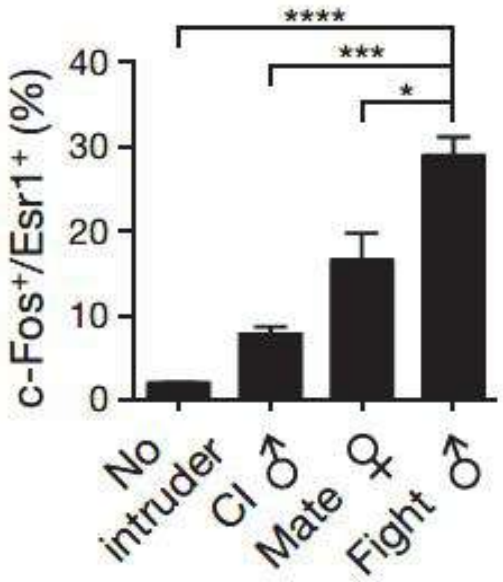


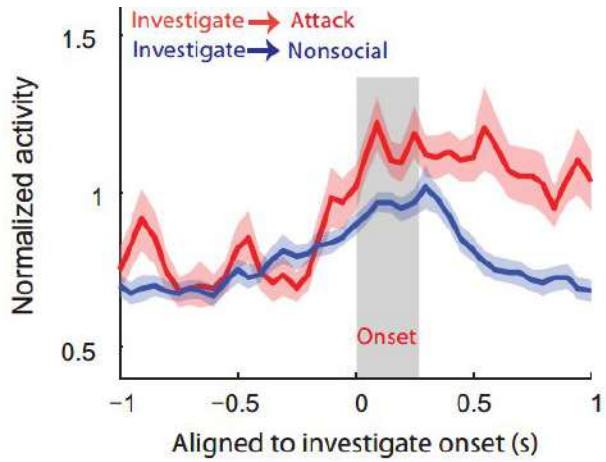
(Kennedy, Asahina et al. 2014)

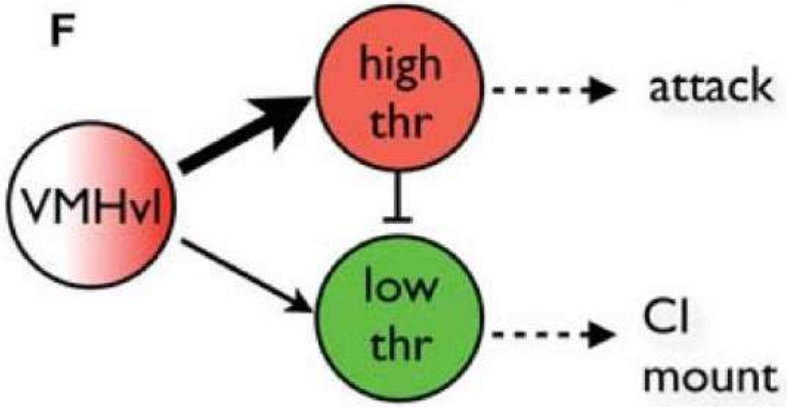
The scalable manner reflects the number or type of active neurons in the population

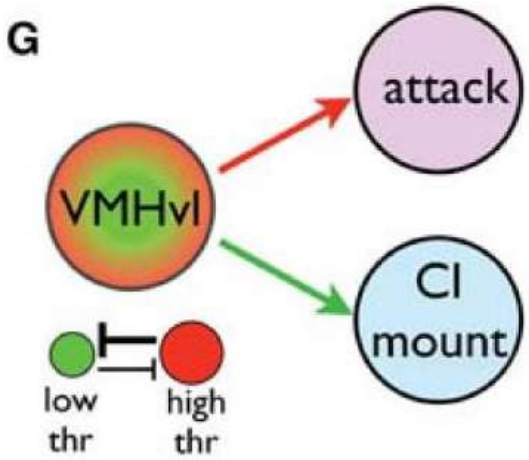




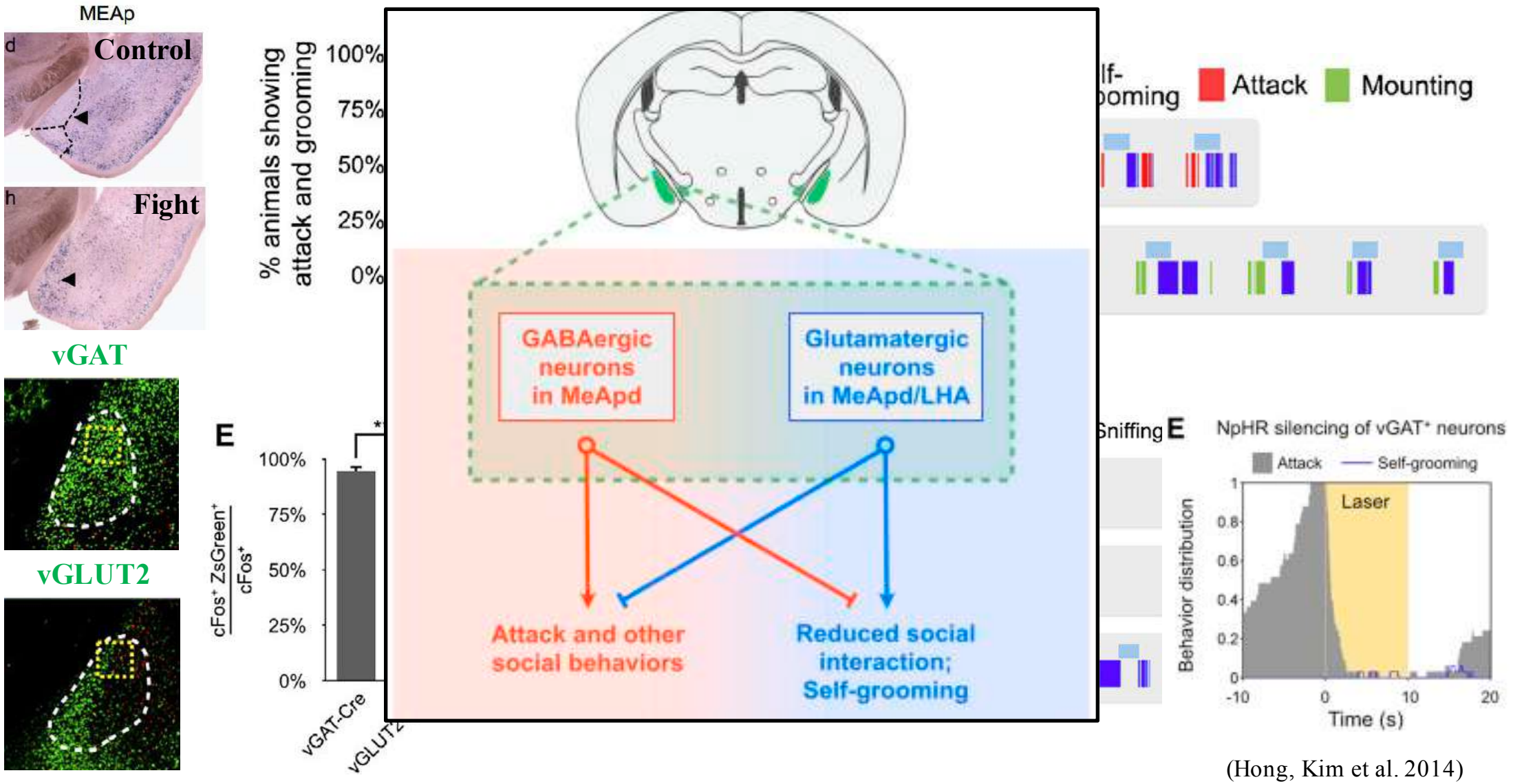








Antagonistic control of social versus asocial behaviors by separable MeA neurons



(Hong, Kim et al. 2014)

(Lin, Boyle et al. 2011) Nature

(Lee, Kim et al. 2014) Nature

(Hong, Kim et al. 2014) Cell

(Asahina, Watanabe et al. 2014) Cell

(Hoopfer, Jung et al. 2015) elife

(Watanabe, Chiu et al. 2017) Neuron

Tachykinin-expressing neurons control male-specific aggressive arousal in Drosophila

Kenta Asahina [1], Kiichi Watar
González [3], Eyrún Arna Eyjólf

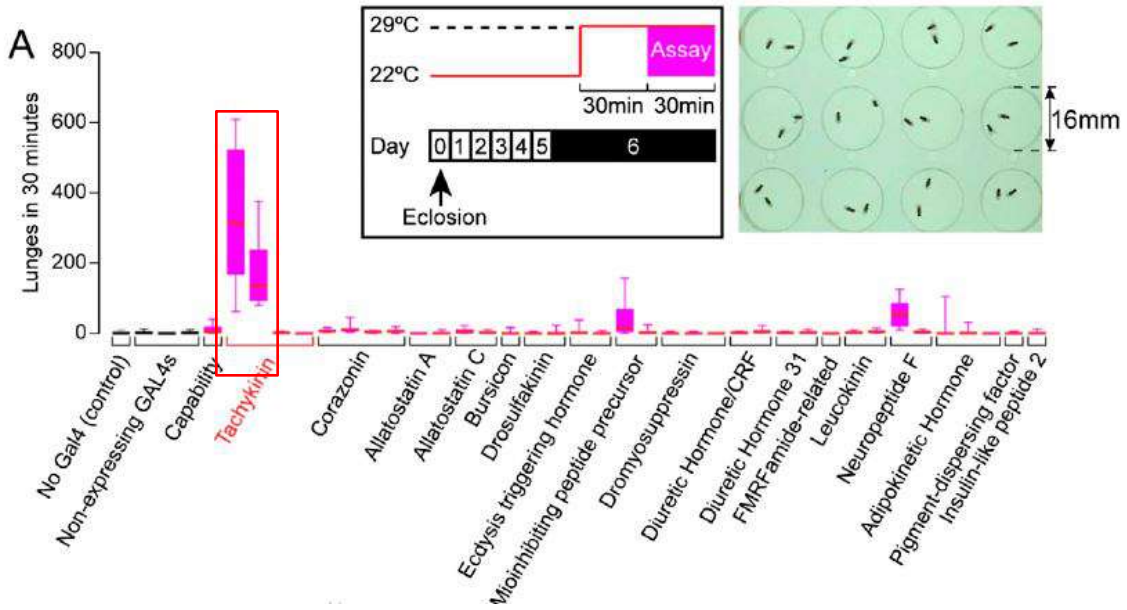
P1 interneurons promote a persistent internal state that enhances inter-male aggression in Drosophila

Eric D Hoopfer [1] [2], Yonil Jung [2], Hid

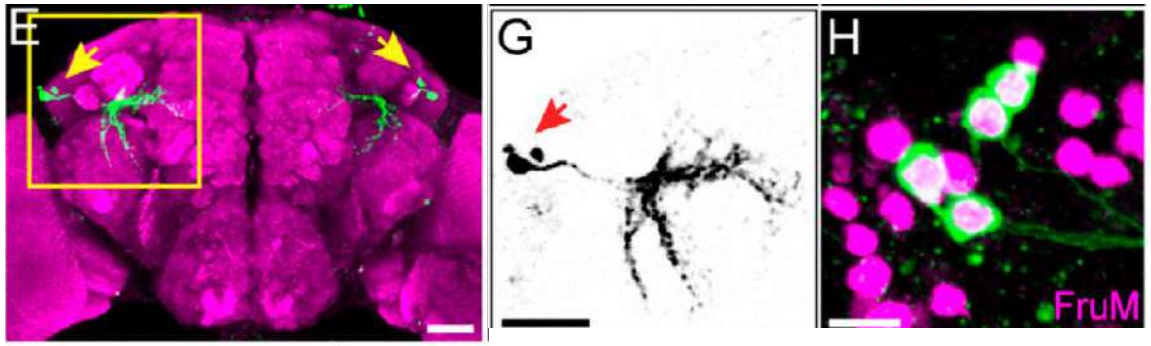
A Circuit Node that Integrates Convergent Input from Neuromodulatory and Social Behavior-Promoting Neurons to Control Aggression in Drosophila

Kiichi Watanabe [1], Hui Chiu [1], Barret D Pfeiffer [2], Allan M Wong [2], Eric D Hoopfer [3], Gerald M Rubin [4], David J Anderson [5]

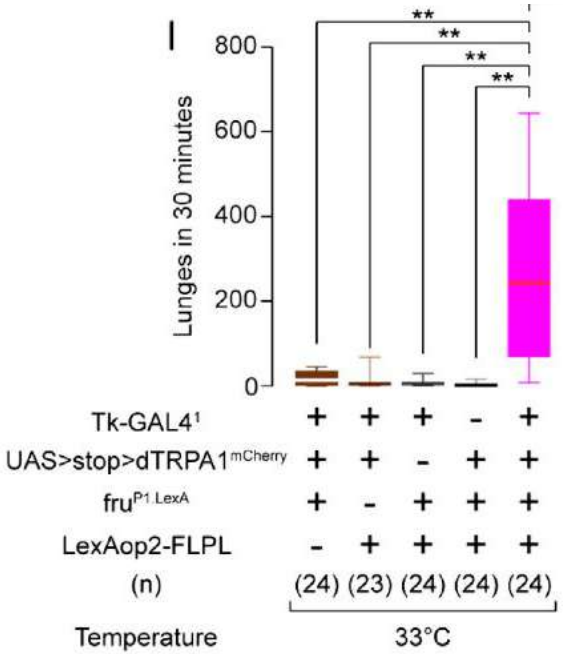
Sexually dimorphic Fru^{M+} TK-expressing neurons control male aggression

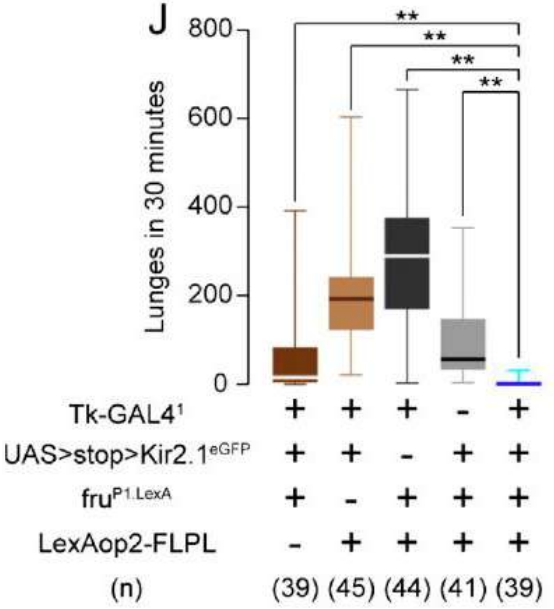


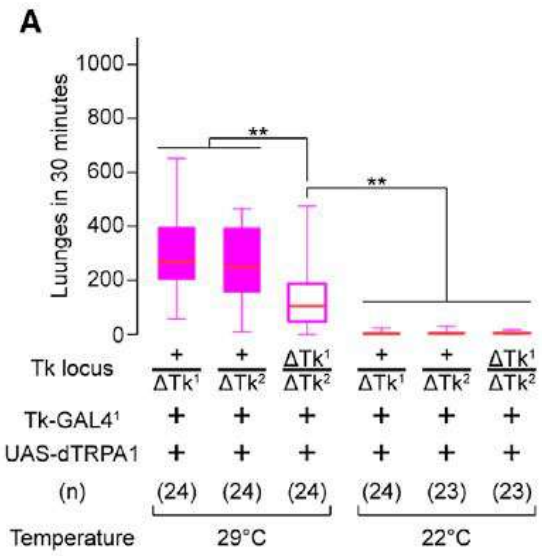
TK Fru^{M+} neurons

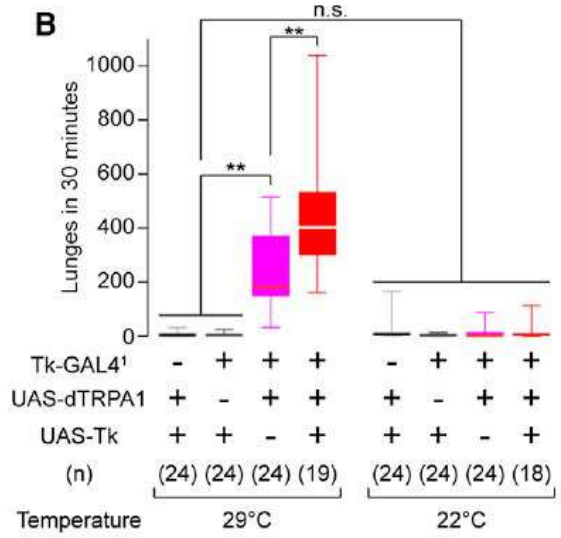


(Asahina, Watanabe et al. 2014)

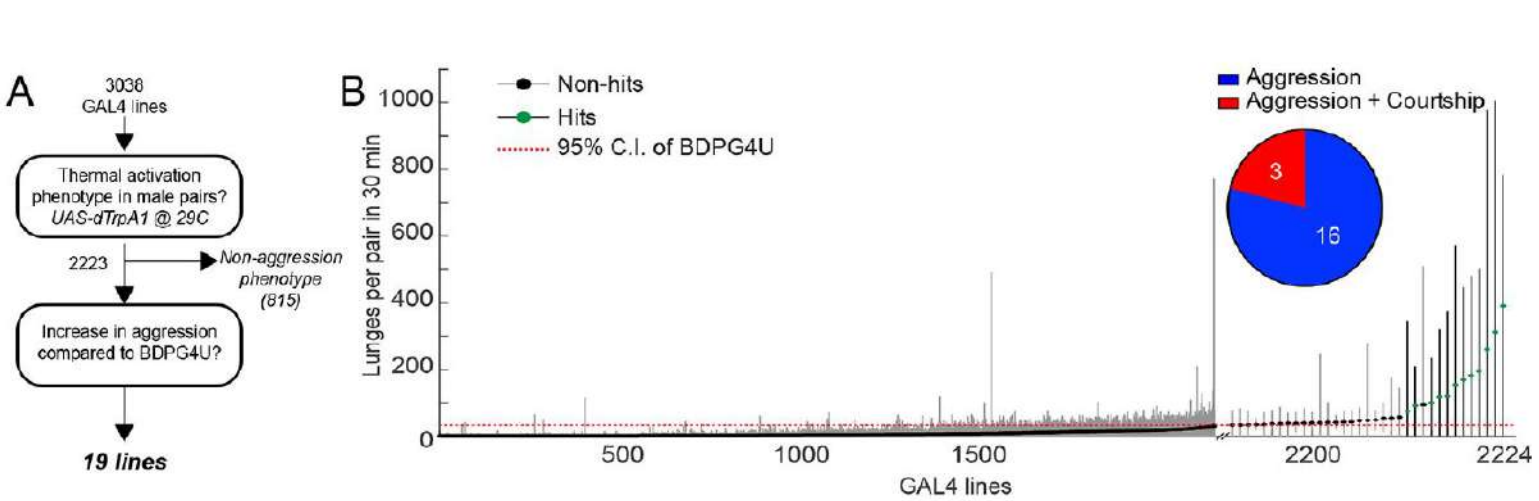


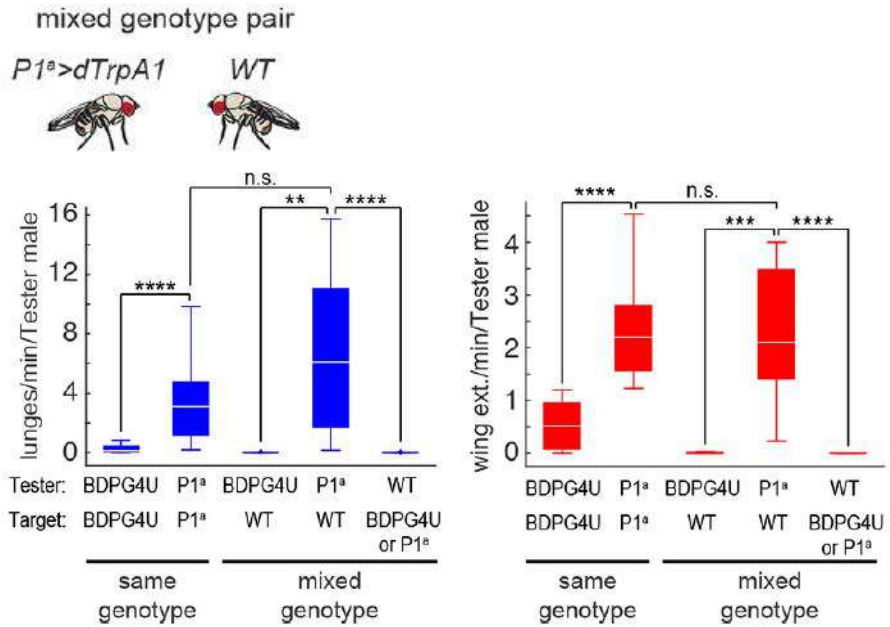


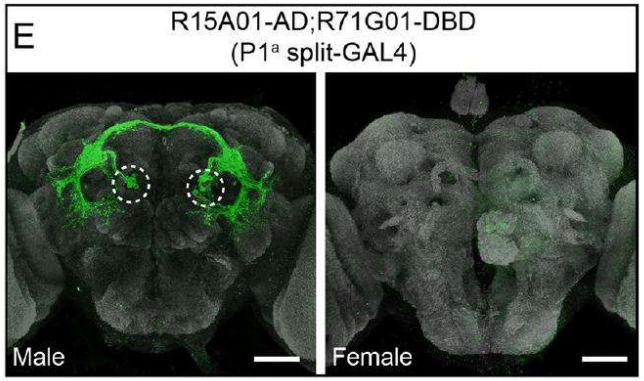


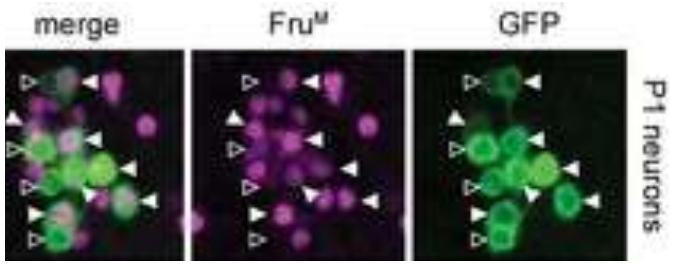


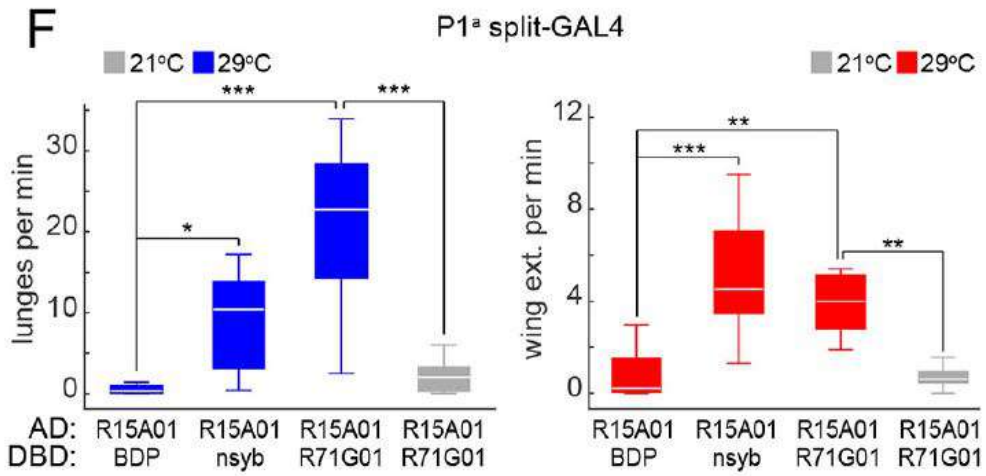
P1 neurons may be a potentially 'motif' for the control of social behaviors





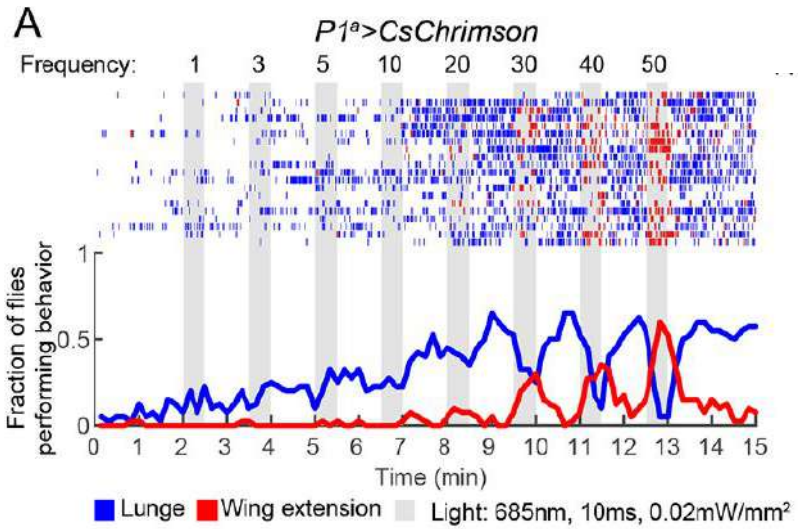


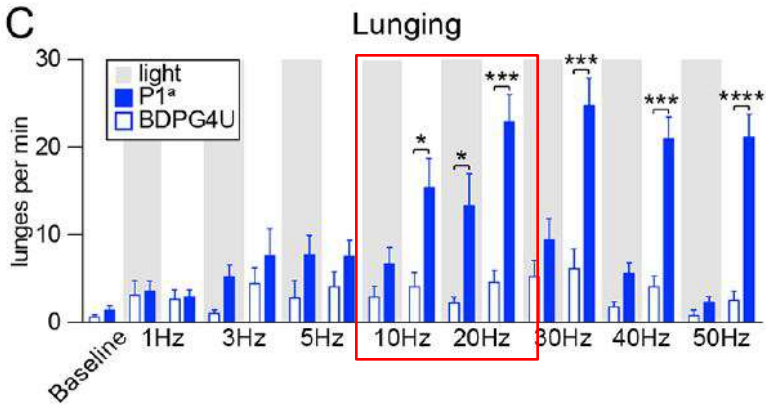


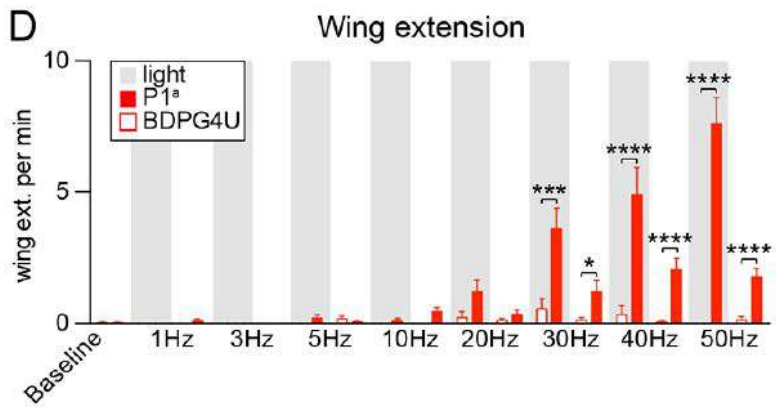


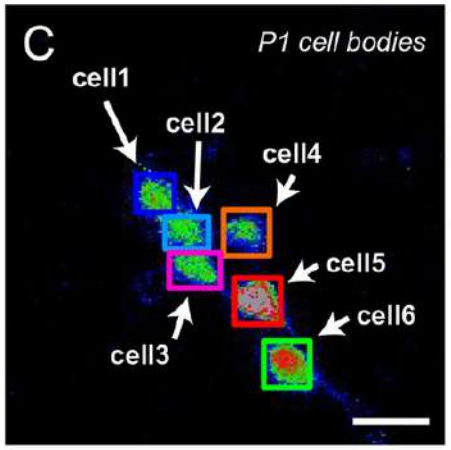
(Hoopfer, Jung et al. 2015)

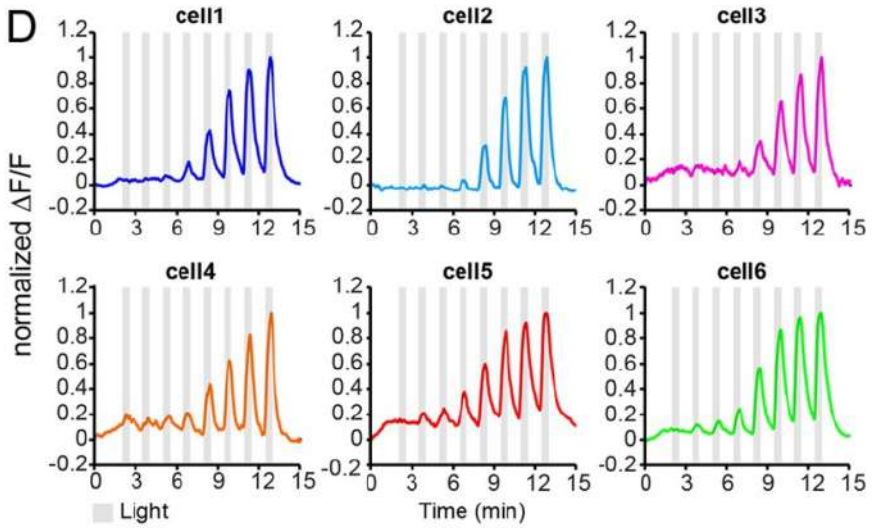
P1 neurons promote social behaviors in a threshold-dependent, inverse manner

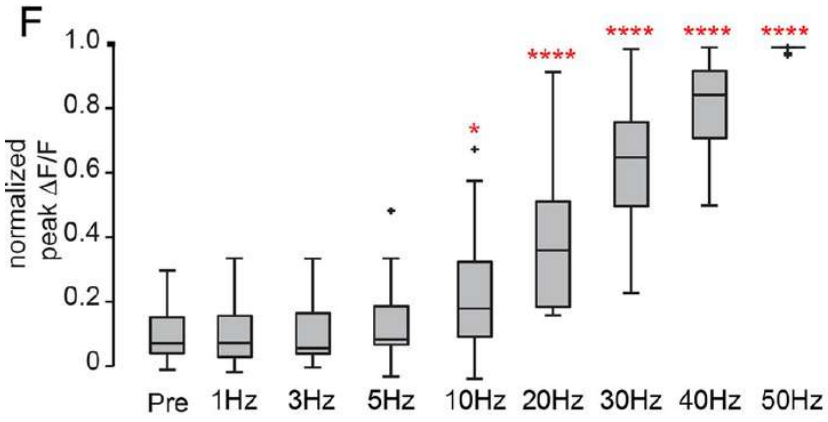


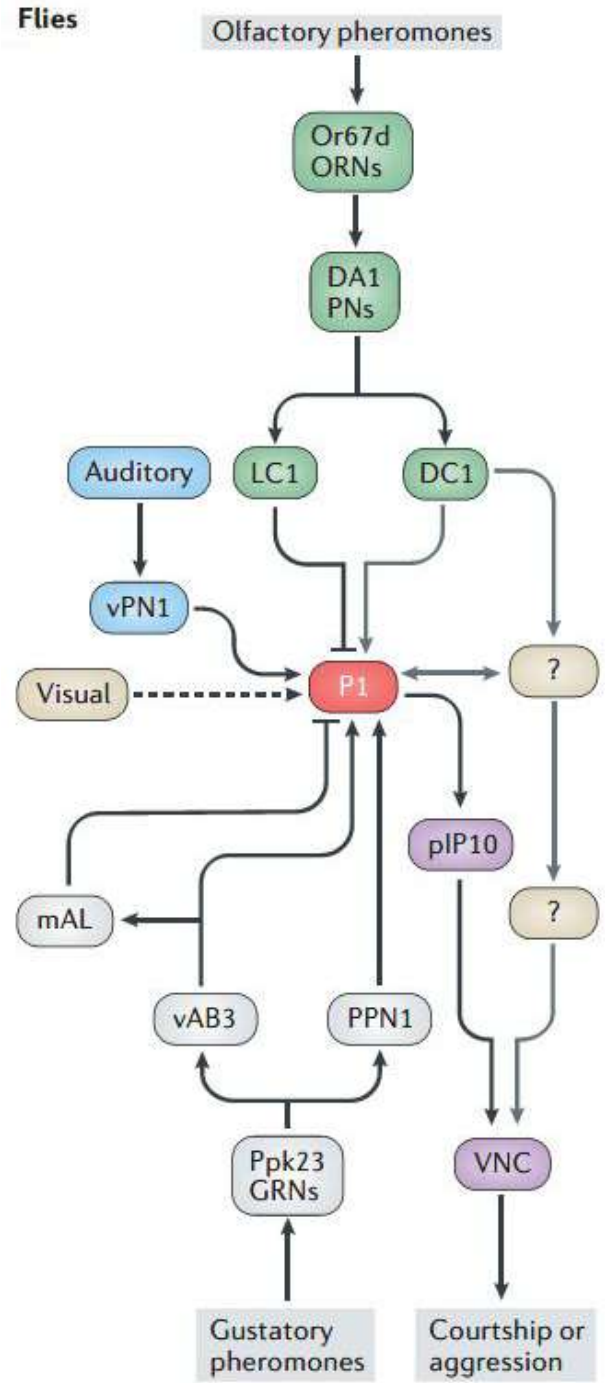


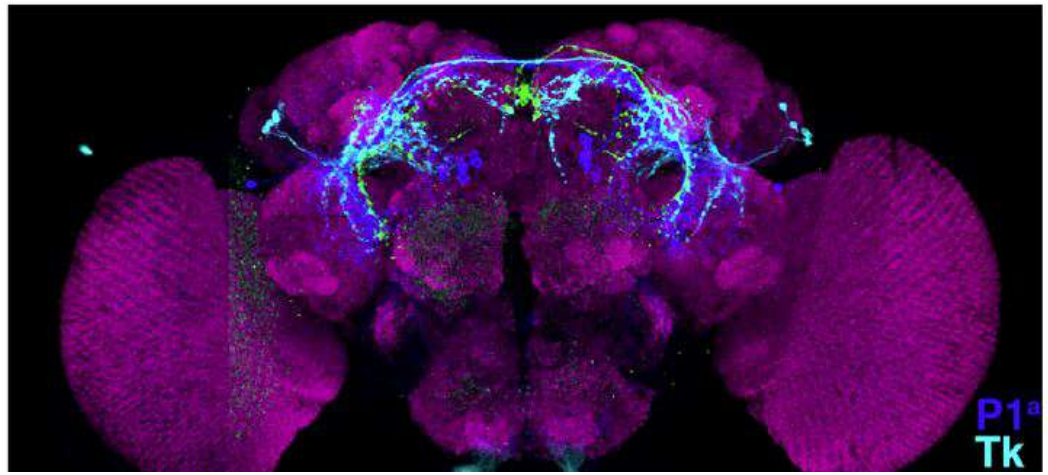




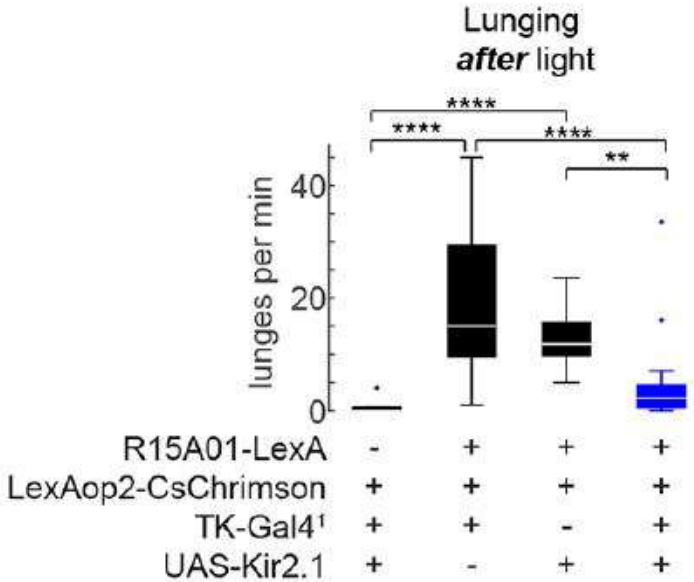




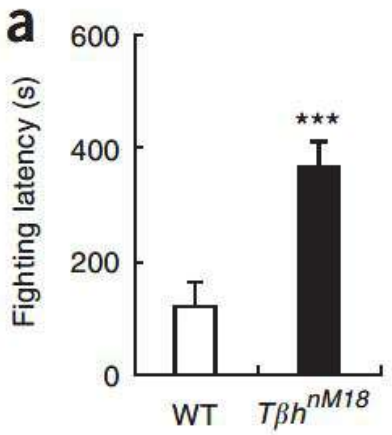


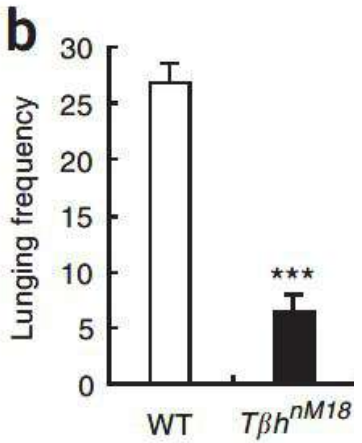


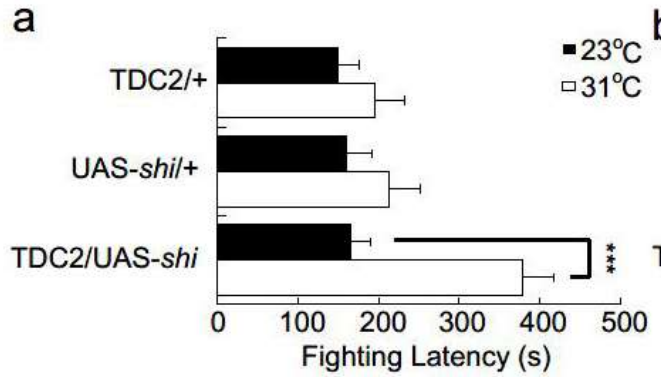
P1 *(R15A01-LexA>CsChrimson)* → ? → **TK^{FruM}** *(TK-GAL4^{1}>Kir2.1)*

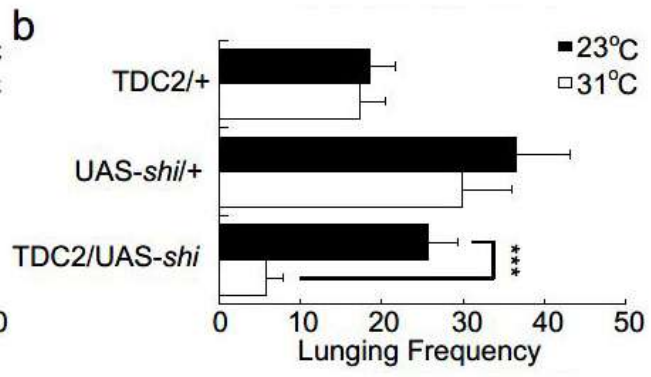


OA is essential for normal levels of aggression

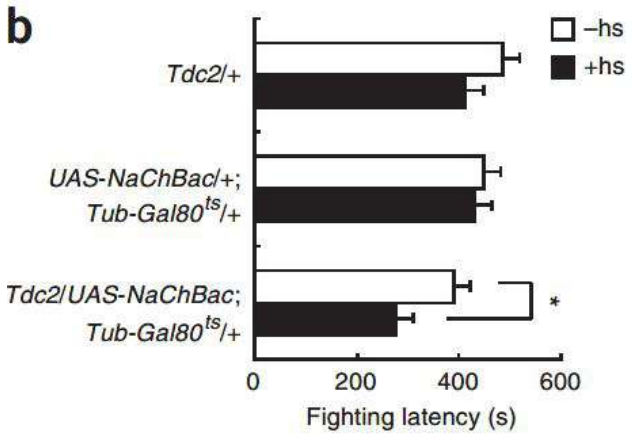


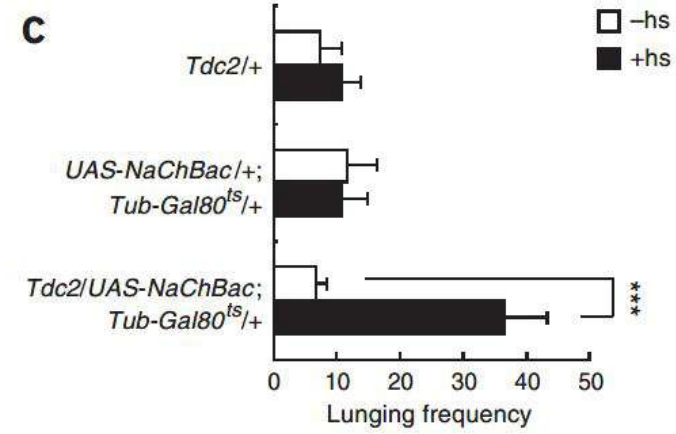






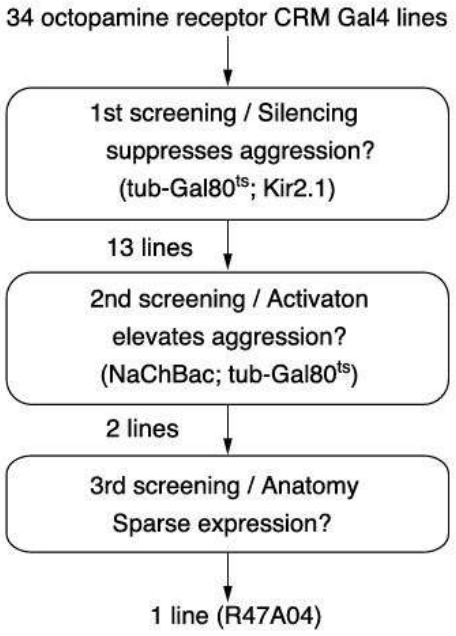
Only NaChBac and only in grouped flies

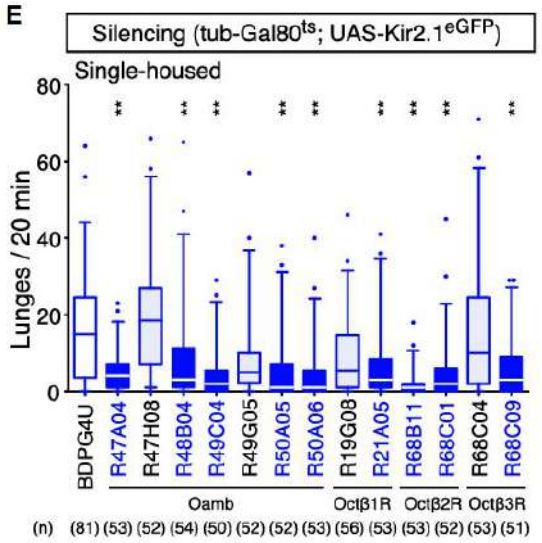


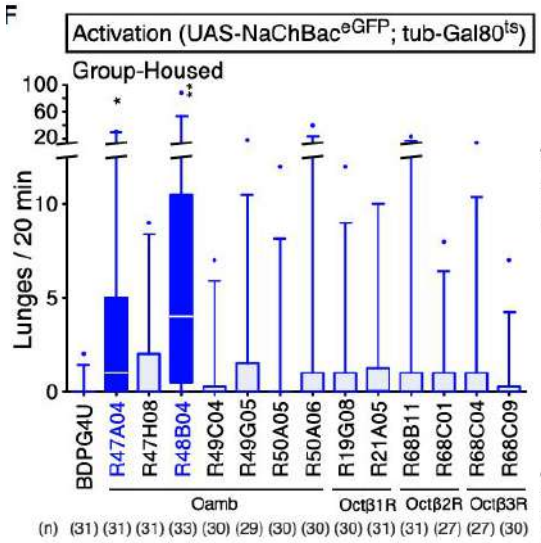


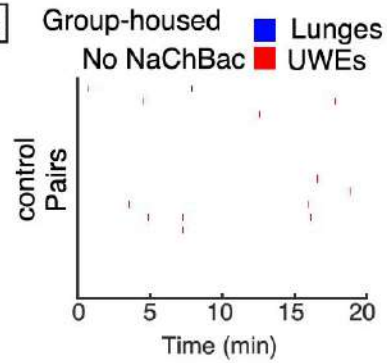
(Hoyer, Eckart et al. 2008)(Zhou, Rao et al. 2008)

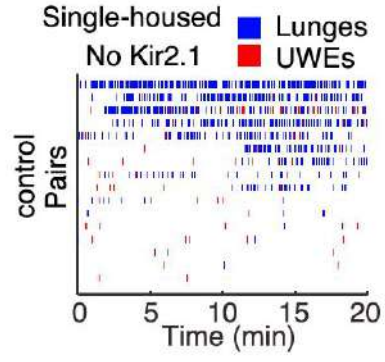
fru-expressing OAR^{+} aSP2 neurons' activity is required for normal levels of aggression

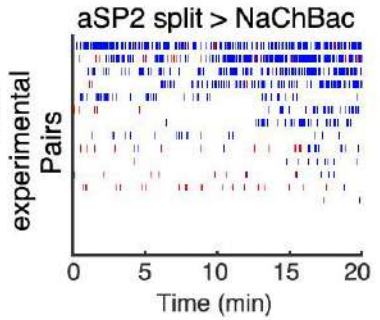


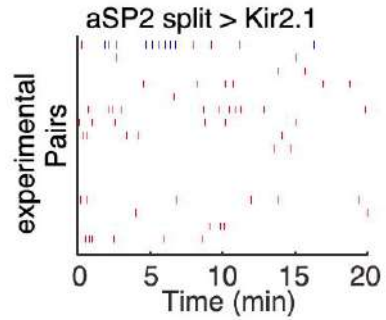




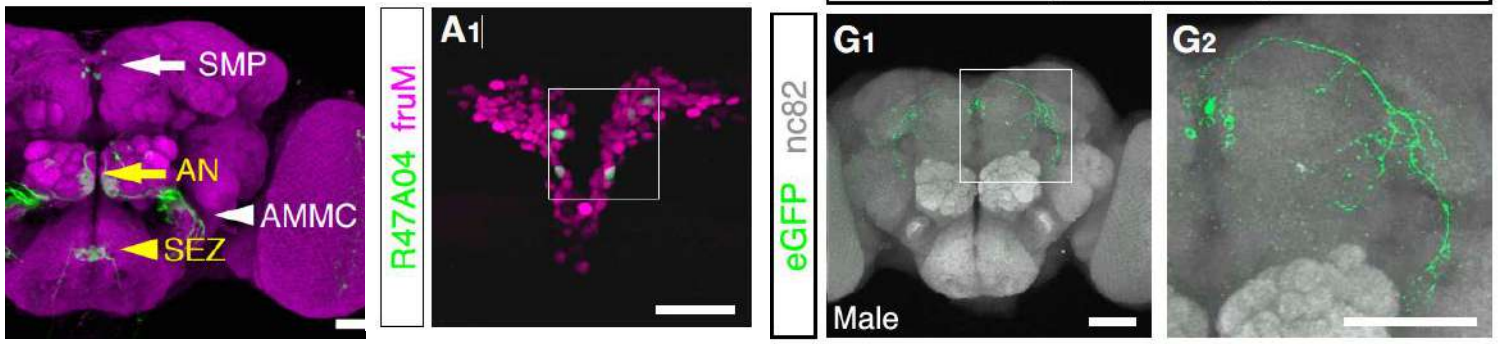








R47A04

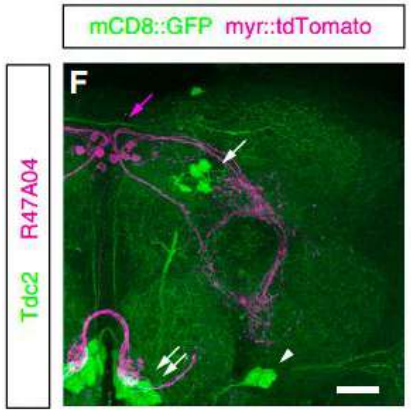


NaChBac: increase neuronal excitability

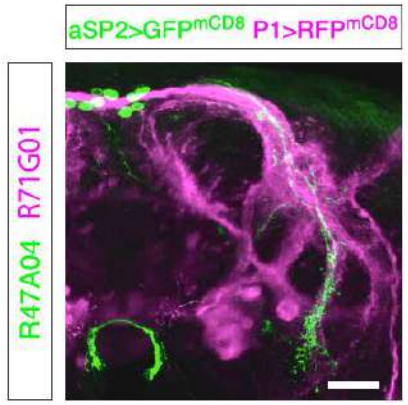
dTrpA1/Chrimson: acutely promote spiking
did not evoke aggression

(Watanabe, Chiu et al. 2017)

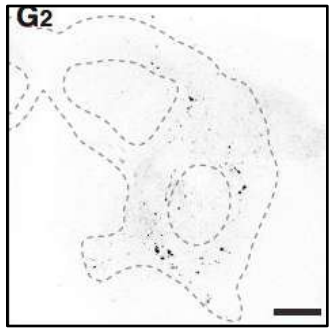
aSP2 neurons bias output from a social behavior network to promote aggression

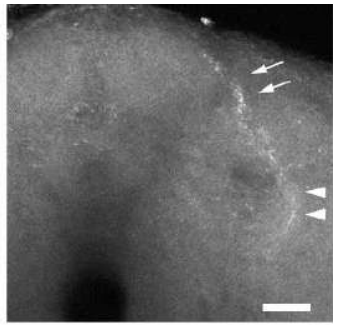


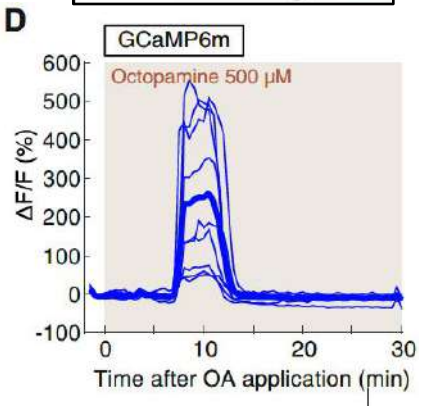
aSP2:Tdc2 GRASP

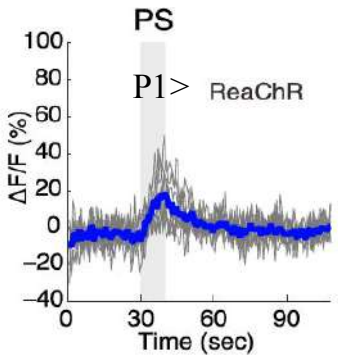


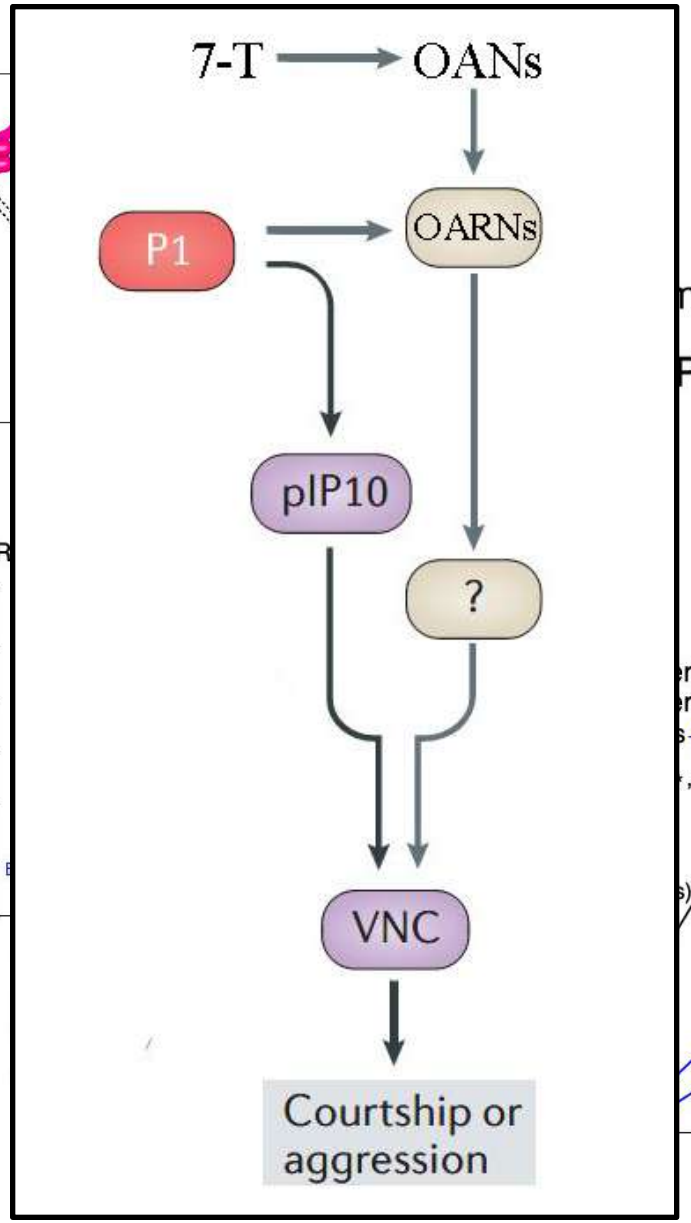
aSP2:P1 GRASP

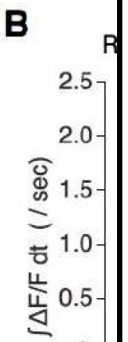


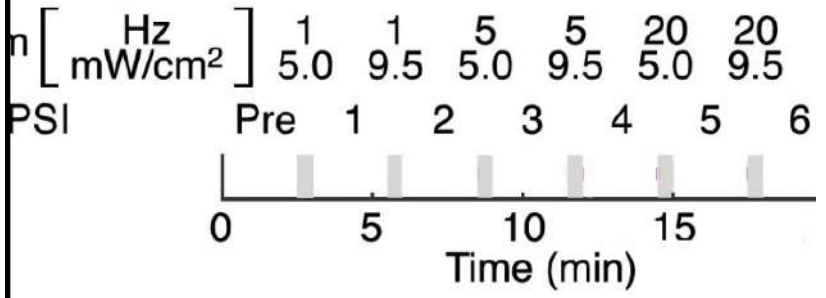


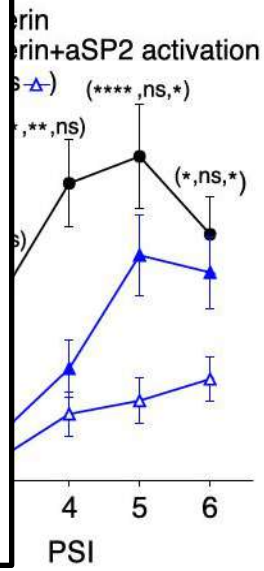


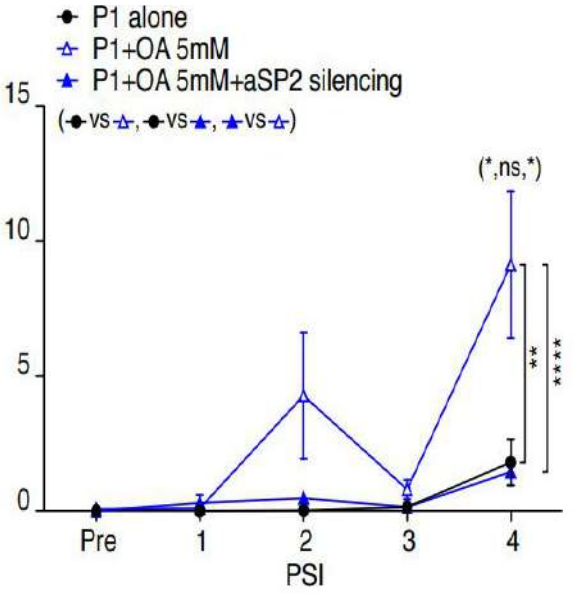








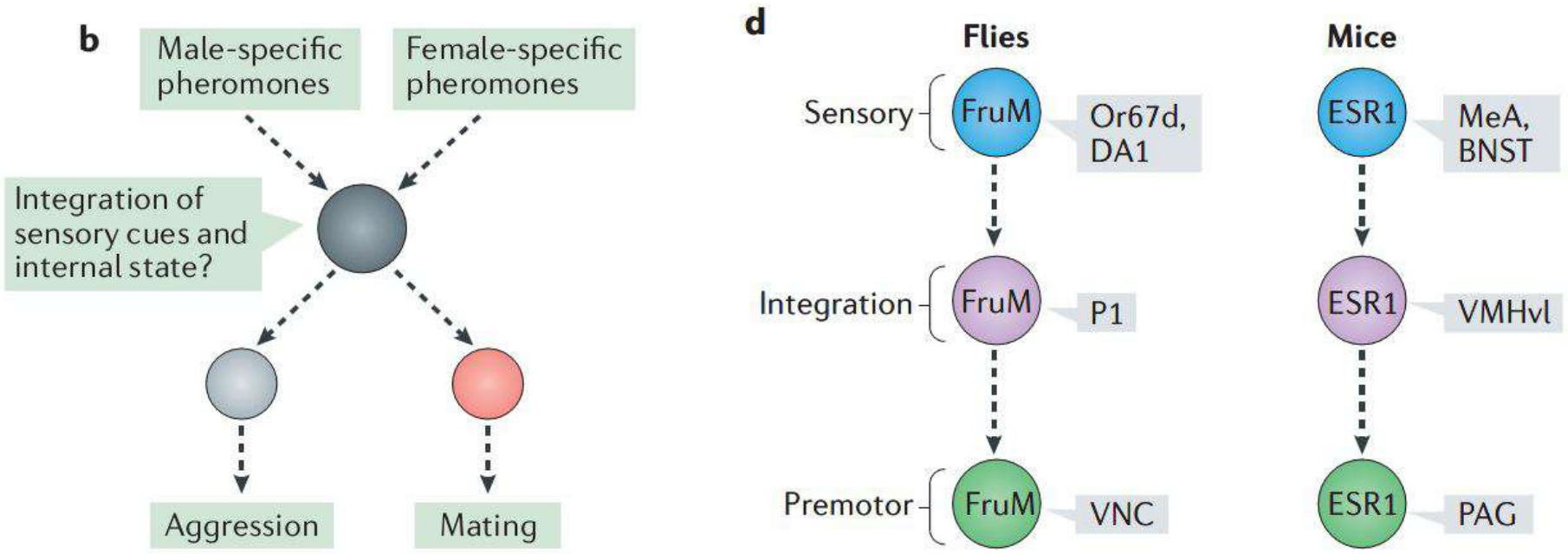




Conclusion

The circuits that regulate social behaviors are highly intertwined

Scalable control may be a general feature of cell populations controlling social behaviors



(Anderson 2016)

Social Influence

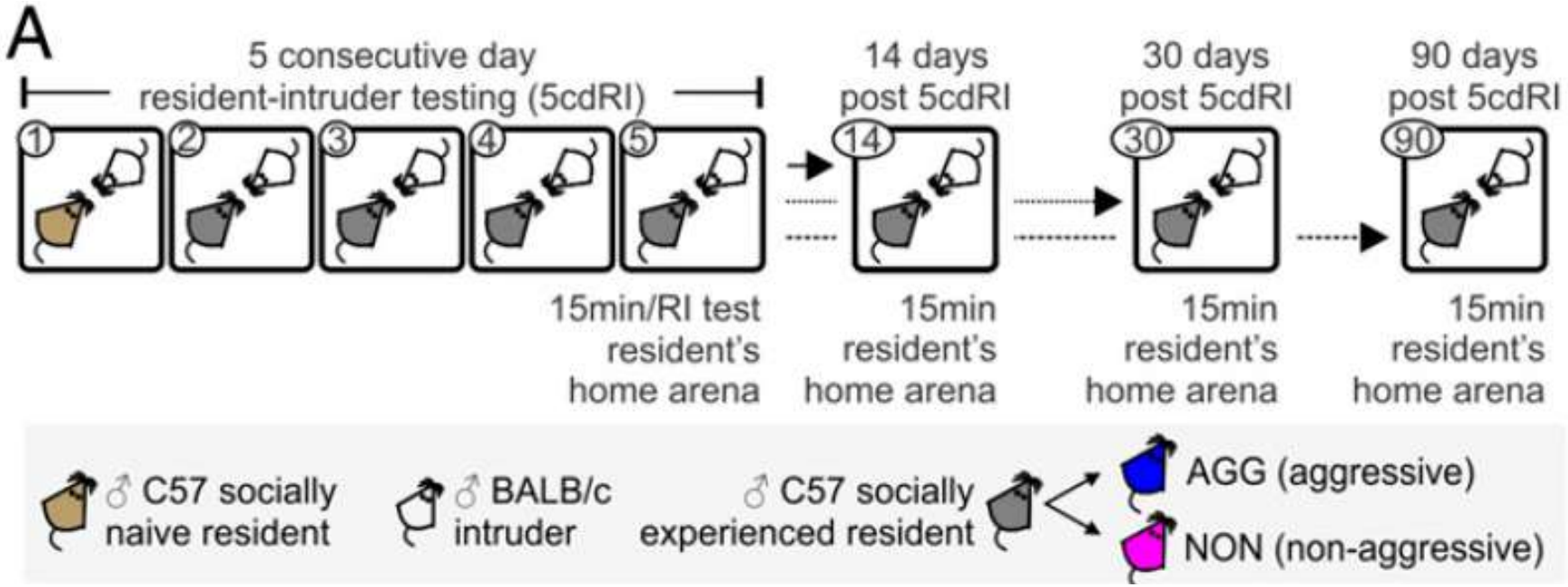
2020 11 12

朱寰

How do **social experience** cast a shadow on……

- Aggression?
- Stress reaction?
- Conspecifics recognition?

AGGRESSION



(Stefanos Stagkourakis, et al, 2020)

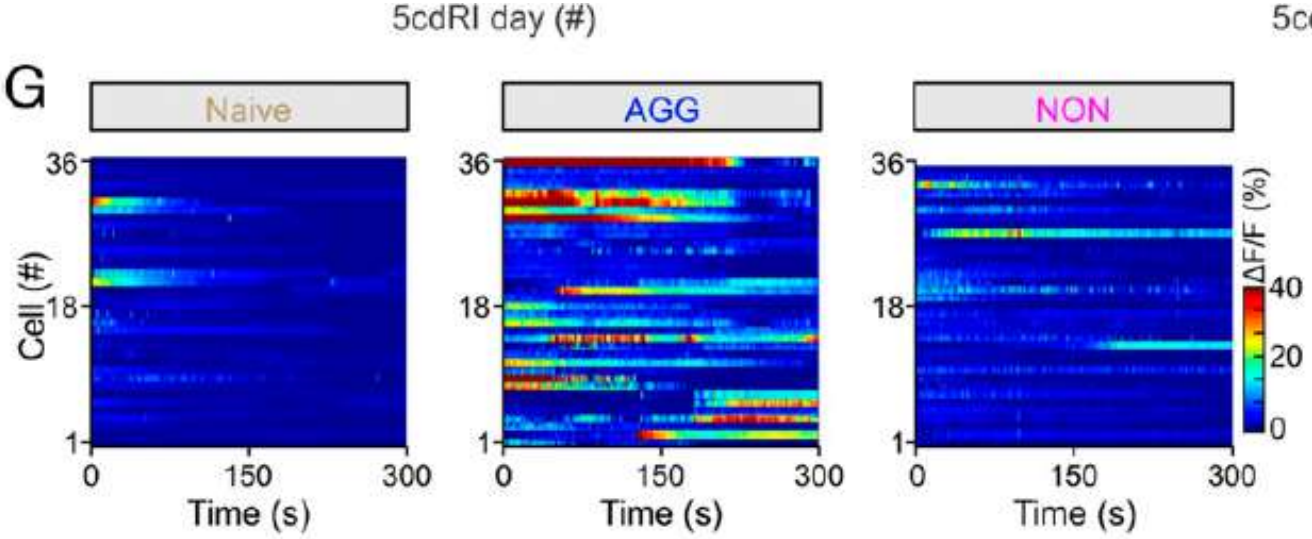
VMHvl esr1^{+} neurons activate after 5-day trial

ARTICLE

doi:10.1038/nature09736

Functional identification of an aggression locus in the mouse hypothalamus

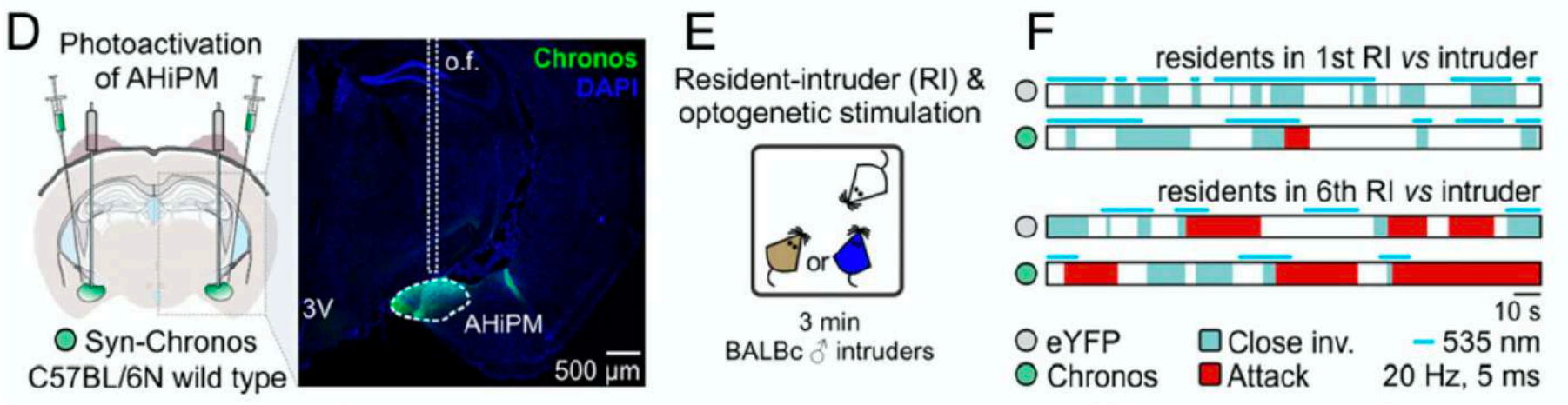
Dayu Lin[1,2], Maureen P. Boyle[3], Piotr Dollar[4], Hyosang Lee[1], E. S. Lein[3], Pietro Perona[4] & David J. Anderson[1,2]

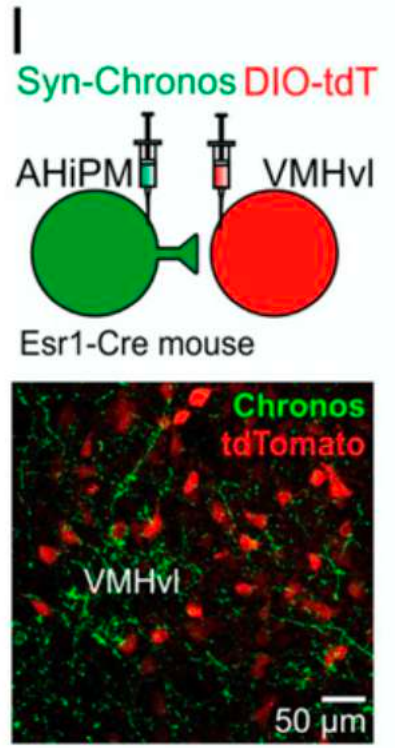


(VMHvl esr1+ neurons,
estrogen receptor 1-expressing neurons in ventrolateral subdivision of the ventromedial hypothalamus,
腹侧下丘脑的雌激素腹侧子侧的、表达雌激素受体1的神经元)

(Stefanos Stagkourakis, et al, 2020)

Upstream AHiPM engages

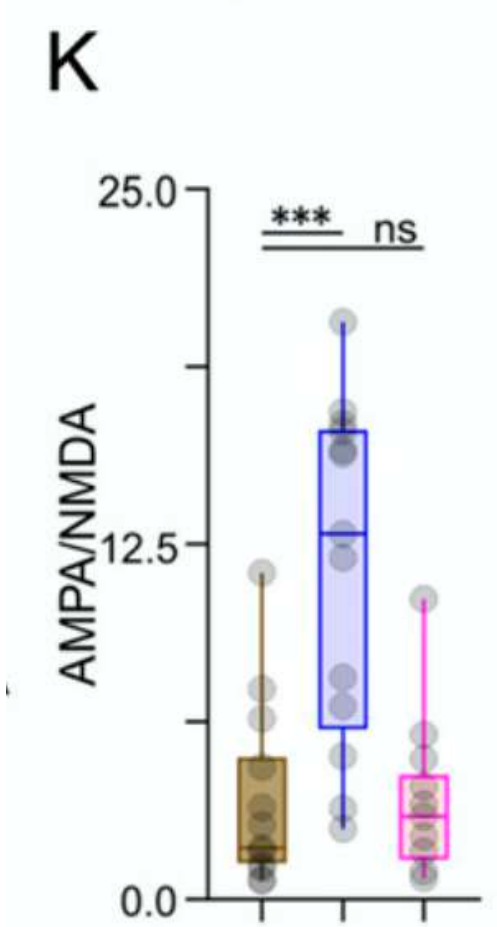


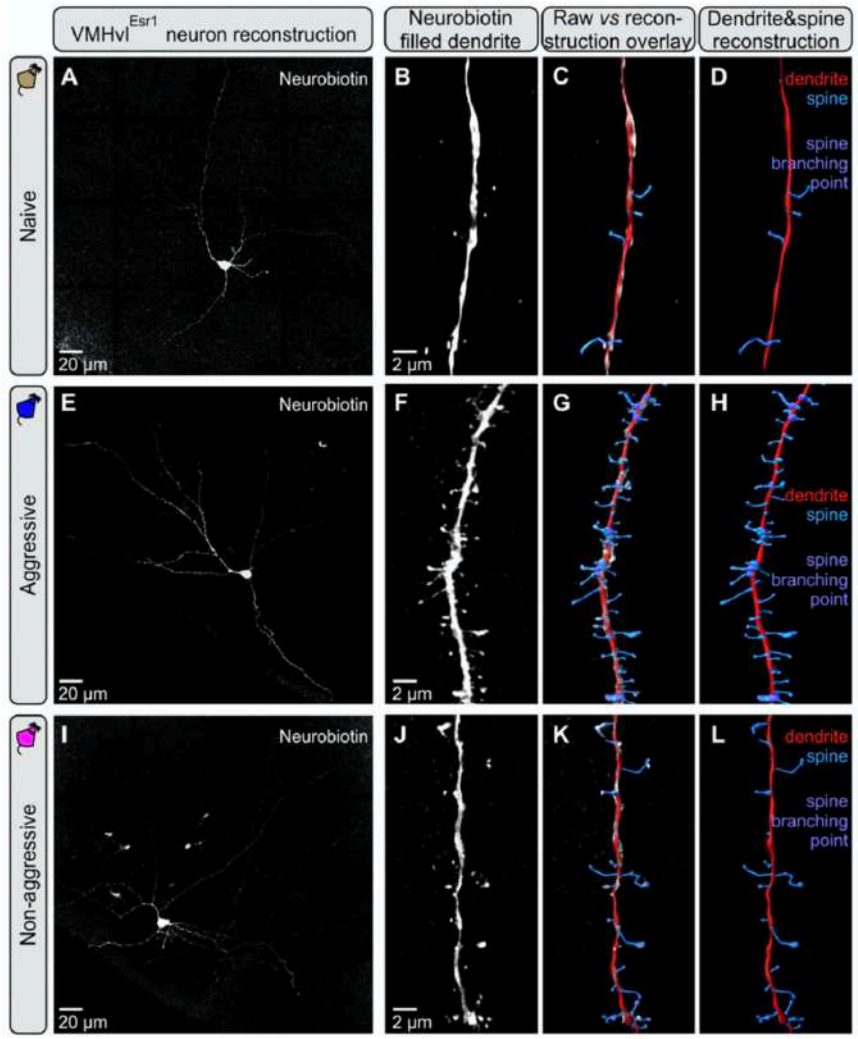


(AHiPM, amygdalohippocampal area, 扁桃体海马区)

(Stefanos Stagkourakis, et al, 2020)

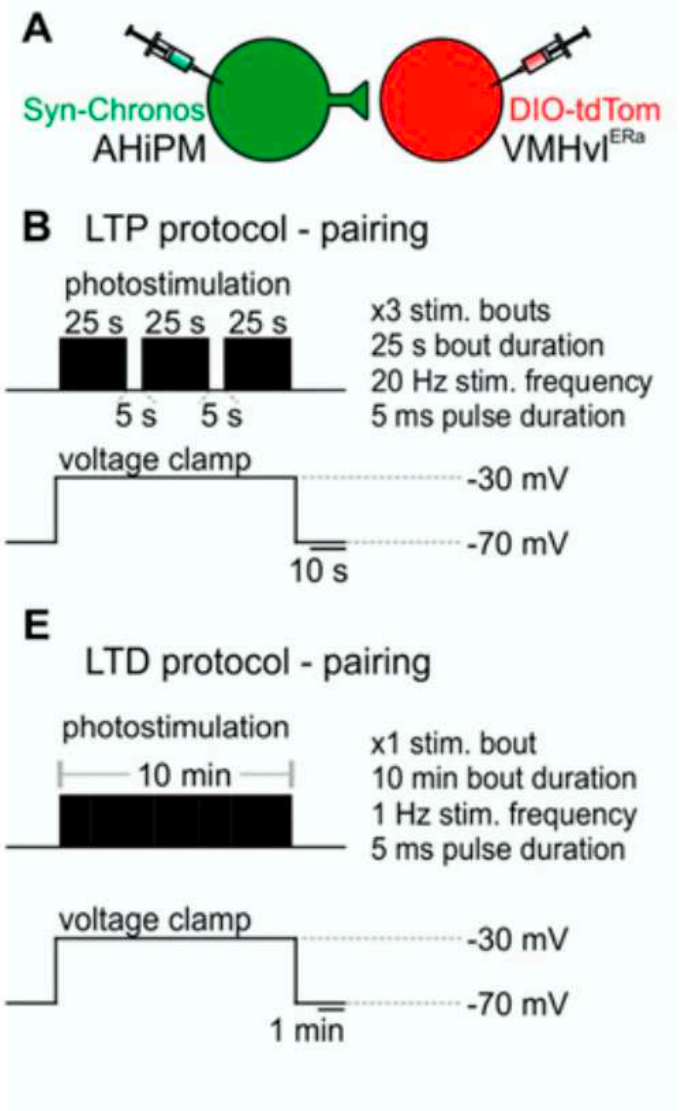
AMPA/NMDA level rises after social experience.
Dendritic spine complexity increases also.

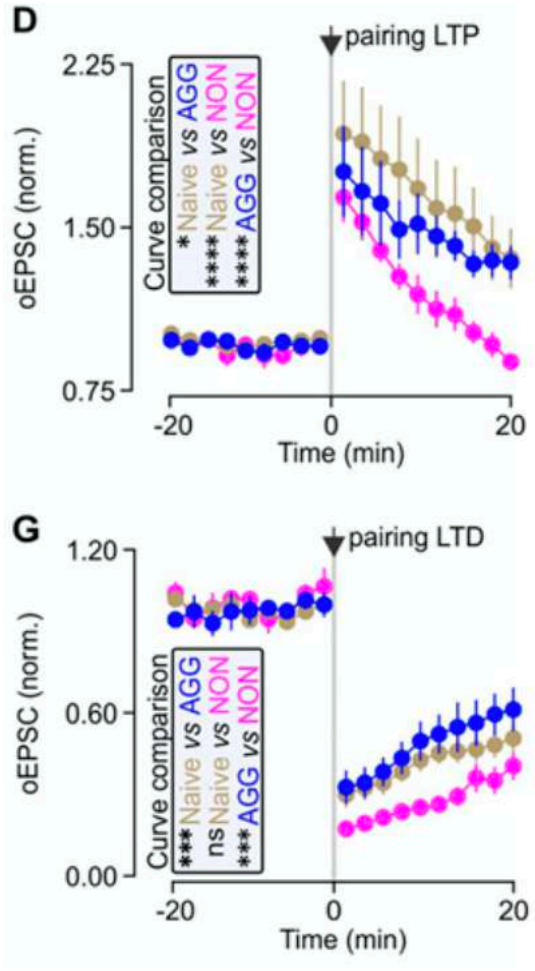




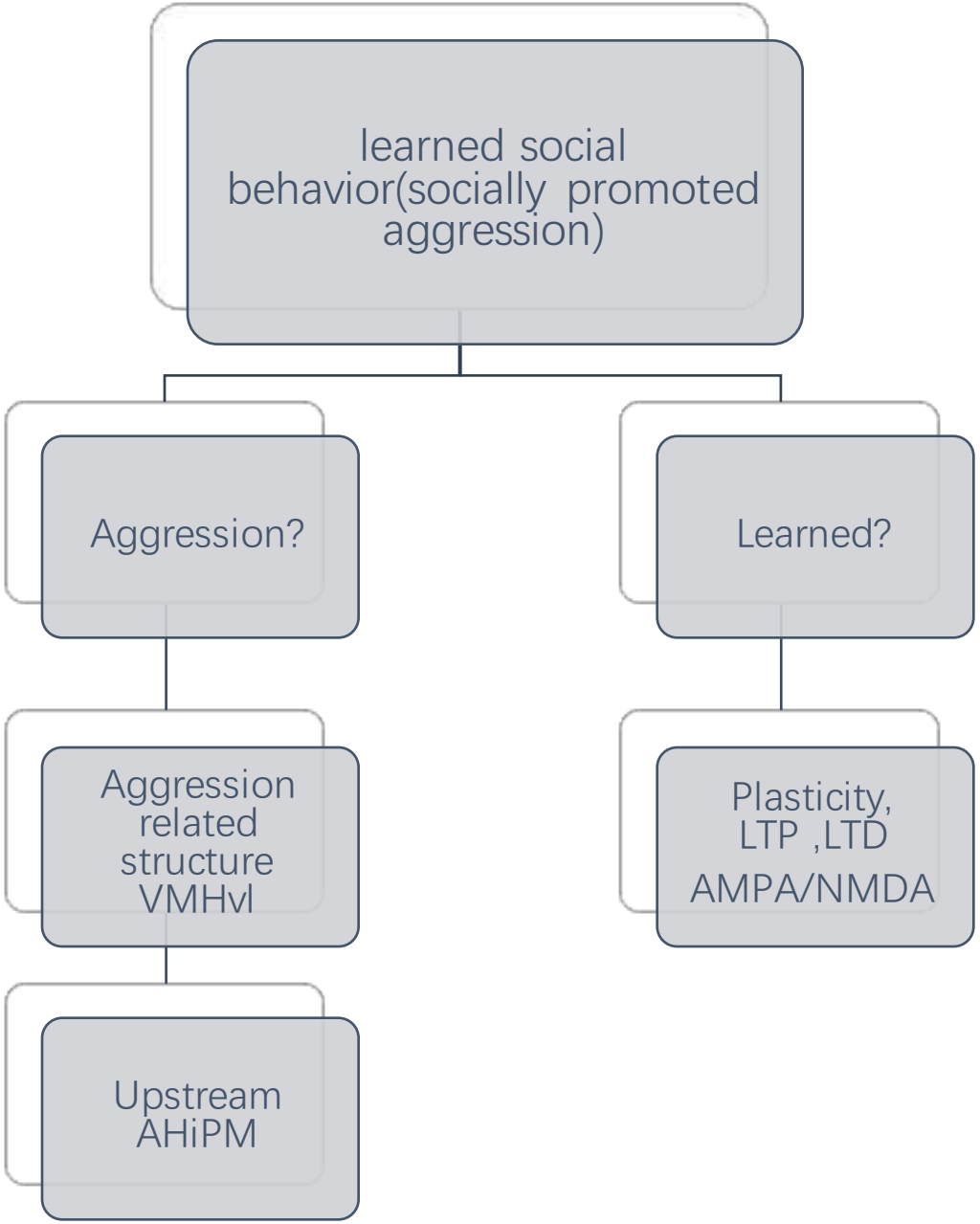
(Stefanos Stagkourakis, et al, 2020)

VMHvl dEPSC amplitudes after optically induced LTP
And attenuates after optically induced LTD

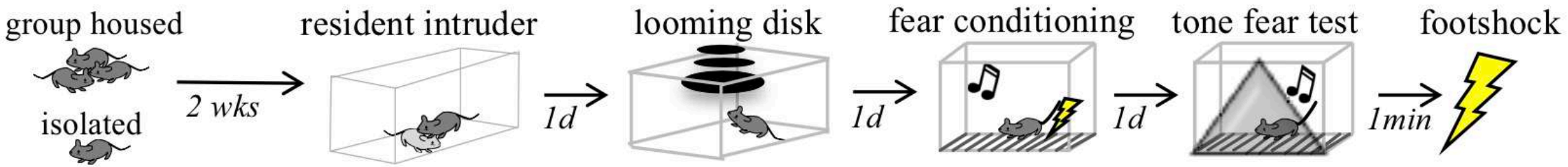




(Stefanos Stagkourakis, et al, 2020)


learned social behavior(socially promoted aggression)
Aggression?
Learned?
Aggression related structure VMHvl
Plasticity, LTP ,LTD AMPA/NMDA
Upstream AHiPM

STRESS REACTION



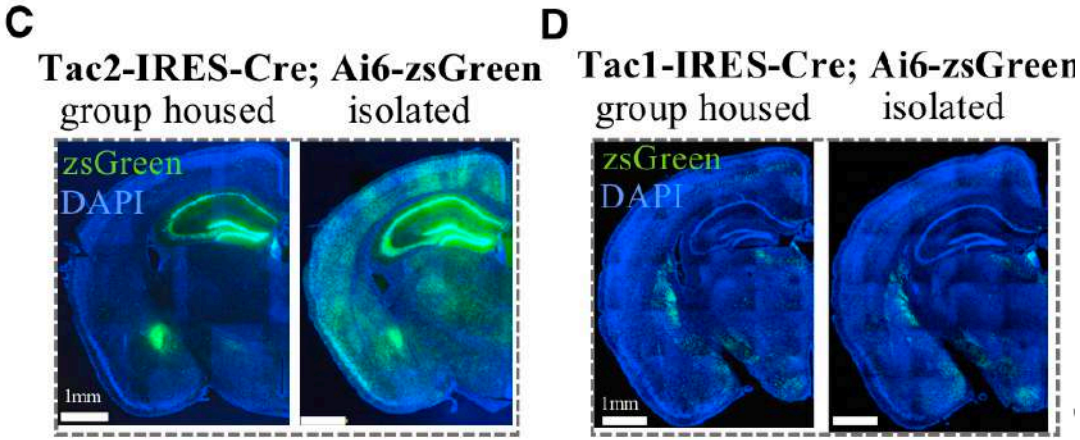
(Moriel Zelikowsky, et al, 2018)

Legacy from previous study , Tac2

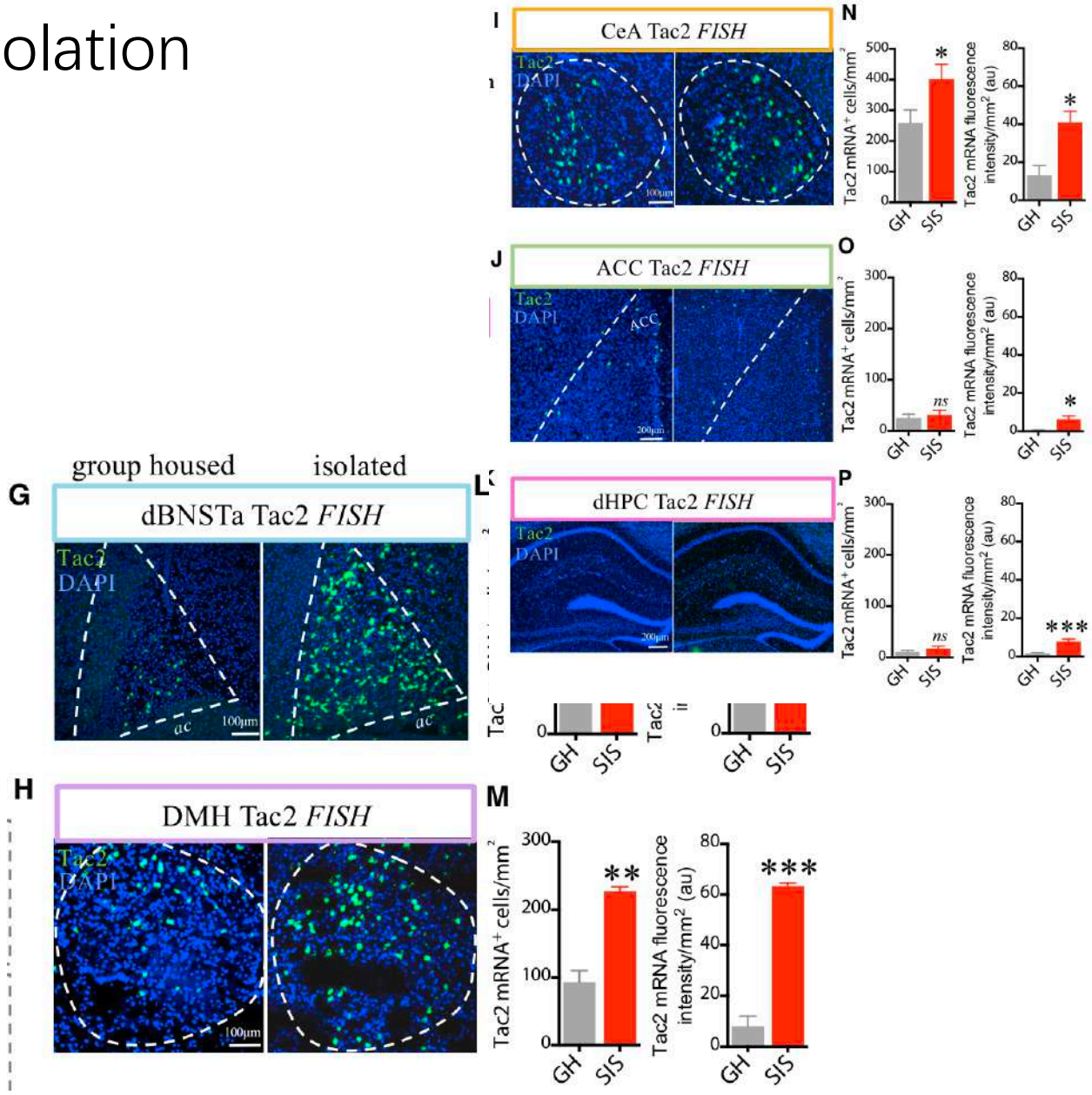
not yet clear (Figures 1A–1D). Guided by our previous studies of aggression in *Drosophila* (Wang et al., 2008; Asahina et al., 2014), we have investigated a potential role for tachykinins in mediating SIS-induced aggression in mice (Maggio, 1988). Studies of the neuropeptide tachykinin 2 (Tac2)/neurokinin B (NkB) in the central amygdala have implicated the peptide in fear memory consolidation (Andero et al., 2014, 2016), suggesting a role in fear learning and expression. Here, we report a broader and unanticipated role for Tac2/NkB as an important peptide mediator of the effects of chronic SIS. Tac2/NkB is dramatically upregulated by SIS throughout the brain and coordinates a pervasive change in brain state, affecting not only aggression but also many other behaviors via distributed local actions in multiple brain regions.

In *Drosophila*, an unbiased screen of peptidergic neurons identified DTK (*Drosophila* tachykinin)-expressing neurons and the DTK peptide as required for social isolation-induced aggression (Asahina et al., 2014). To determine whether this function might be conserved, we investigated the role of tachykinins in SIS. In rodents, the tachykinin gene family comprises *Tac1* and *Tac2* (Maggio, 1988). *Tac1* encodes the peptides substance P (SP),

TK expression increases after social isolation

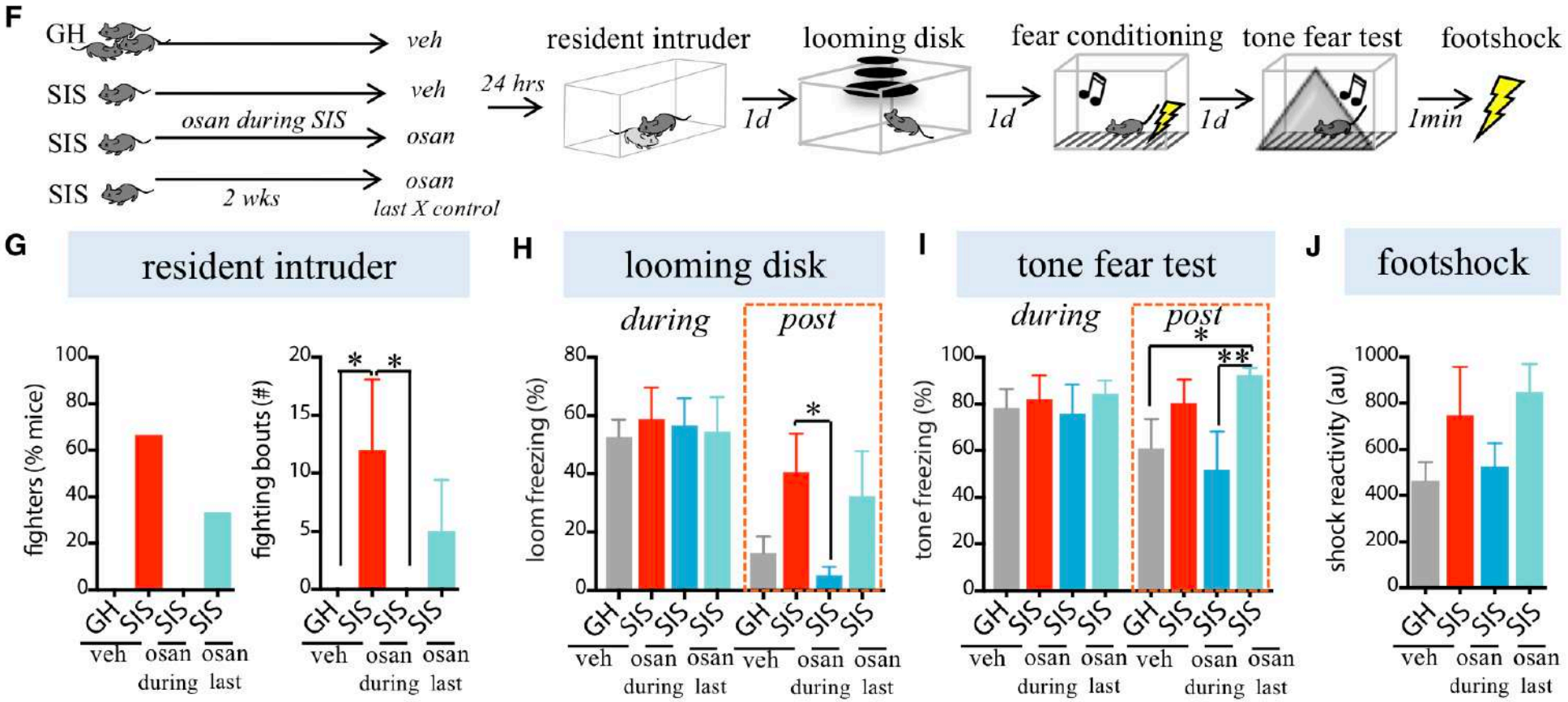


anterior dorsal bed nucleus of the stria terminalis (dBNSTa)
纹状体终端前背床核
central nucleus of the amygdala (CeA)
杏仁核中央核
dorsomedial hypothalamus (DMH)
背中下丘脑
anterior cingulate cortex （ ACC ）
前扣带回皮层
Dorsal hippocampus（ dHPC ）
背侧海马



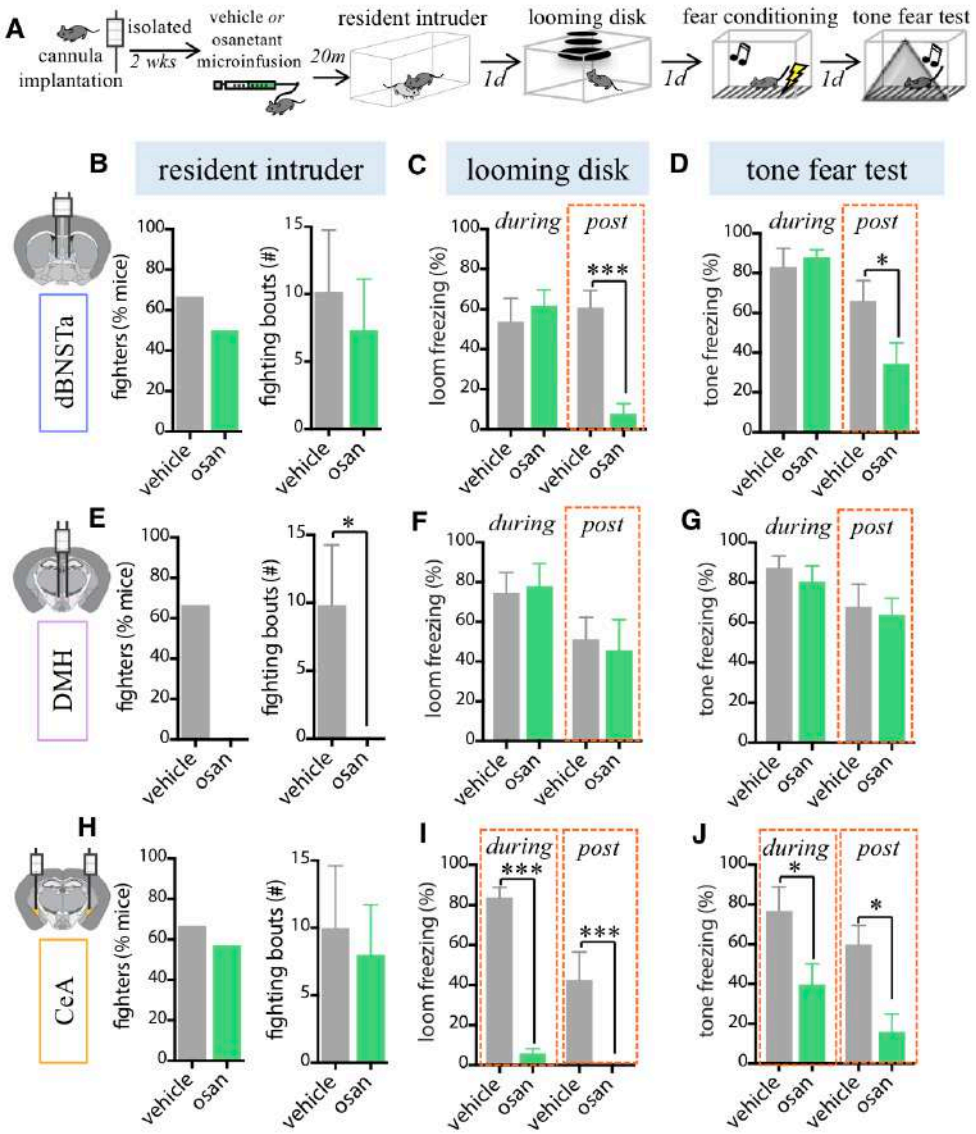
(Moriel Zelikowsky, et al, 2018)

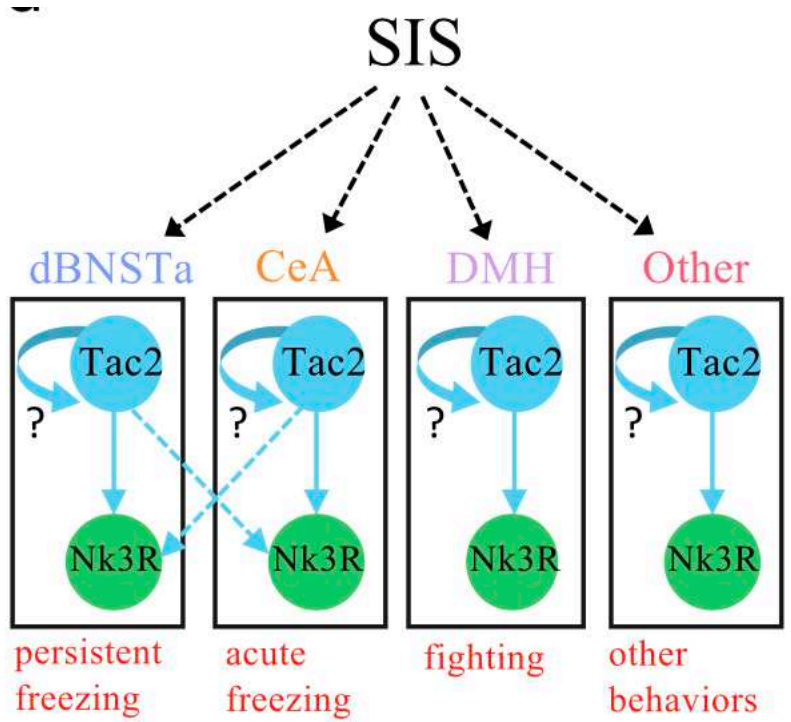
Neurokinin B and its antagonist osanetant attenuates effects of SIS



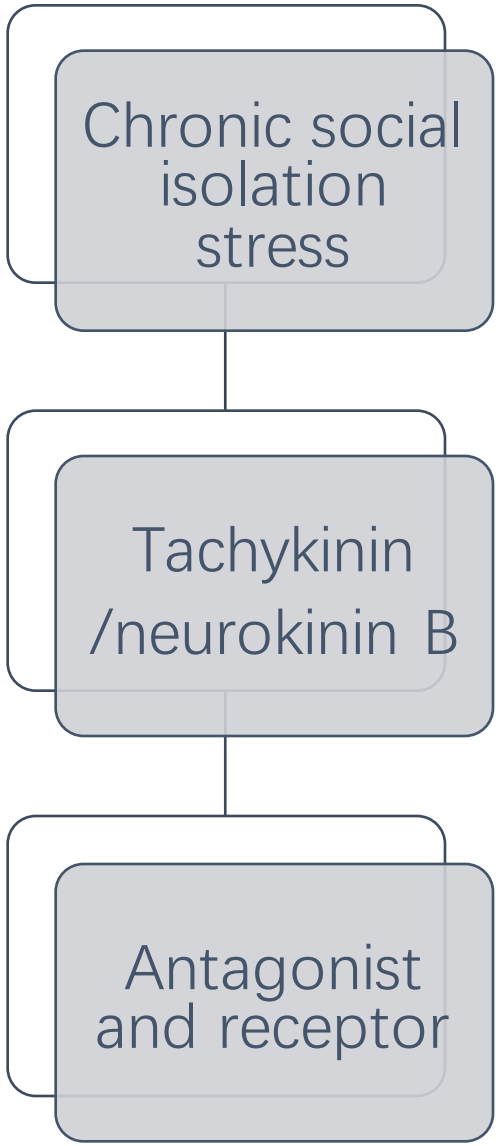
(Moriel Zelikowsky, et al, 2018)

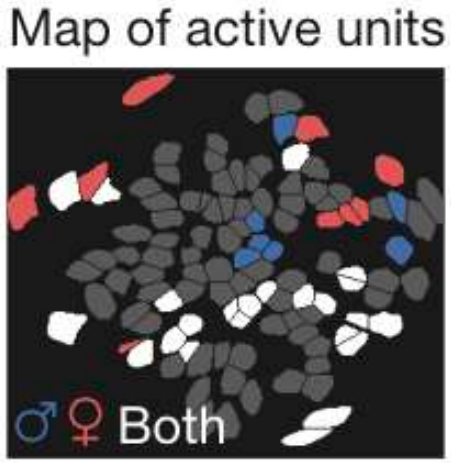
Targeted NK3R antagonism in different area attenuates different effects of SIS

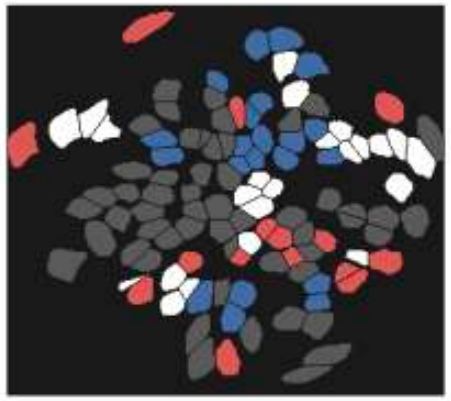


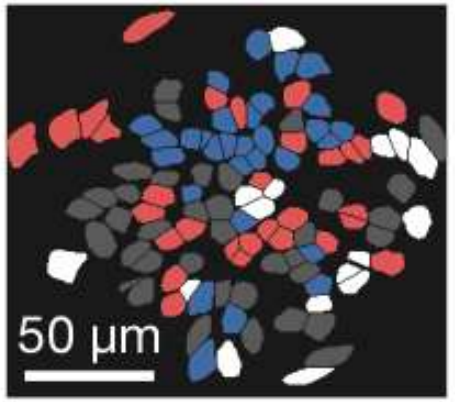


(Moriel Zelikowsky, et al, 2018)


Chronic social isolation stress
Tachykinin /neurokinin B
Antagonist and receptor



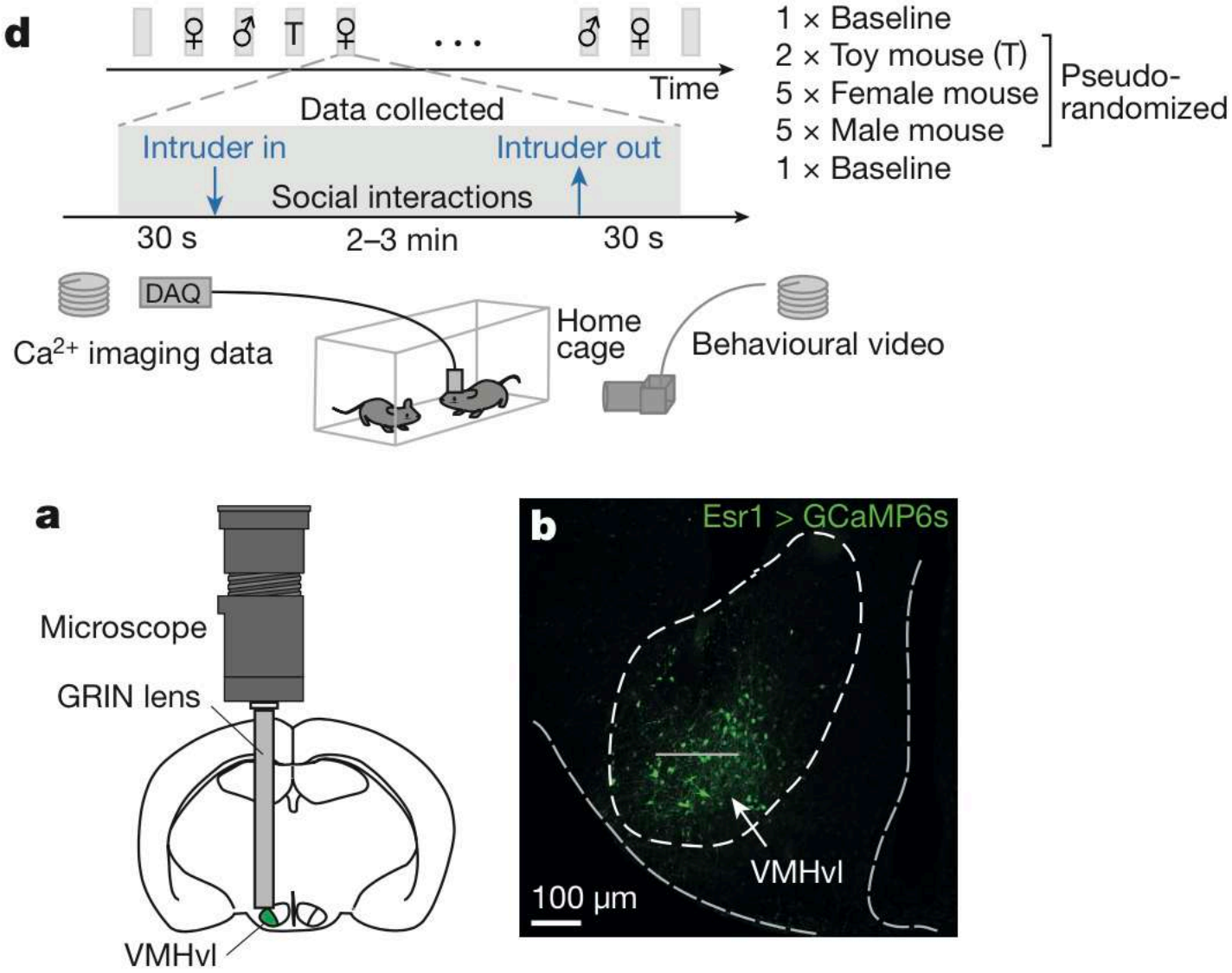




CONSPECIFIC RECOGNITION

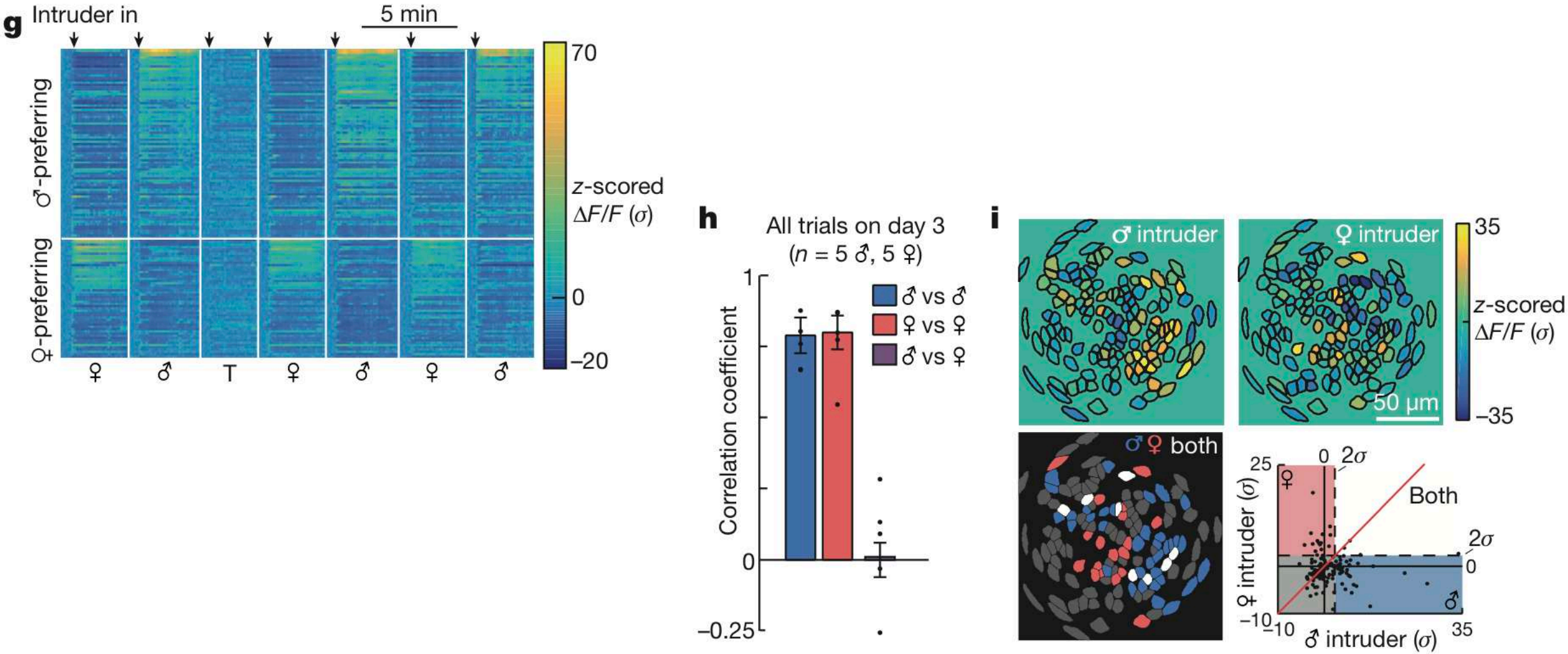
(Remedios R, et al, 2017)

VMHvl calcium imaging



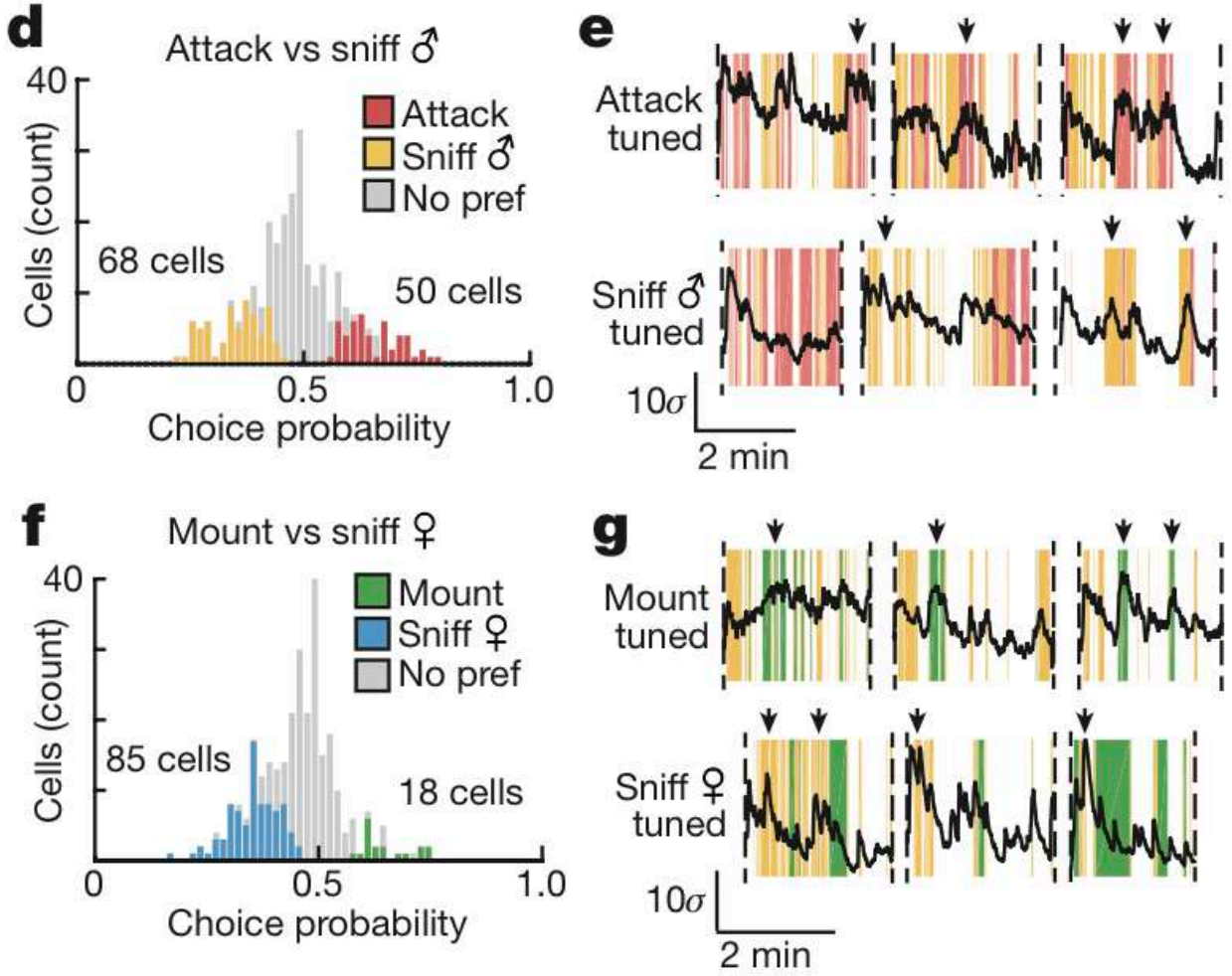
(Remedios R, et al, 2017)

Some neurons prefer one specific sex



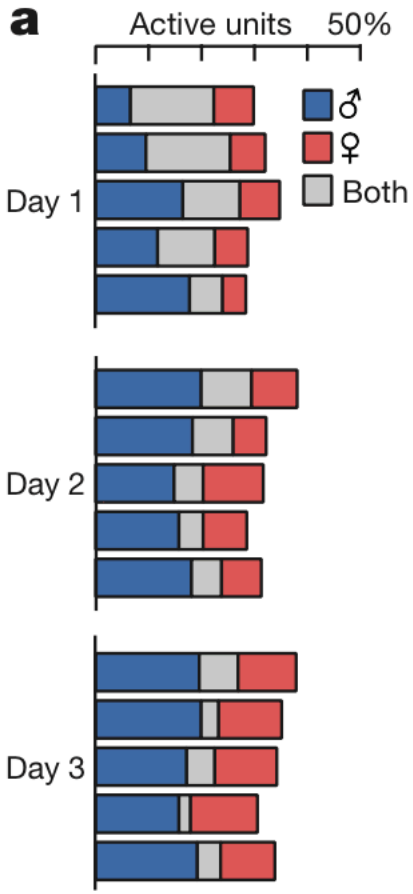
(Remedios R, et al, 2017)

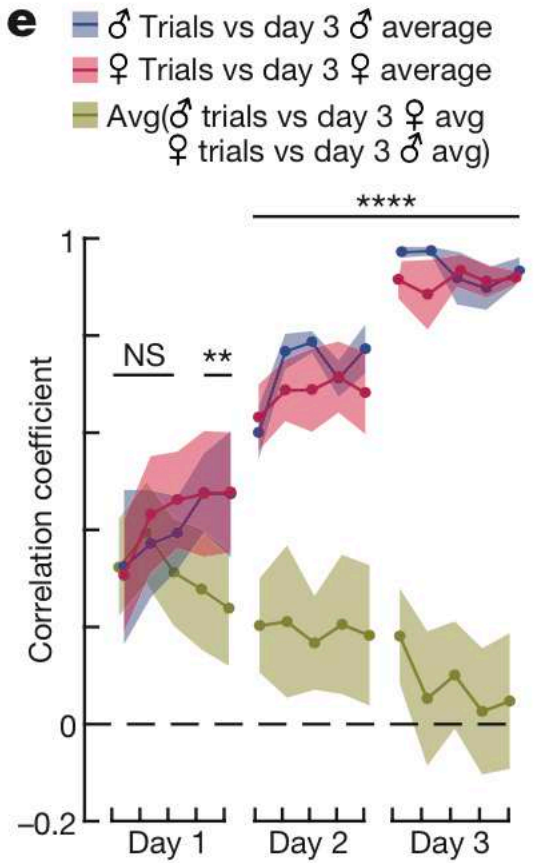
Cell activity represents different social behavior



(Remedios R, et al, 2017)

Neurons' sex preference polarizes during sex experience

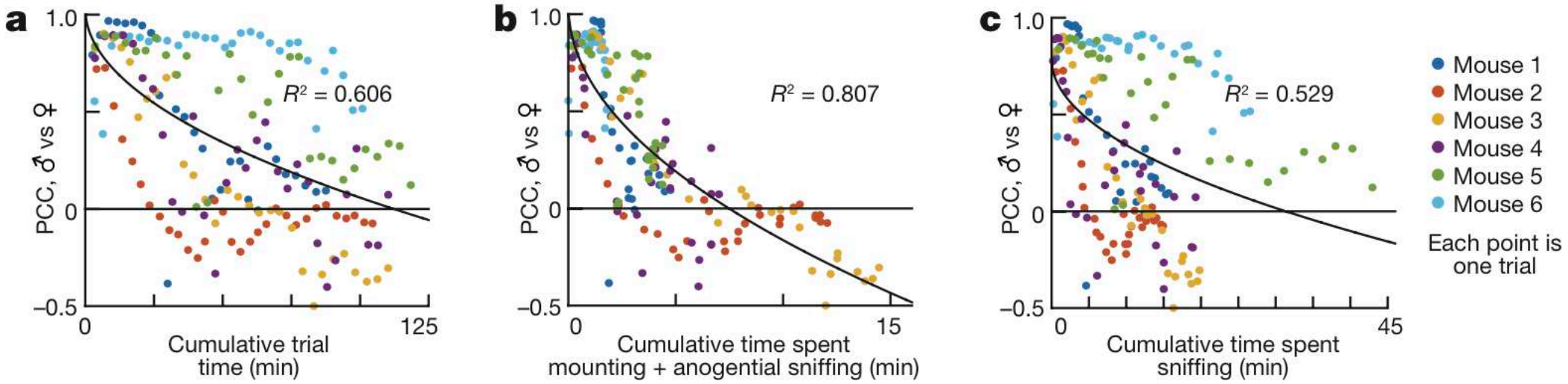




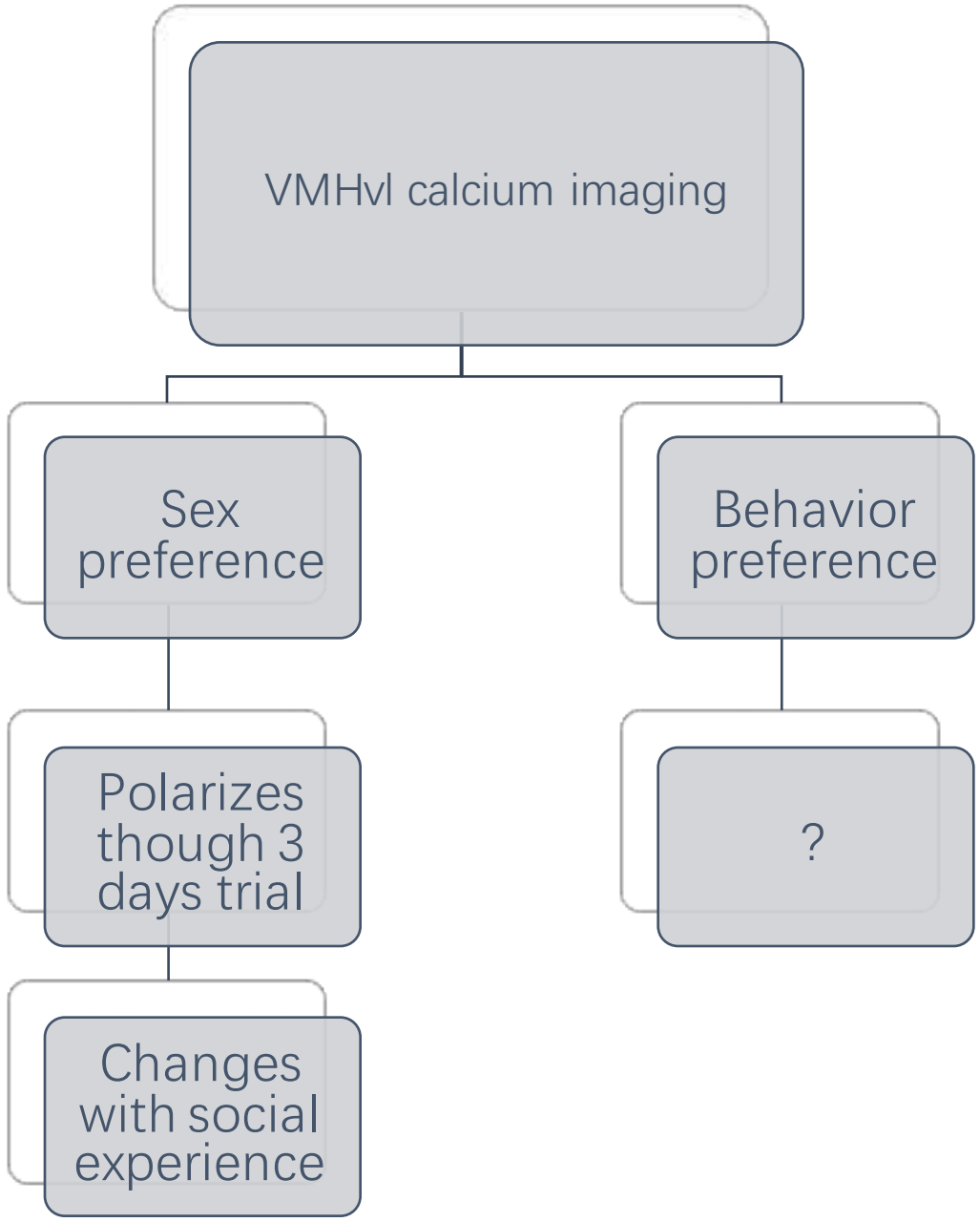
PCC, Pearson's correlation coefficient

(Remedios R, et al, 2017)

polarization dynamic



(Remedios R, et al, 2017)


VMHvl calcium imaging
Sex preference
Behavior preference
Polarizes though 3 days trial
?
Changes with social experience

Reference

- Stagkourakis S, Spigolon G, Liu G, Anderson DJ. Experience-dependent plasticity in an innate social behavior is mediated by hypothalamic LTP. Proc Natl Acad Sci U S A. 2020;117(41):25789-25799. doi:10.1073/pnas.2011782117
- Zelikowsky M, Hui M, Karigo T, et al. The Neuropeptide Tac2 Controls a Distributed Brain State Induced by Chronic Social Isolation Stress. Cell. 2018;173(5):1265-1279.e19. doi:10.1016/j.cell.2018.03.037
- Remedios R, Kennedy A, Zelikowsky M, Grewe BF, Schnitzer MJ, Anderson DJ. Social behaviour shapes hypothalamic neural ensemble representations of conspecific sex. Nature. 2017;550(7676):388-392. doi:10.1038/nature23885
- Lee H, Kim DW, Remedios R, et al. Scalable control of mounting and attack by Esr1+ neurons in the ventromedial hypothalamus. Nature. 2014;509(7502):627-632. doi:10.1038/nature13169
- Dankert, Heiko et al. (2009) Automated monitoring and analysis of social behavior in Drosophila. Nature Methods, 6 (4). pp. 297-303. ISSN 1548-7091. http://resolver.caltech.edu/CaltechAUTHORS:20090601-135542919

Reference

- Wang, Liming et al. (2011) Hierarchical chemosensory regulation of male-male social interactions in Drosophila.Nature Neuroscience, 14 (6). pp. 757-762. ISSN 1097-6256.http://resolver.caltech.edu/CaltechAUTHORS:20110614-081823526
- Burgos-Artizzu, Xavier P. et al. (2012) Social behavior recognition in continuous video. In: 2012 IEEE Conference on Computer Vision and Pattern Recognition (CVPR). IEEE , Piscataway, NJ, pp. 1322-1329. ISBN 978-1-4673-1226-4 http://resolver.caltech.edu/CaltechAUTHORS:20120731-115125060
- Adolphs, Ralph and Anderson, David (2013) Social and emotional neuroscience: Editorial overview. Current Opinion in Neurobiology, 23 (3). pp. 291-293. ISSN 0959-4388.http://resolver.caltech.edu/CaltechAUTHORS:20130919-125746689
- Hong, Weizhe and Kennedy, Ann and Burgos-Artizzu, Xavier P. et al. (2015) Automated measurement of mouse social behaviors using depth sensing, video tracking, and machine learning. Proceedings of the National Academy of Sciences, 112 (38). E5351-E5360. ISSN 0027-8424. PMCID PMC4603510.http://resolver.caltech.edu/CaltechAUTHORS:20150914-091025001

Reference

- David J. Anderson. (2016) Circuit modules linking internal states and social behaviour in flies and mice. Nature Reviews Neuroscience 17 pp. 692-704. doi:10.1038/nrn.2016.125
- Anderson, David J. (2016) Social behavior circuits in flies and mice. Chemical Senses, 41 (9). E111. ISSN 0379-864X. http://resolver.caltech.edu/CaltechAUTHORS:20161117-131559559
- Remedios, Ryan and Kennedy, Ann and Zelikowsky, Moriel et al. (2017) Social behaviour shapes hypothalamic neural ensemble representations of conspecific sex. Nature, 550 (7676). pp. 388-392. ISSN 0028-0836. http://resolver.caltech.edu/CaltechAUTHORS:20171019-073428081
- Watanabe, Kiichi and Chiu, Hui and Pfeiffer, Barret D. et al. (2017) A Circuit Node that Integrates Convergent Input from Neuromodulatory and Social Behavior-Promoting Neurons to Control Aggression in Drosophila. Neuron, 95 (5). pp. 1112-1128. ISSN 0896-6273. http://resolver.caltech.edu/CaltechAUTHORS:20170914-102103491