



Aug. Journal Club

# Unveiling Emotional States: Decoding the Emotional World of Animals

Gao Can  
Xing Limin  
Ma Mingze  
2023/ 8/ 31

# Basic emotions of human



喜  
Happiness



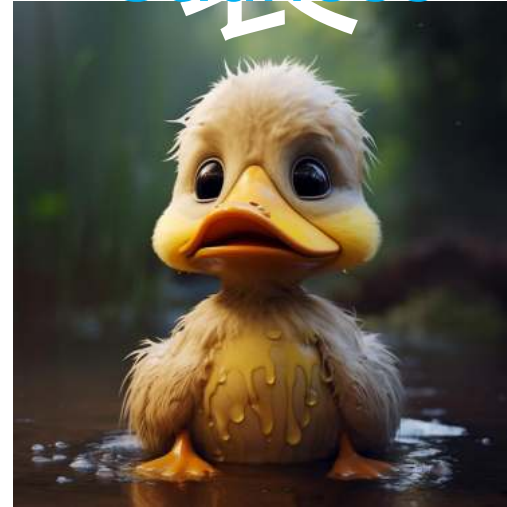
怒  
Anger



哀  
Sadness



惧  
Fear



- **Do animals have emotions like us?**

Gao Can

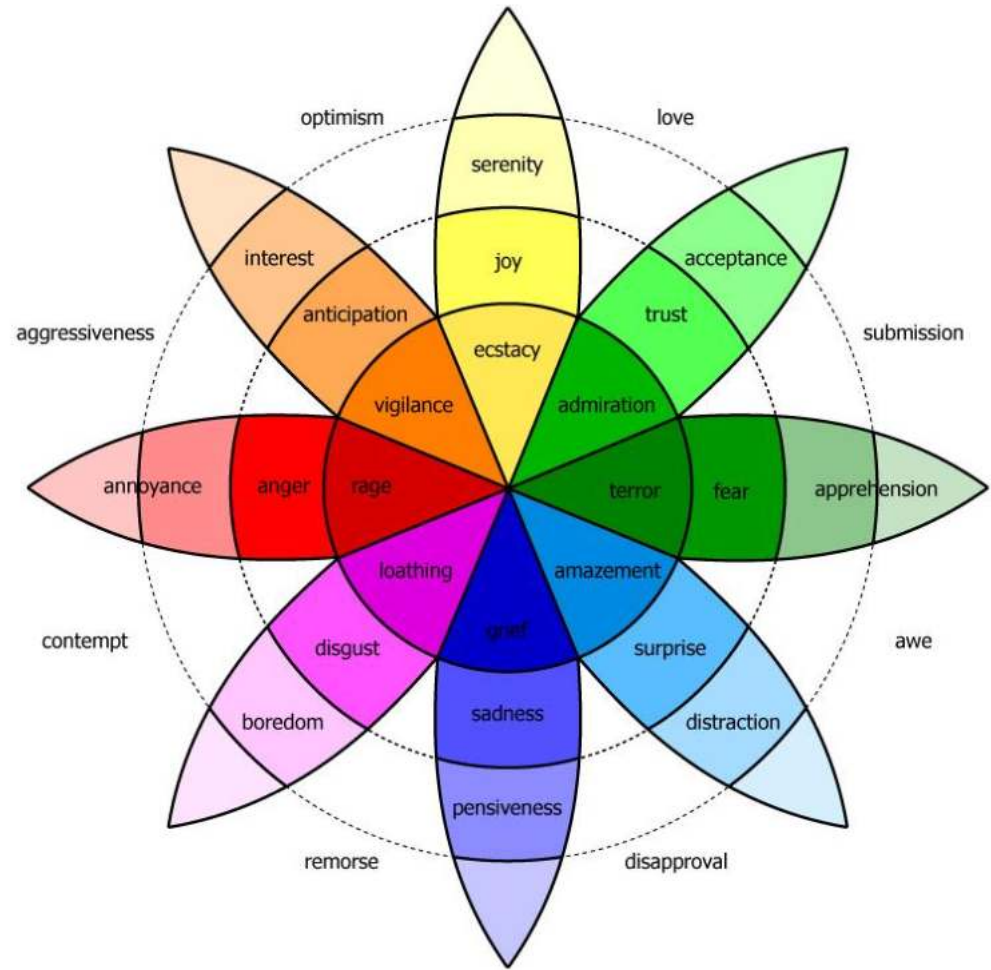
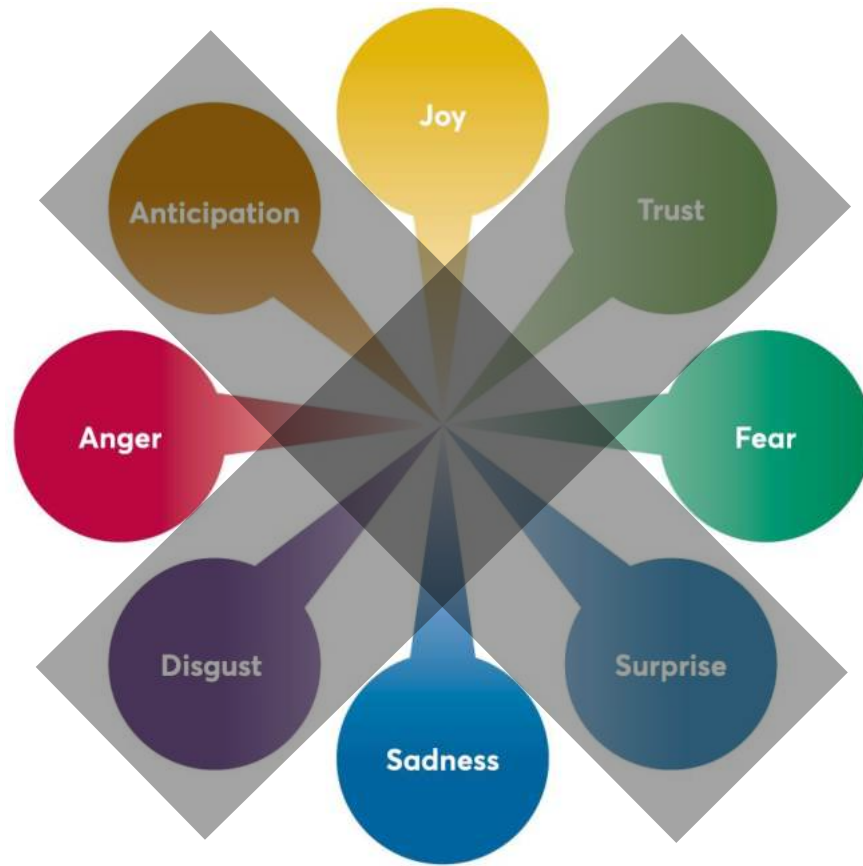
- **How to study emotion-like behaviors in animals?**

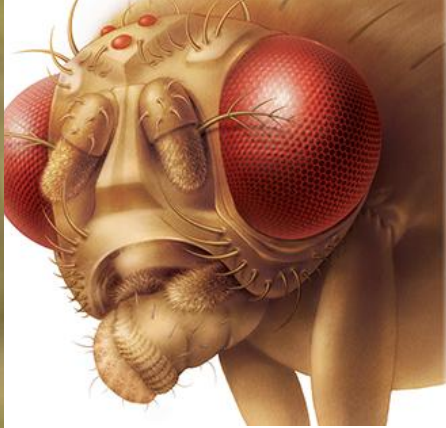
Ma Mingze

- **Impact of animal emotions on behavior.**

Xing Limin

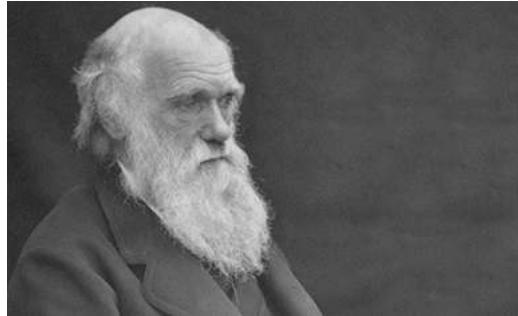
# Basic emotions of human



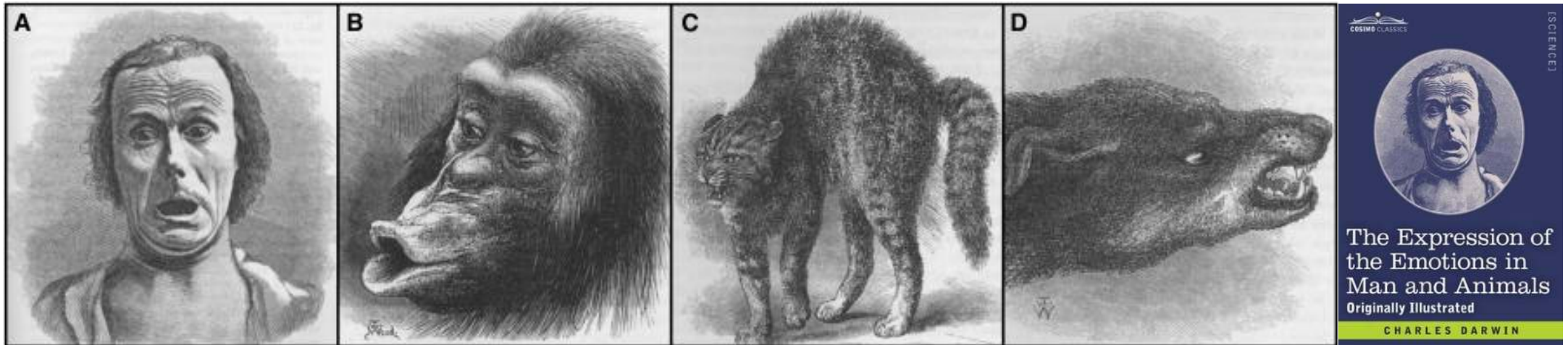


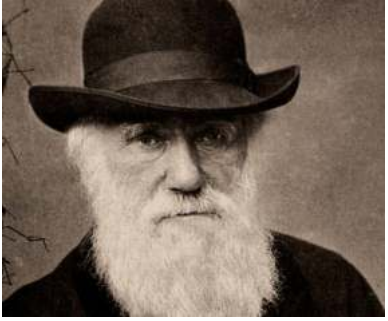
**Do they *feel*  
the emotion?**





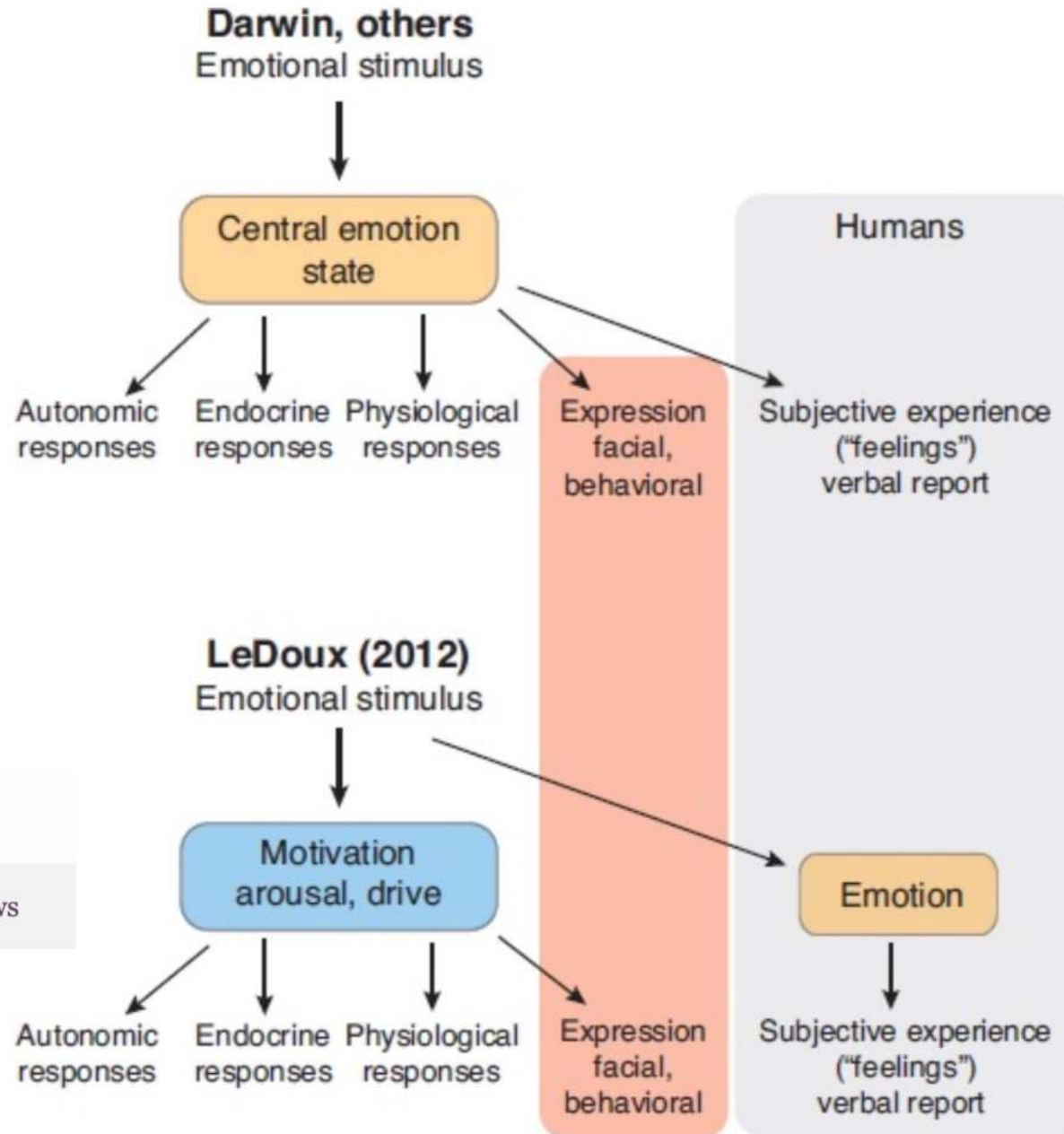
“Even insects express anger, terror, jealousy and love, by their stridulation.”—Charles Darwin, *The Expression of the Emotions in Man and Animals*





Joseph E. LeDoux, PhD

MUSICIAN: Music Videos & Slideshows



- Joseph LeDoux - A River of Hope and Love Flows Through a Dark Abyss (full album) [2018]
- Slideshow: "So We Are" at Sidewalk
- Slideshow: THE BRAIN IN WORDS AND MUSIC: "THEORY OF MY MIND" - The musicians on the stage September 29, 2010. Don Hill's, NYC
- Fearing - The Amygdaloids
- Slideshow: "All in Our Minds" EP Release Party
- Slideshow: The Amygdaloids (with Mark Mitton) at the Sidewalk Cafe 5-9-2012
- Mind Over Matter - The Amygdaloids (with Rosanne Cash)
- Brainstorm - The Amygdaloids
- Slideshow: The Amygdaloids: "THEORY OF MY MIND" RELEASE PARTY at Don Hill's, Sept. 29, 2010
- The making of 'All in Our Minds'-- a new EP by The Amygdaloids
- The Amygdaloids' "Map of Your Mind"

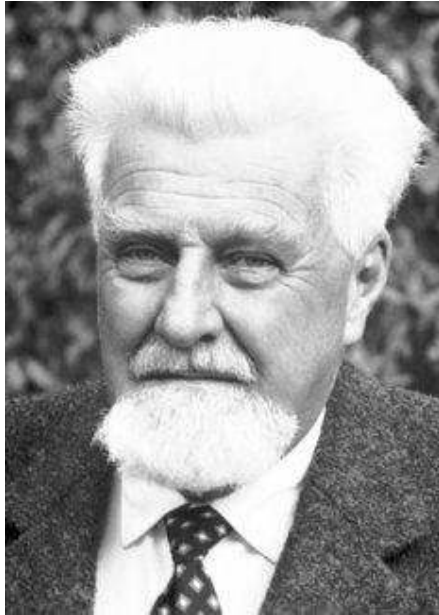
# The Amygdaloids'

## "Map of Your Mind"



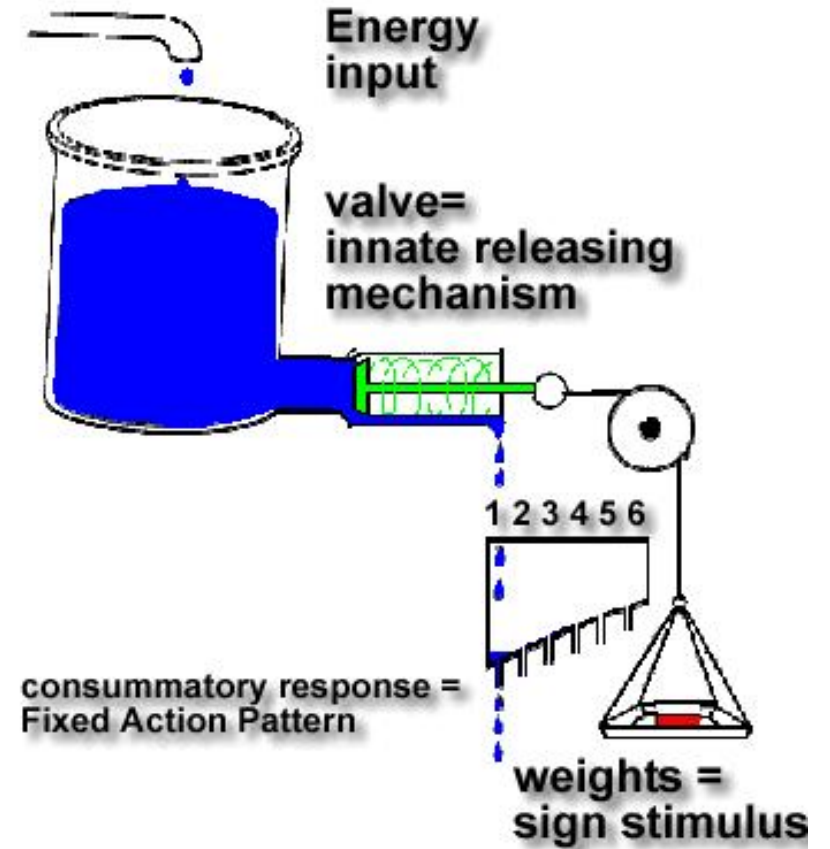
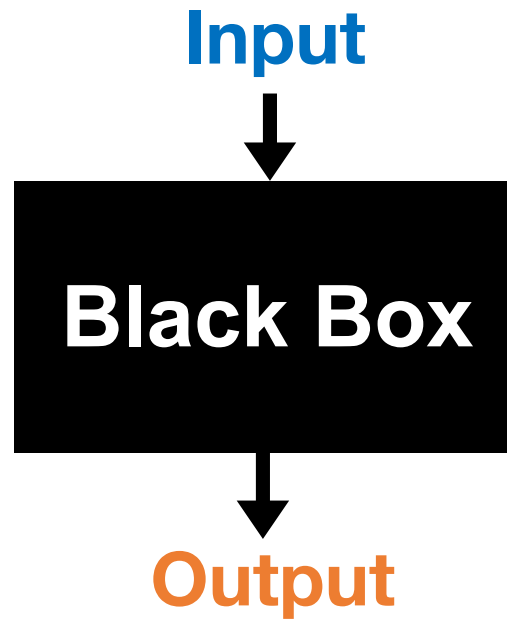
What is **EMOTON**?

# Lorenz's Psycho hydraulic Model

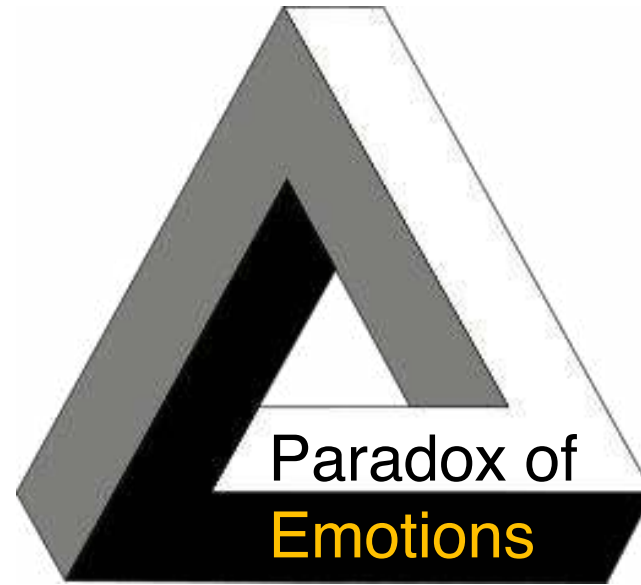


**Konrad  
Lorenz**

1973 Nobel Prize in  
Physiology or  
Medicine



Self-evident and  
obvious



Extremely difficult to define  
in objective scientific terms

We excise the word “emotion” altogether from our scientific  
vocabulary. [LeDoux J. Neuron. 2012](#)

But how can we study a topic so important if we cannot even  
agree on operational criteria for what it is? --David Anderson

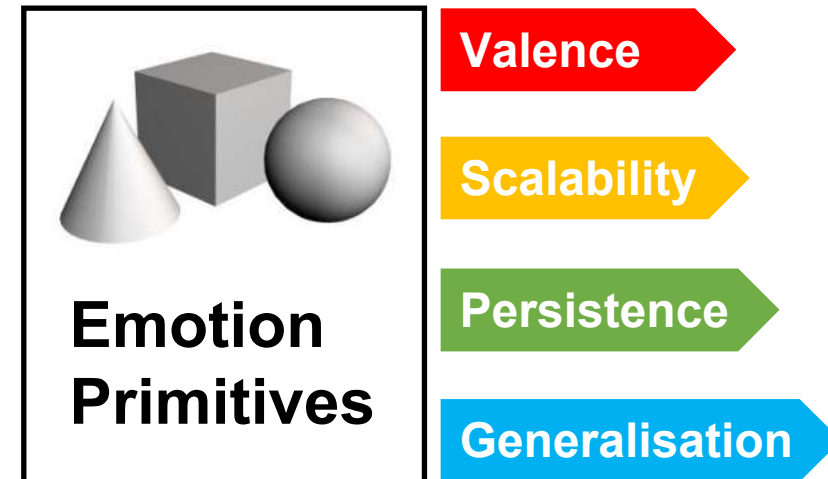
# What is emotion?

Emotion, *émouvoir*, which means "to stir up"

**Emotions** are [mental states](#) brought on by neurophysiological changes, variously associated with thoughts, feelings, behavioral responses, and a degree of [pleasure](#) or [displeasure](#). Wikipedia

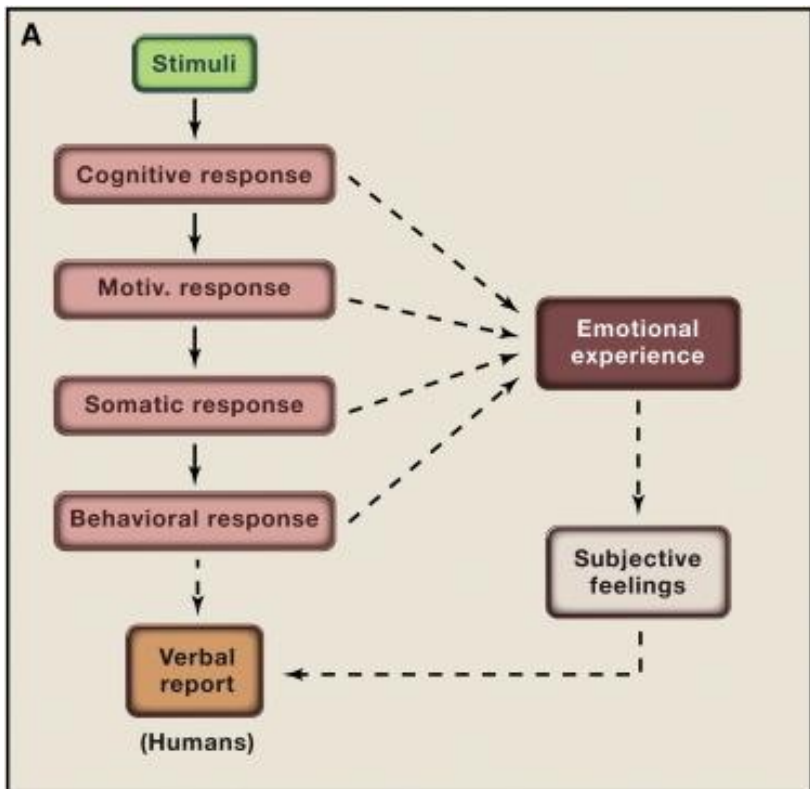
Emotional expression are easily recognizable not only in **humans**, but also in related **mammalian species**, even in **insects**. Darwin

**Emotions** are an **internal CNS state** that gives rise to **physiological, behavioral, cognitive** (& subjective) responses. [Anderson and Adolphs \(2014\)](#)

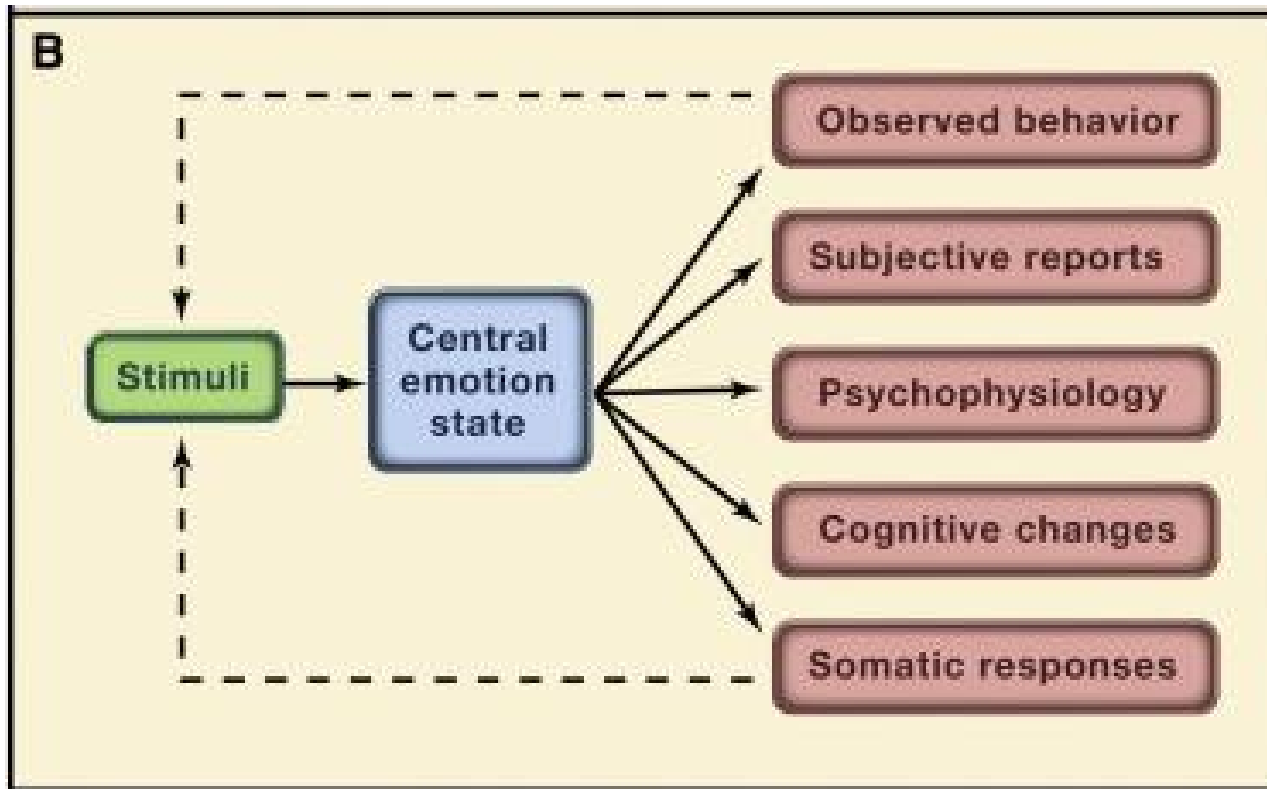


# The causal relationship between emotions and observable behavior

## Conventional views

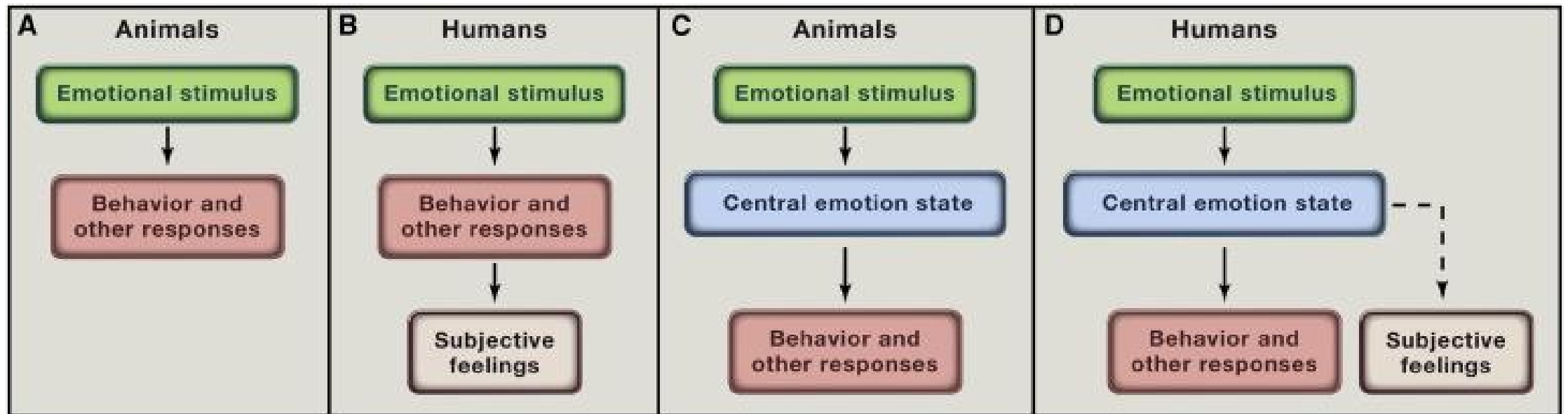


## Anderson's views



# The relationship between central emotion states and subjective feelings

## Behaviorist version of view



I feel 'afraid' because I run from the bear

I cry because I am sad.

## Scalability

“He who will attend to the starting of his horse...will perceive how perfect is the gradation from a mere glance at some unexpected object...to a jump so rapid and violent that the animal probably could not voluntarily whirl round in so rapid a manner.”—Darwin

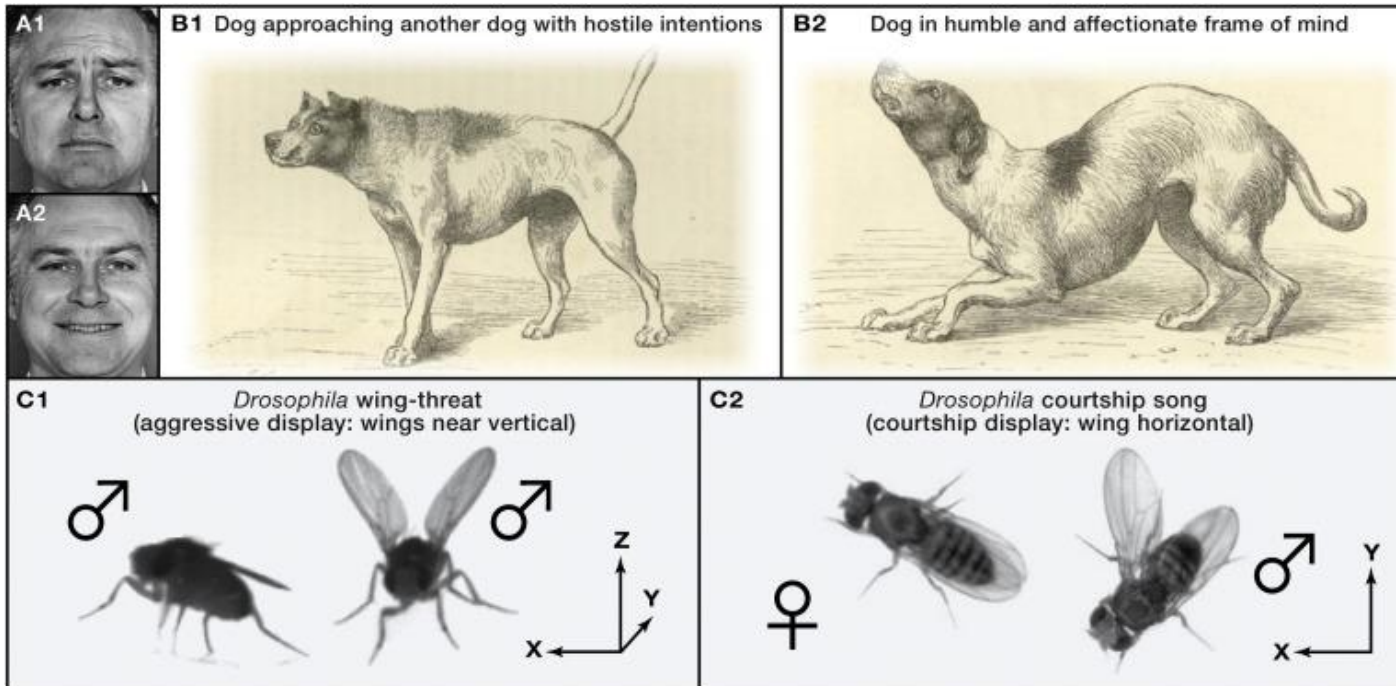
Scalability means different stimuli can create states of different strength.



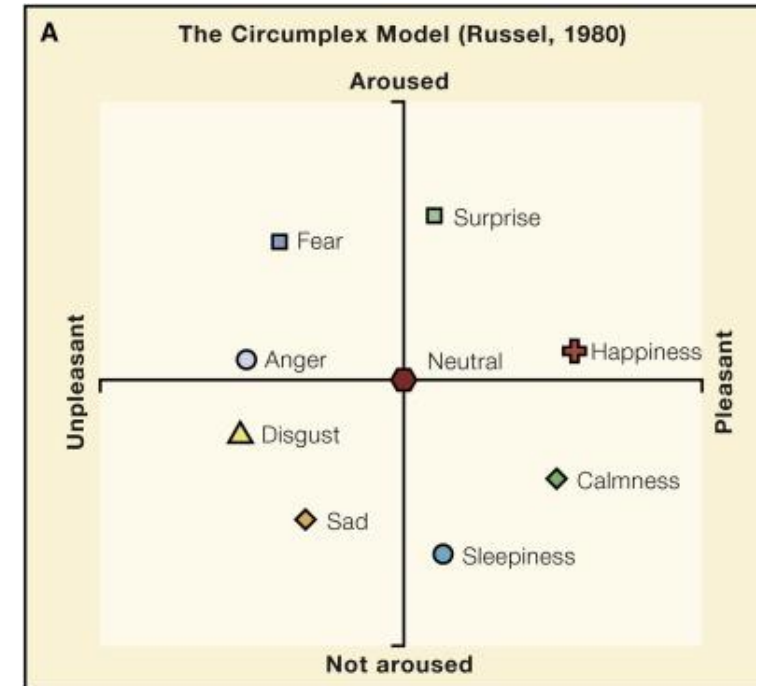
## Valence

“When actions of one kind have become firmly associated with any sensation or emotion, it appears natural that actions of a directly opposite kind...should be unconsciously performed...under the influence of a directly opposite sensation or emotion.”—Darwin

Valence, which means emotion can be positive, negative, or somewhere in between.



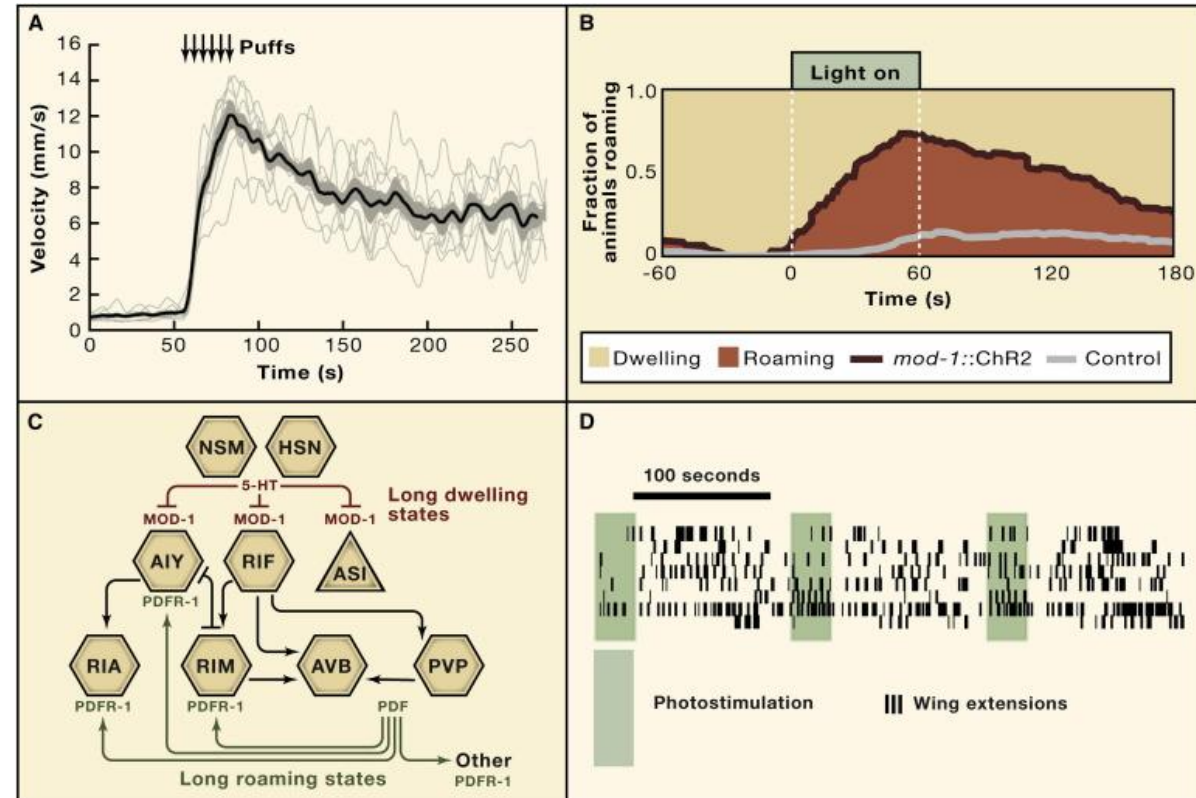
Examples of Darwin's Second Principle of Antithesis



Dimensional Models of Emotion

## Persistence

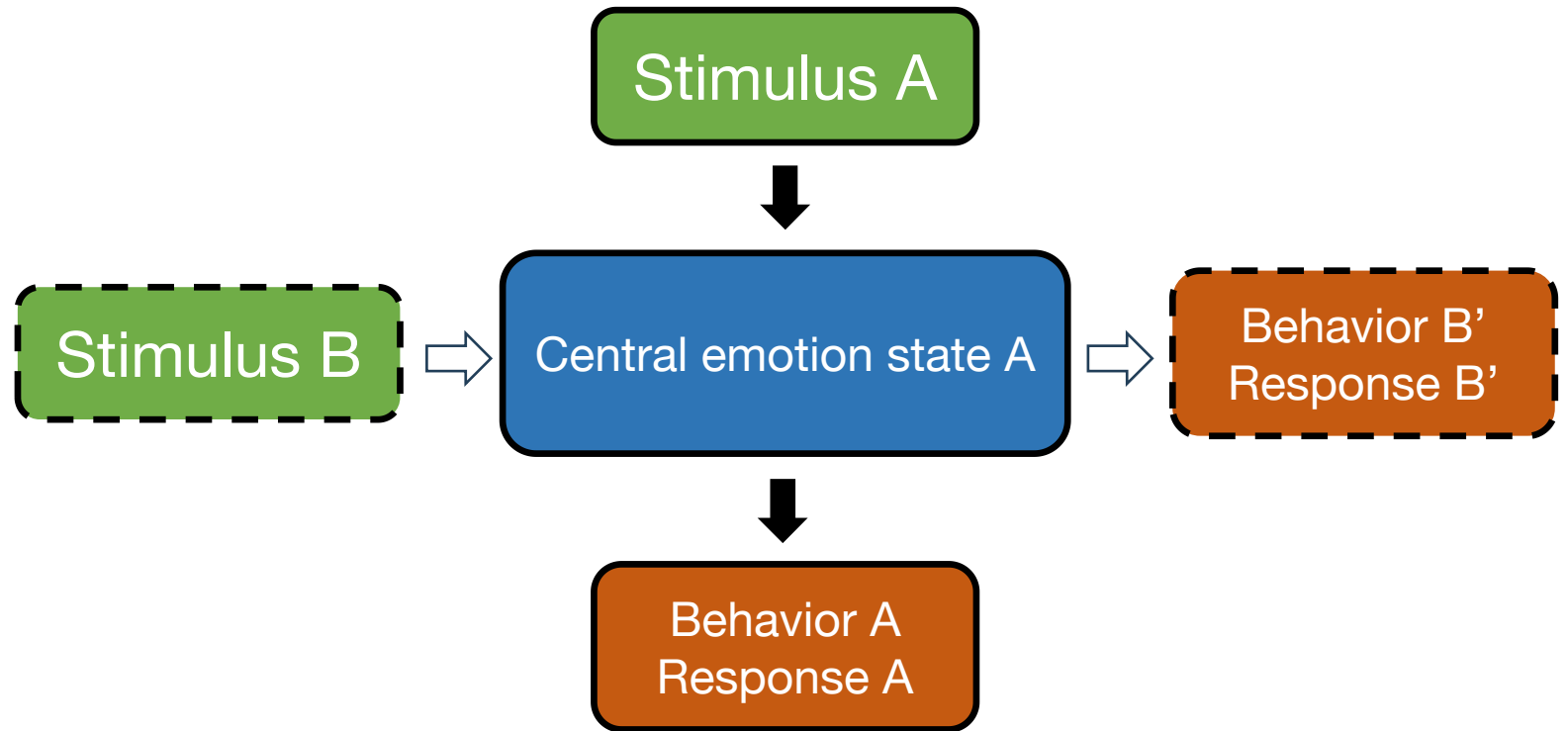
“A man may have his heart filled with the blackest hatred or suspicion, or be corroded with envy or jealousy...these feelings...commonly last for some time.”—Darwin



Experimental Examples of Persistent Activity in Flies and Worms

## Generalization

“When any sensation, desire, dislike, etc. has led during a long series of generations to some voluntary movement, then a tendency to the performance of a similar movement will almost certainly be excited, whenever the same, or any analogous or associated sensation...is experienced.”—Darwin



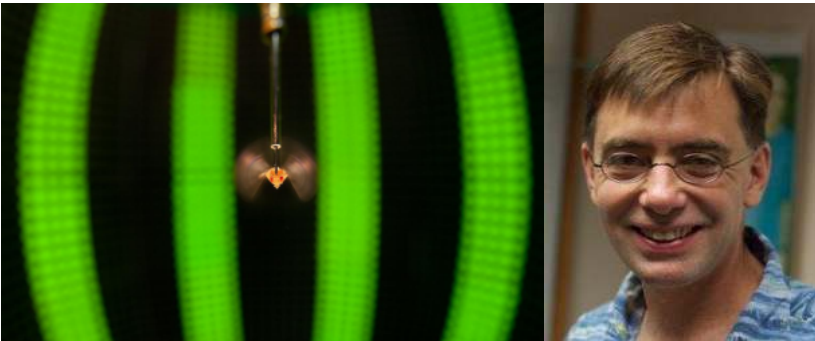
# Are Fleeing Fruit Flies Fraught with Fear?



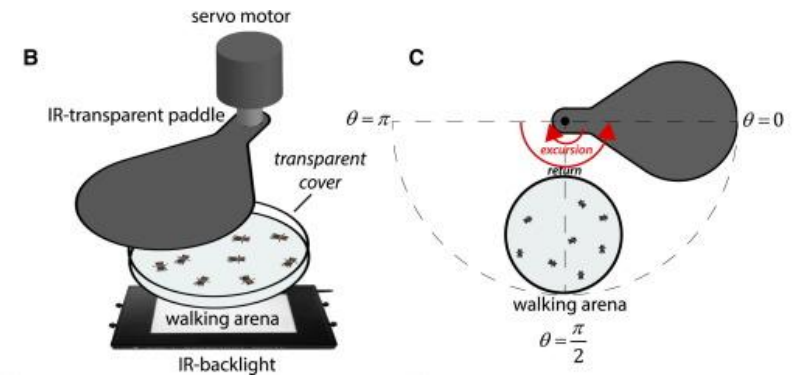
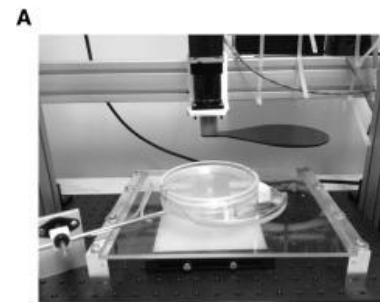
## Gwyneth Card, PhD

Investigator / 2022—Present

Dr. Card is an associate professor of neuroscience at Columbia University and a principal investigator at Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute. She was a group leader at HHMI's Janelia Research Campus from 2010-2022.



Michael H. Dickinson



William T. Gibson et al., 2015



Fraught with Fear?

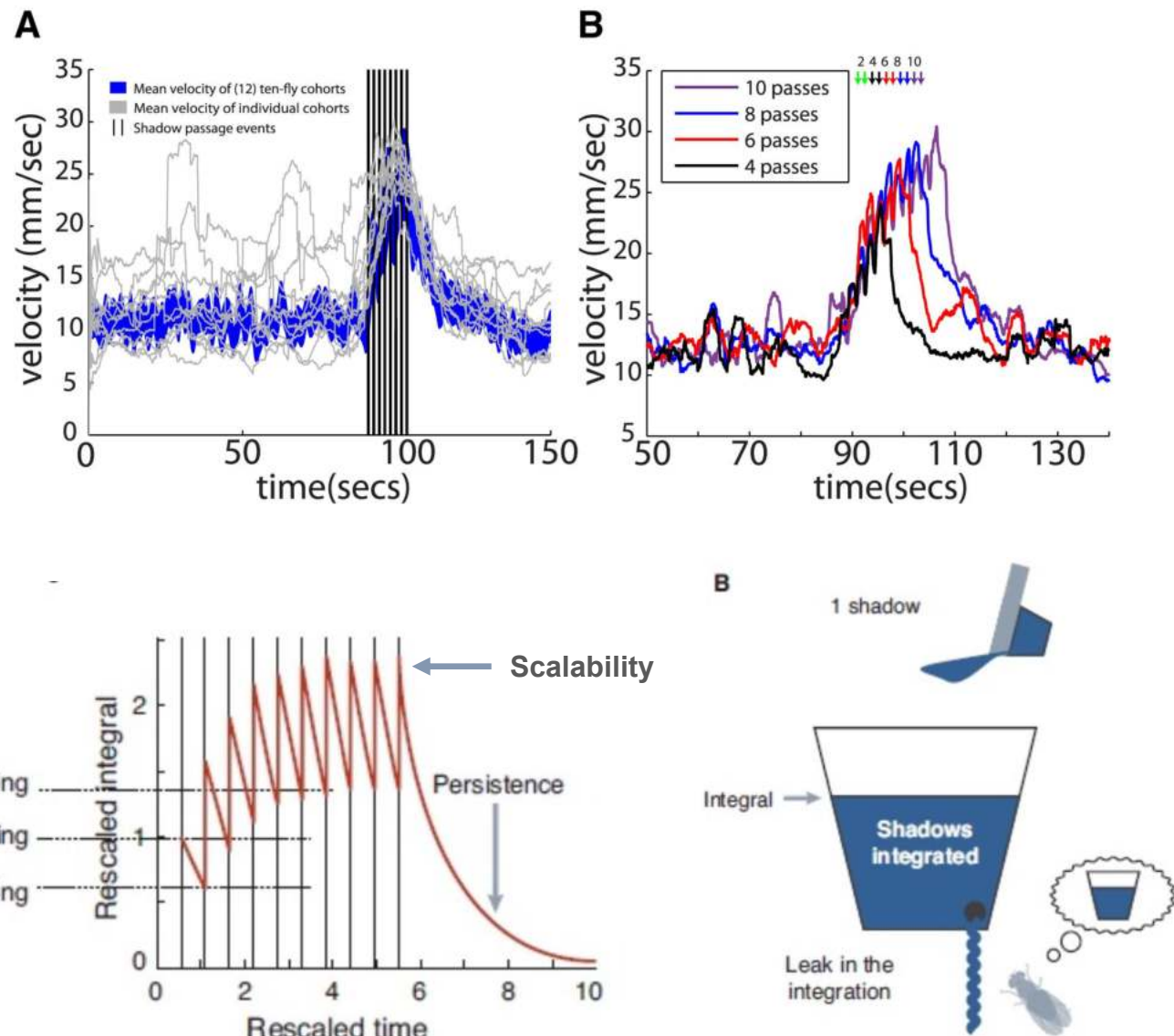
Robotic Escape Reflex?

## Occam's Razor

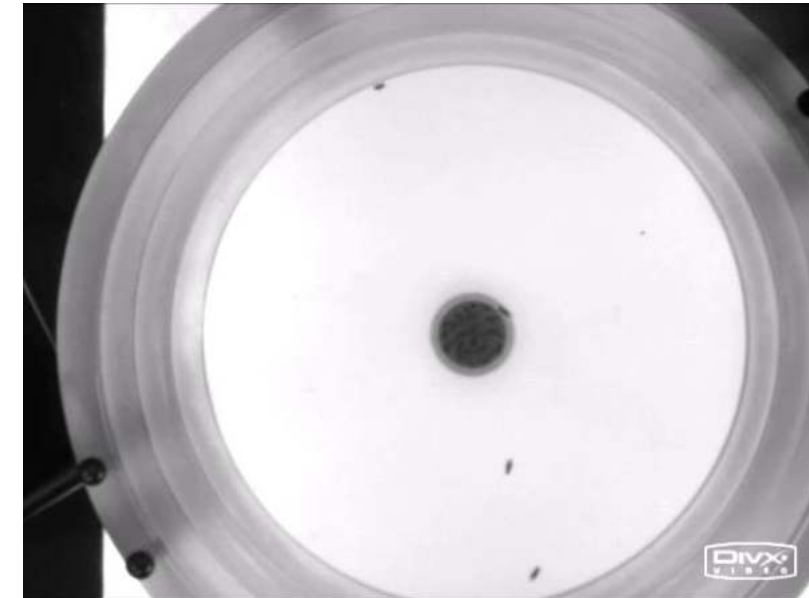
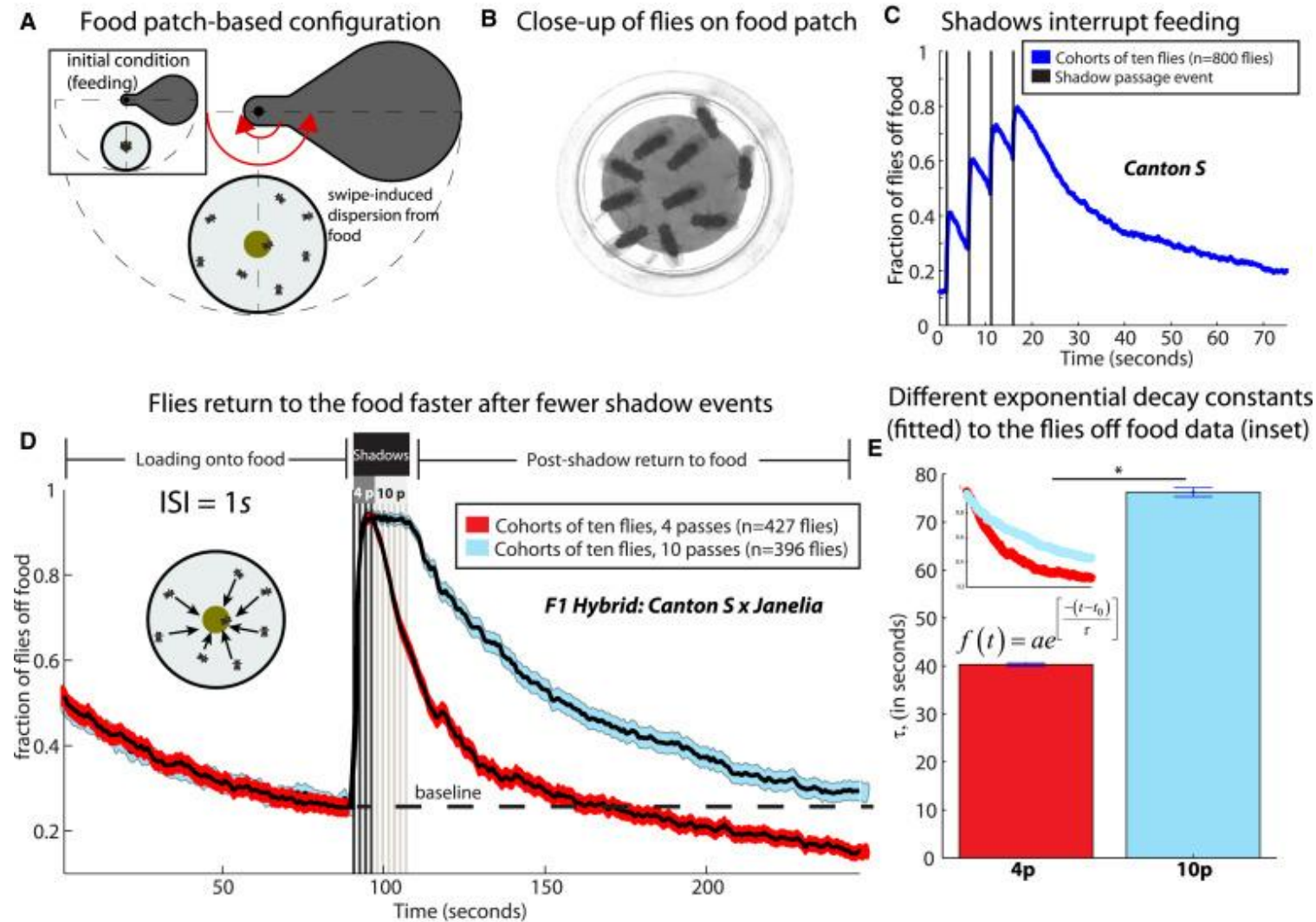


*"When faced with two equally good hypotheses, always choose the simpler."*

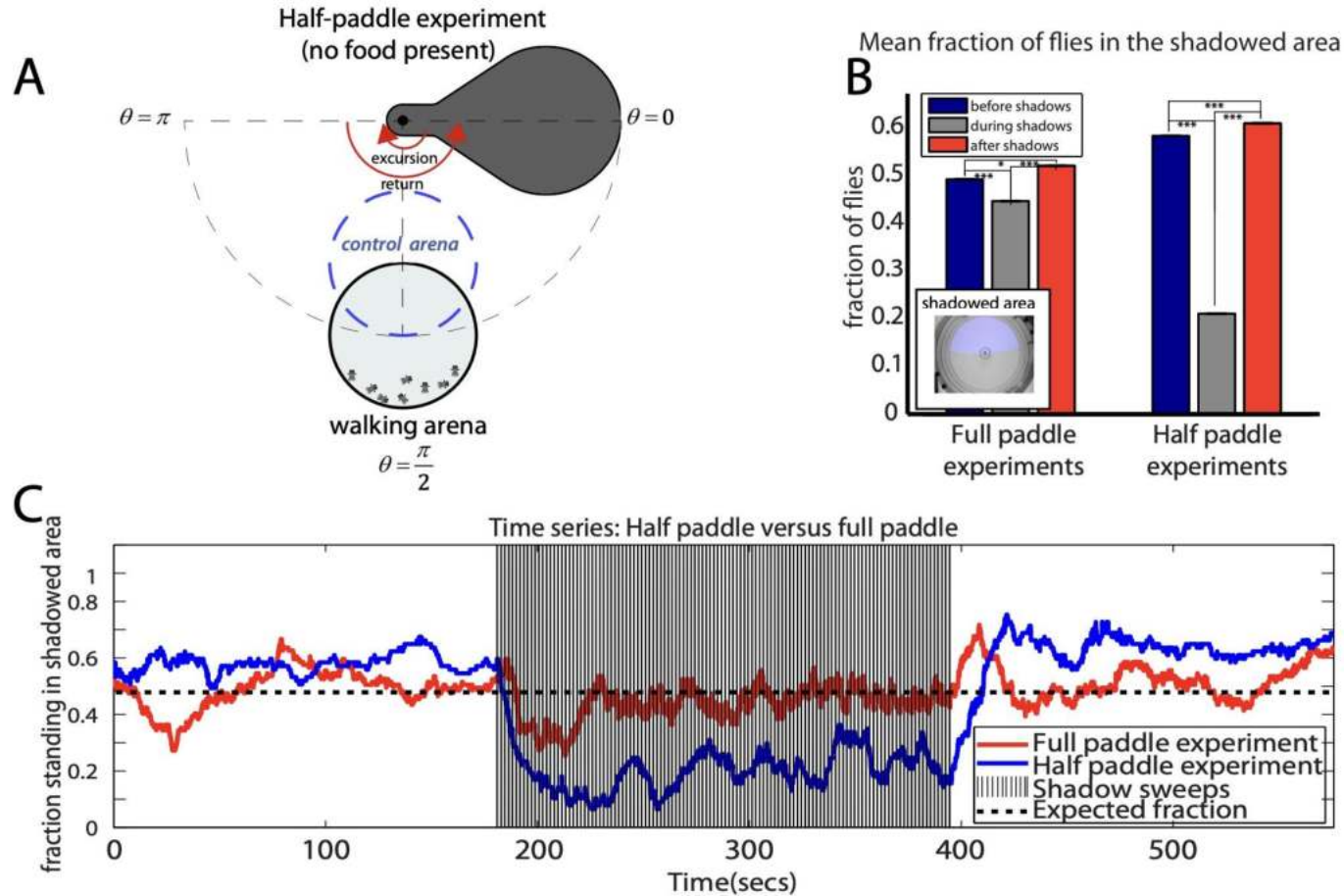
# ReVSA Behaviors Scale with Shadow Number



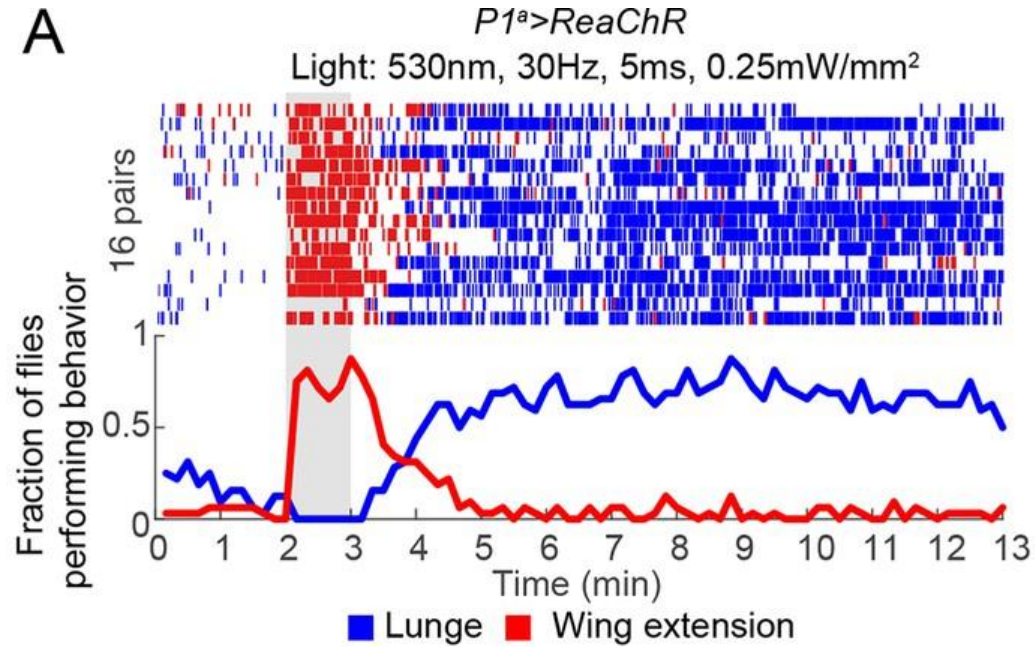
# Return Times in Food-Based ReVSA Assay Scale with Shadow Number



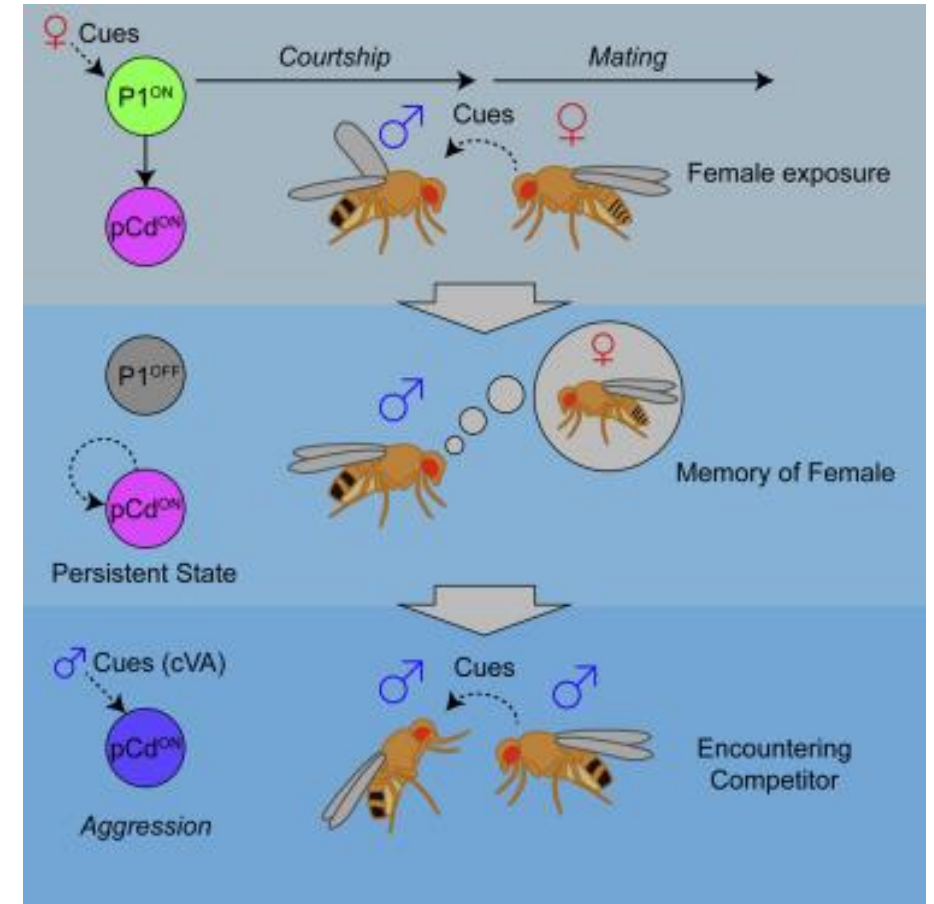
# Drosophila exhibits directed shadow avoidance



## Other evidence indicates that *Drosophila* possesses internal states

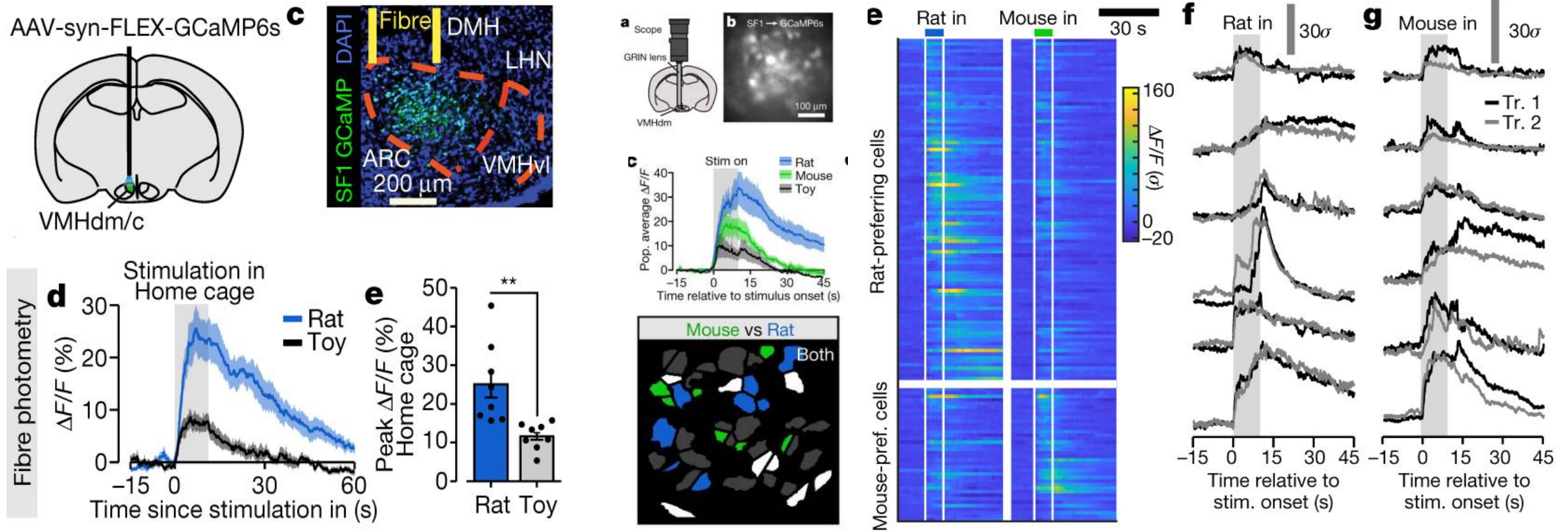


Eric D Hoopfer et al. ,2015



Yonil Jung et al. , 2020

# Stimulus-specific hypothalamic encoding of a persistent defensive state



# Summary

Emotions are an internal CNS state that gives rise to physiological, behavioral, cognitive (& subjective) responses;

Emotions contain generic attributes that are called emotion primitives, which are valence, scalability, persistence, generalization;

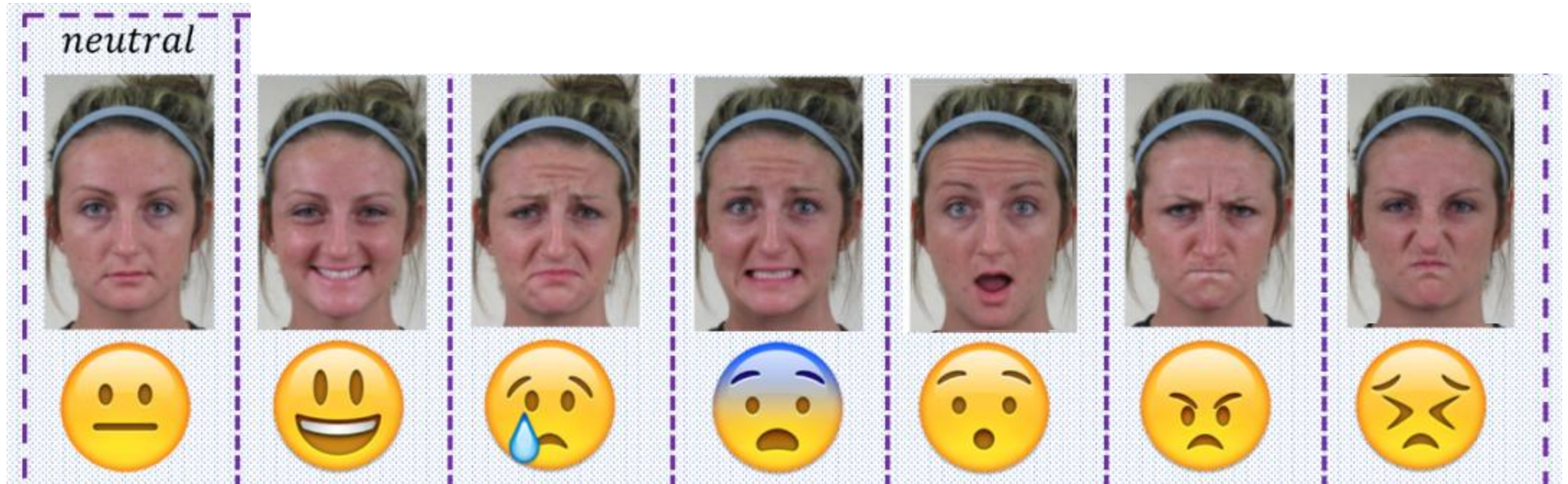
Animal behavior can be characterized by these emotional primitives, but it cannot be equated with “emotions” in the colloquial sense of the word, because we are defining “emotion” as an internal state for scientific purposes.

## PART2:

How to study emotion-like  
behavior in animals?

MMZ

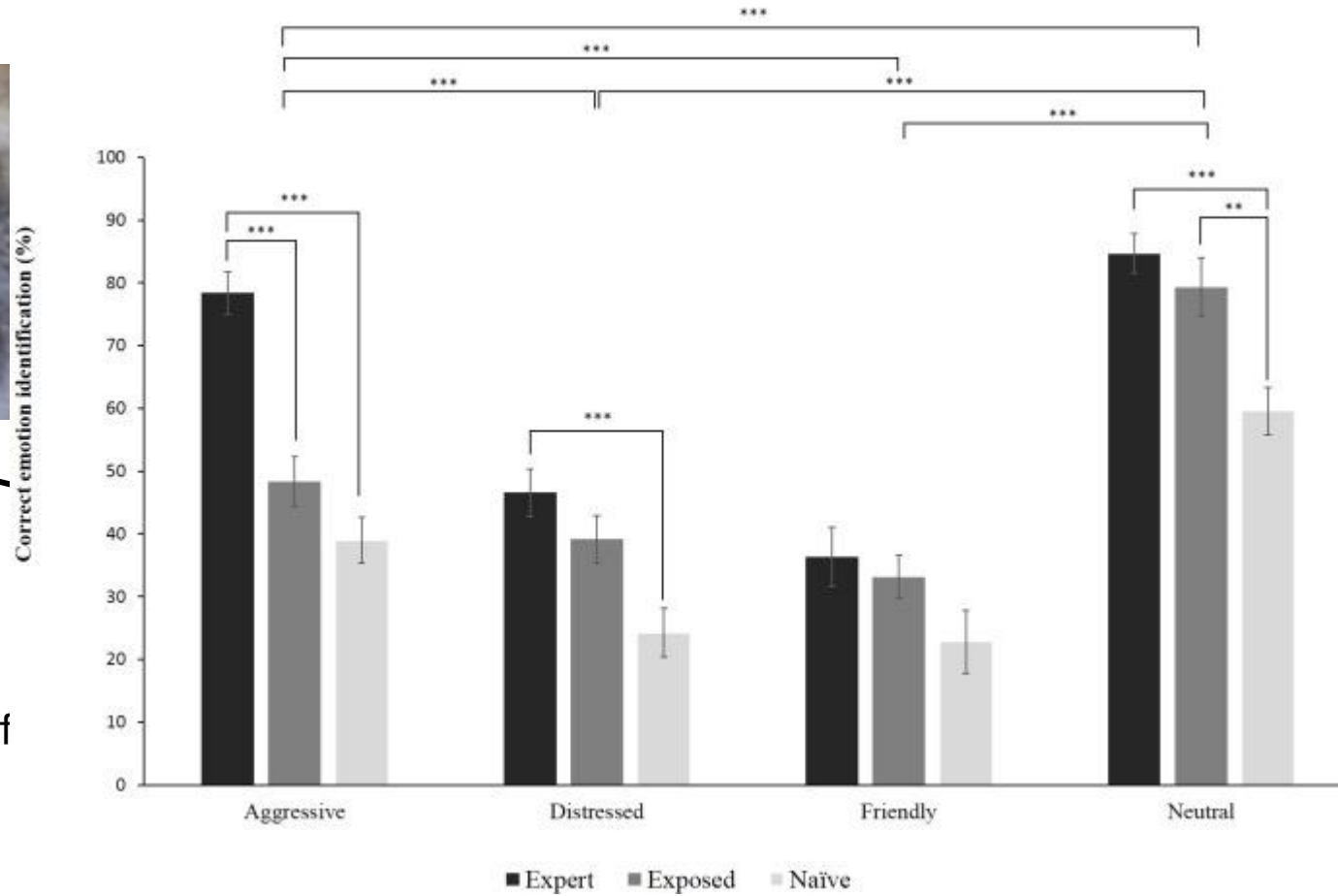
## The six basic emotions of humans



Can you understand the monkey's expression?



Friendly or Aff



ssed or Submissive

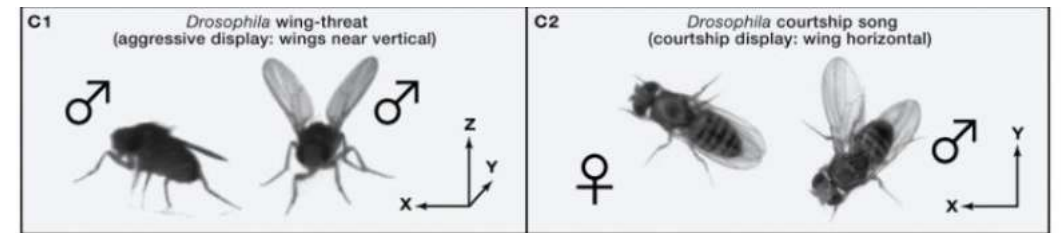
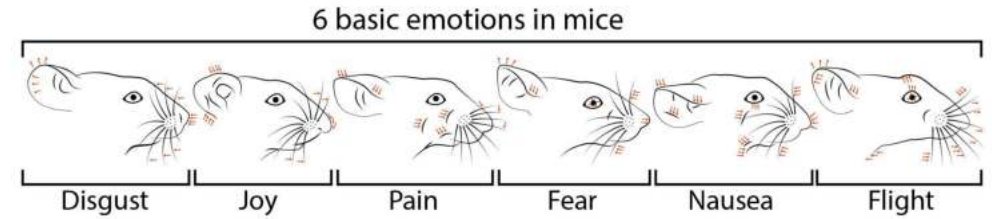
# Steps for Studying Animal Emotions

## Inducing emotions

- Anxious/Fear
- Depressed

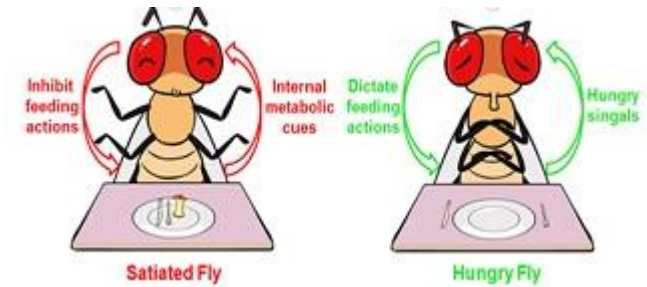
## Measuring emotions

## Emotions and brain

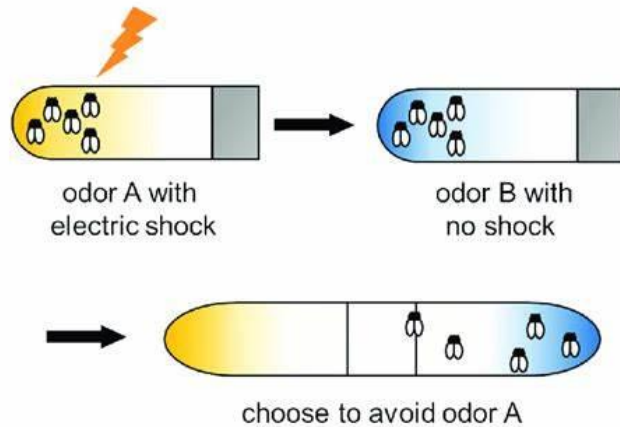


# Inducing insect emotion-like behavior

- Starvation
- Social isolation
- Predators
- Bitter food/poisons
- Noxious stimulation(electric shock, quake)



## SOCIAL ISOLATION



# Induction of mammalian emotions

Transgenic animal

Drug intervention

Social

New environment

Resource deprivation

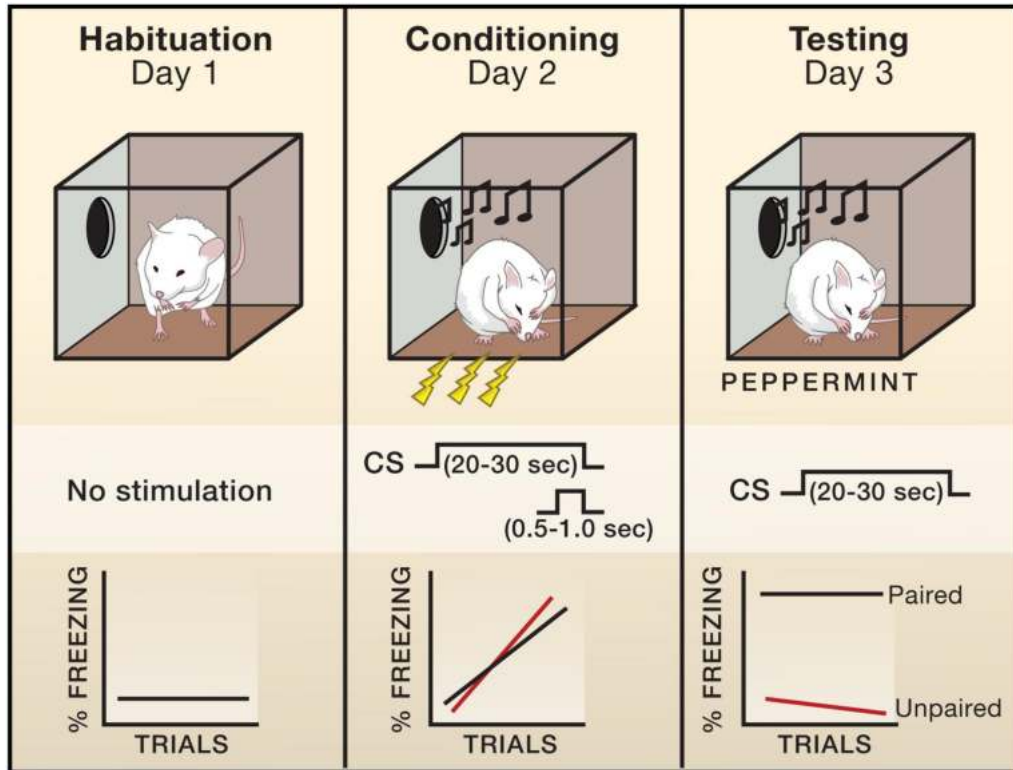
Fear Conditioning Test

Learned Helplessness(Seligman& Maier, 1967)

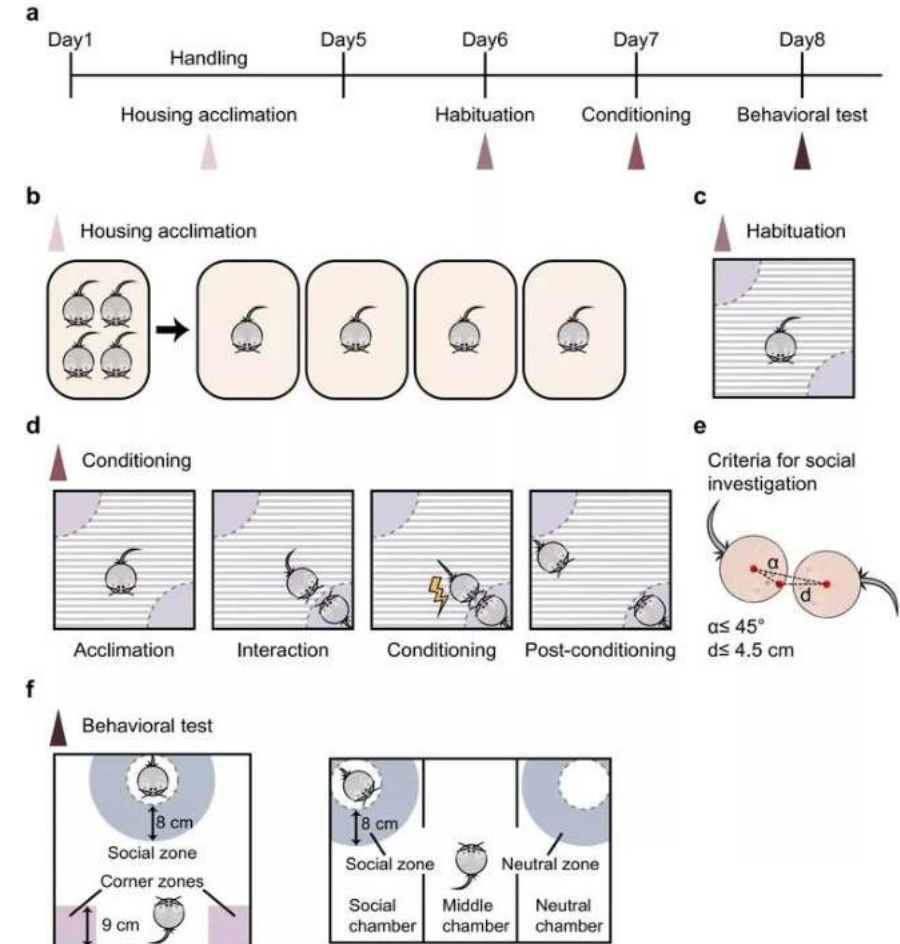
Rat models of postpartum depression

- Gestational Stress Models
- Maternal Separation Models, MS
- Chronic Social Stress, CSS
- Hormone Withdrawal Models

# Fear Conditioning Test

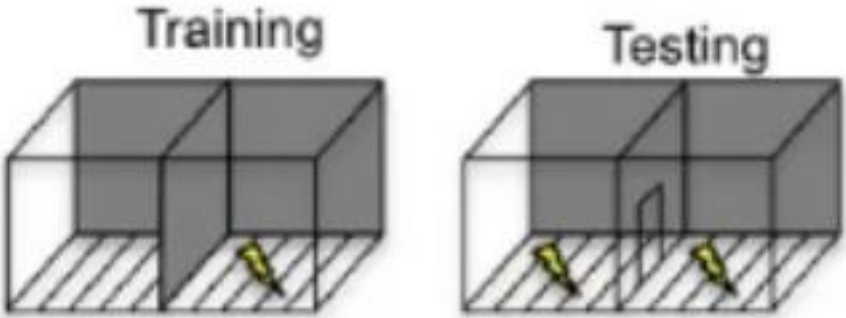
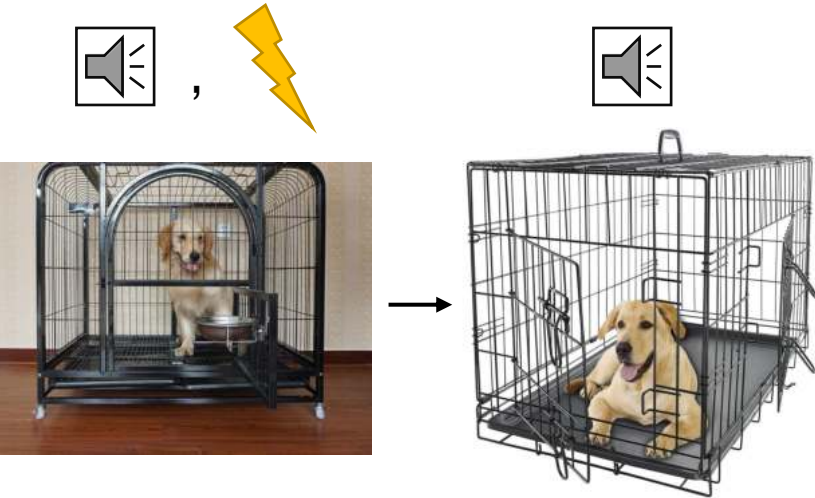


Johansen JP et al., *Cell*, 2011.



Zheng J, et al., *Neurosci Bull.*, 2021.

Learned Helplessness(Seligman& Maier, 1967)



45s shocks per min  
1h  
5d

10s shocks

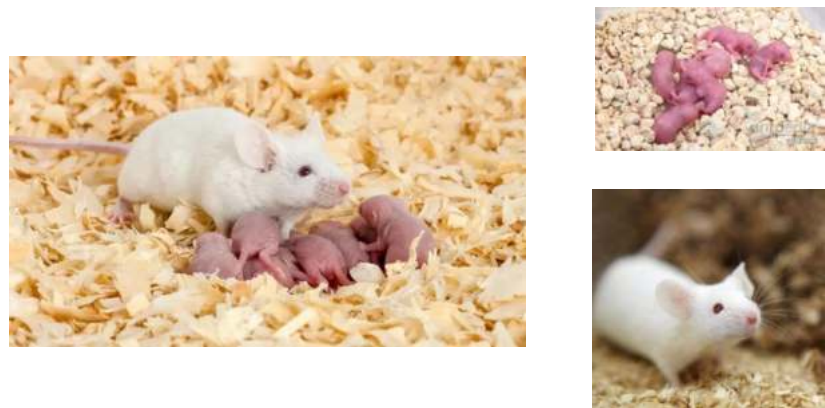
escape rate  
escape latency

# Rat models of postpartum depression

## Gestational Stress Models



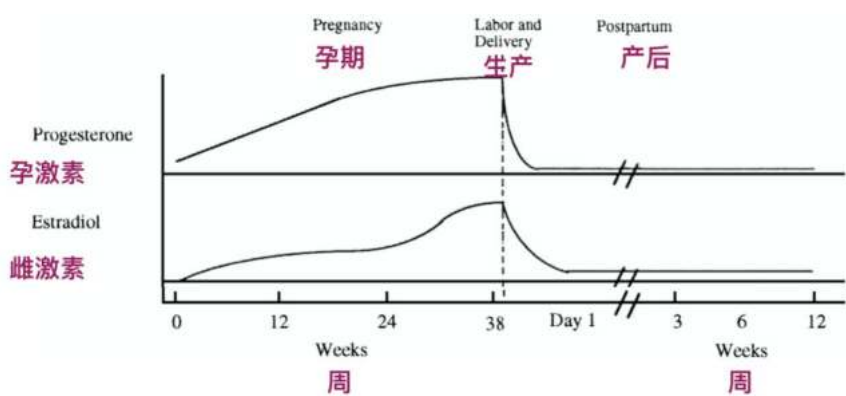
## Maternal Separation Models, MS



## Chronic Social Stress, CSS



## Hormone Withdrawal Models



# The impact of emotions on individuals

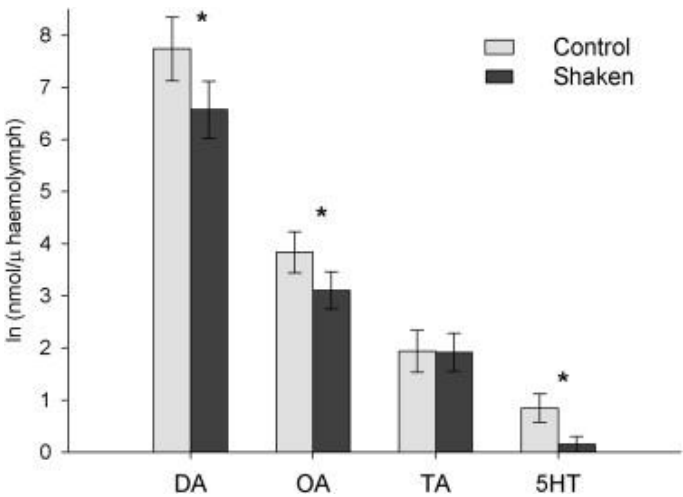
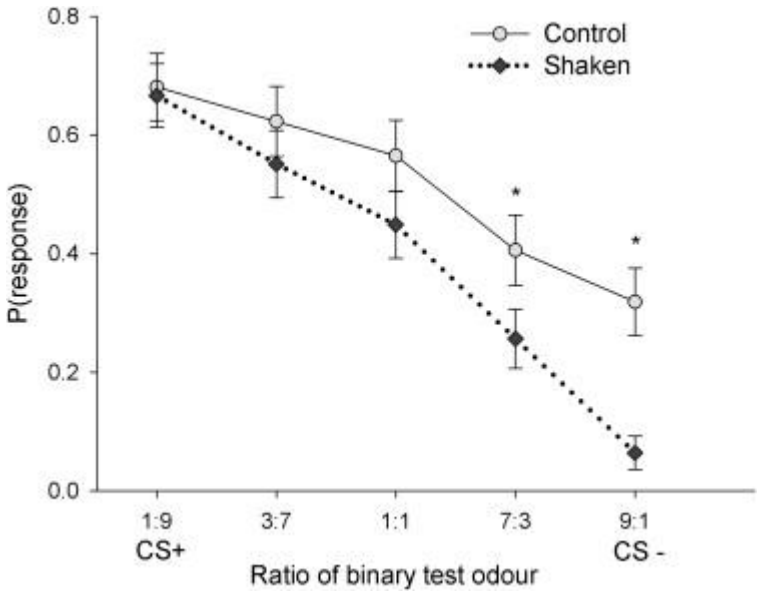
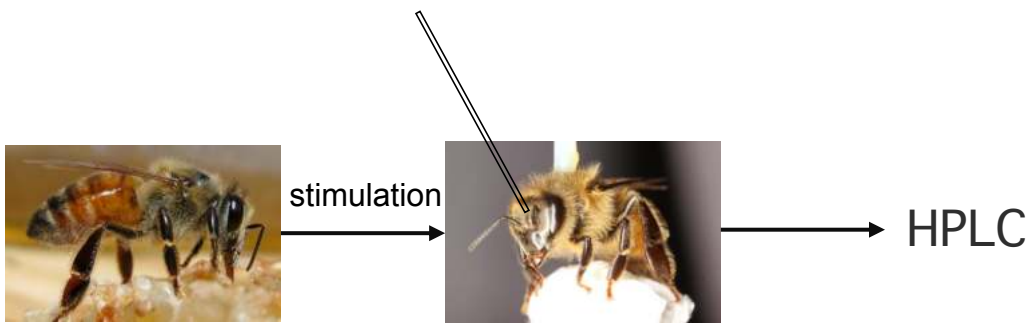
Anxiety-like behavior/Fear

Physiological

Depressive behavior

Cognitive

Behavior

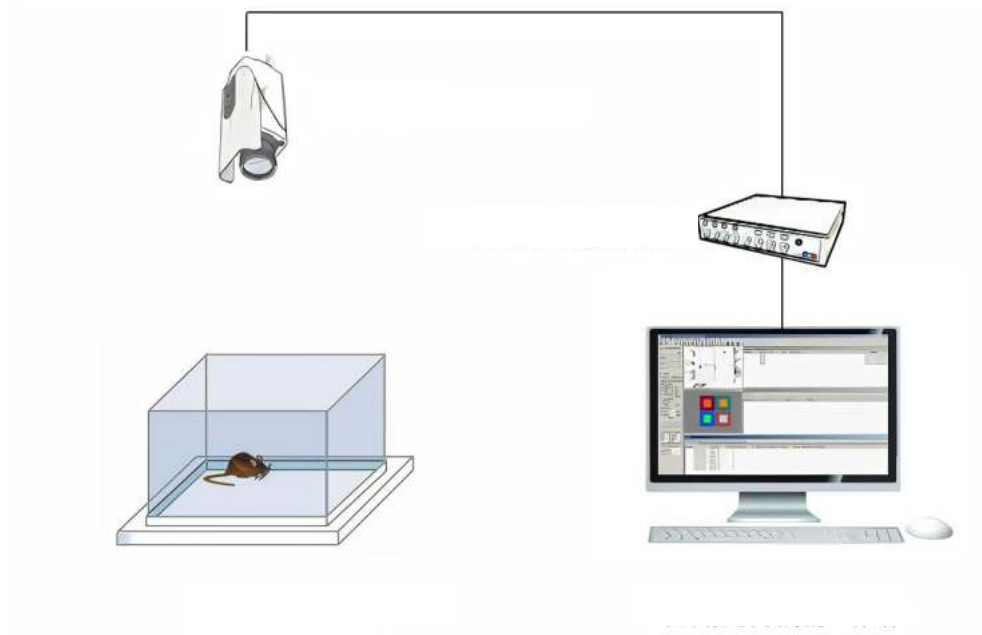


# Experimental methods for anxiety-like behavior

- Fear of a new environment
- Reduction in exploratory behavior



# Open Field Test(OFT)



Walking/Rest Time(Central Grid/Surrounding Grid)

Average Speed

Cross Grid Times

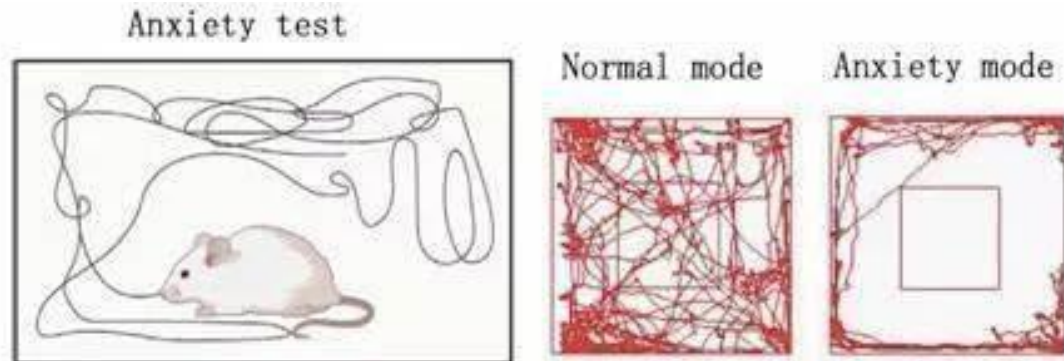
Number of cross grid times in the central grid

Stand Up Times

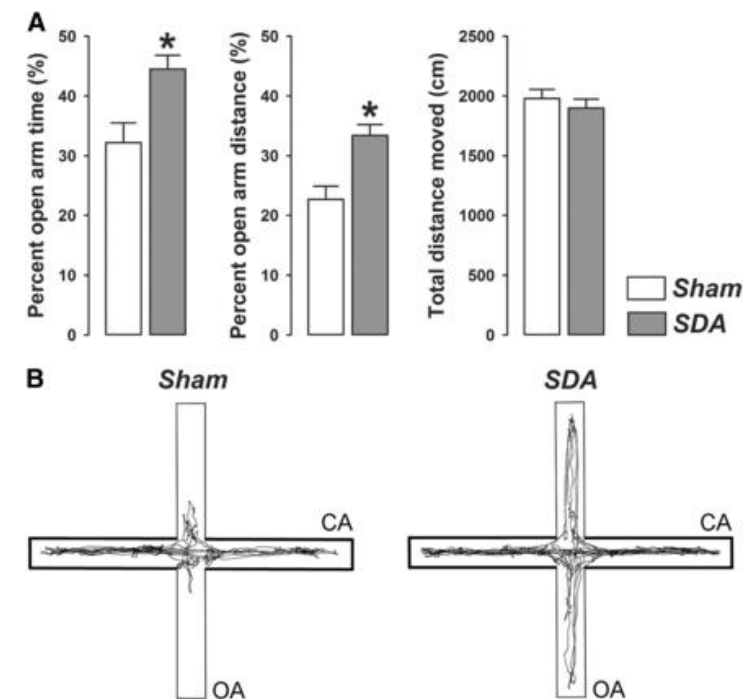
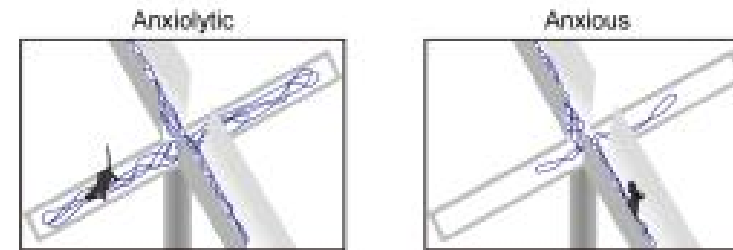
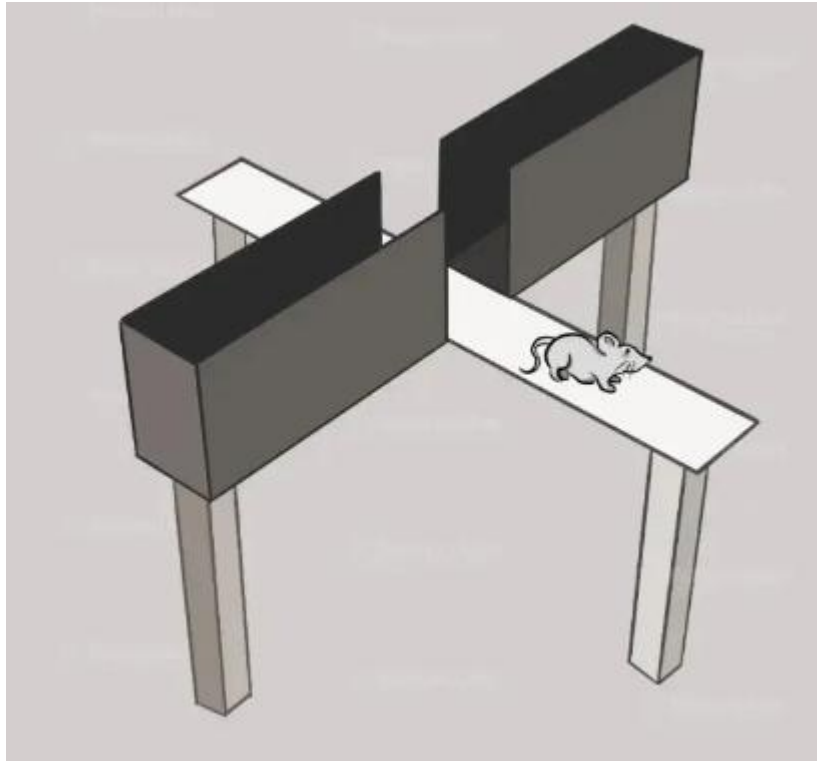
Defecating Time

Grooming frequency

Cross grid level

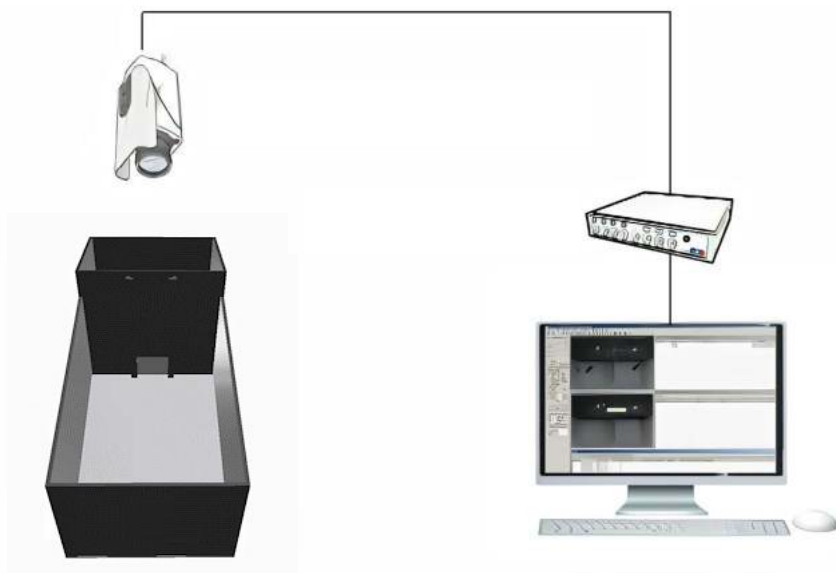


# Elevated Plus Maze

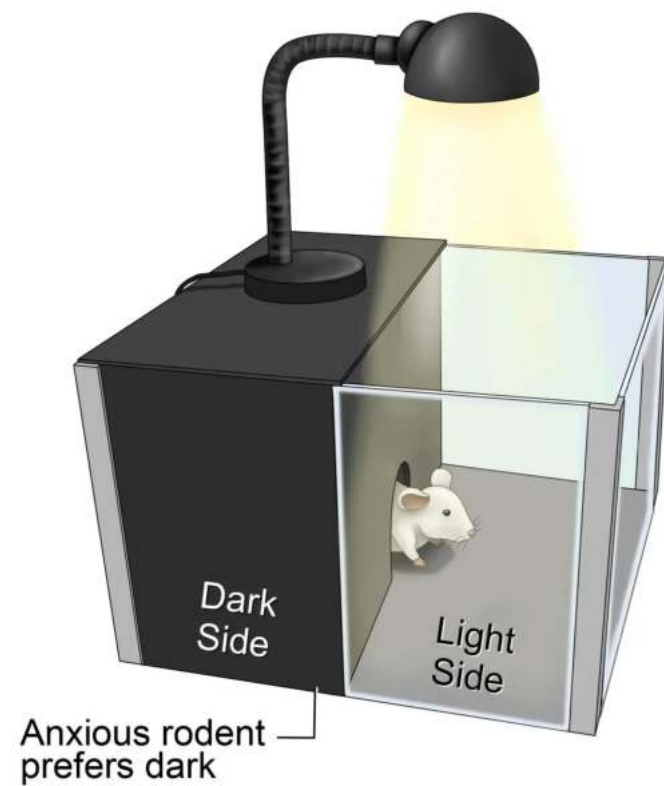
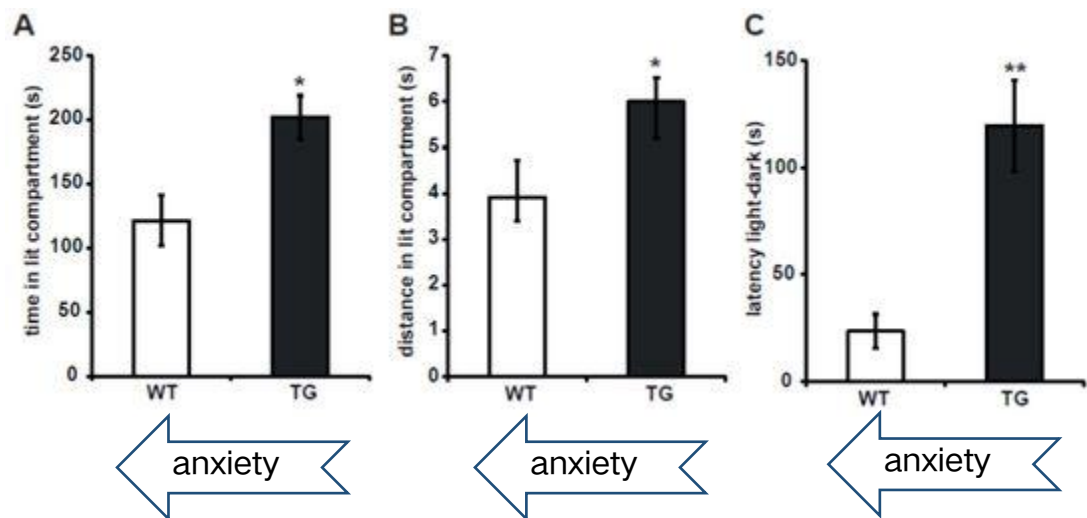


Klarer M, et al., J Neurosci., 2014.

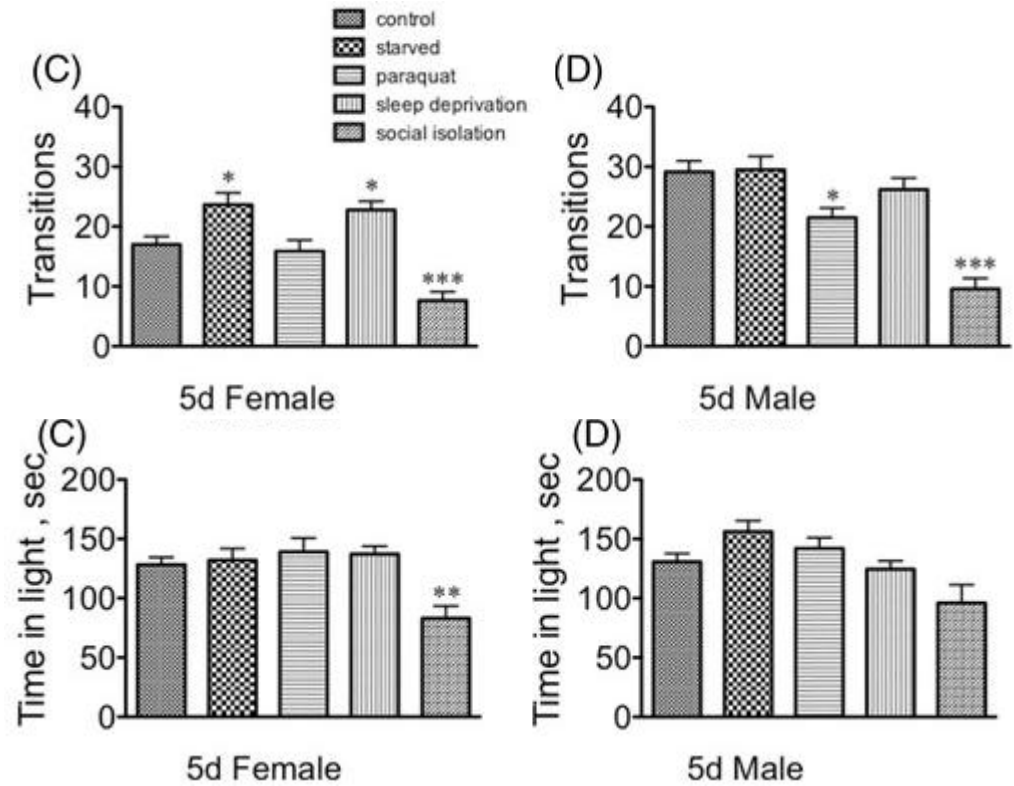
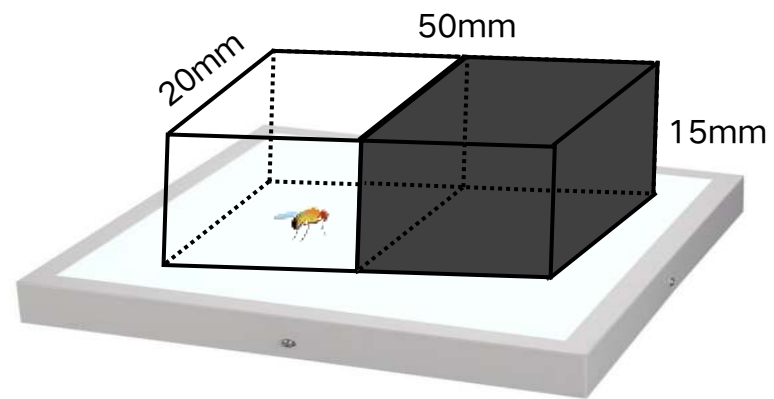
## Light/Dark Box



(Crawley & Goodwin, 1980)



## Light/Dark Box



Neckameyer WS, Nieto-Romero AR., *Stress*, 2015

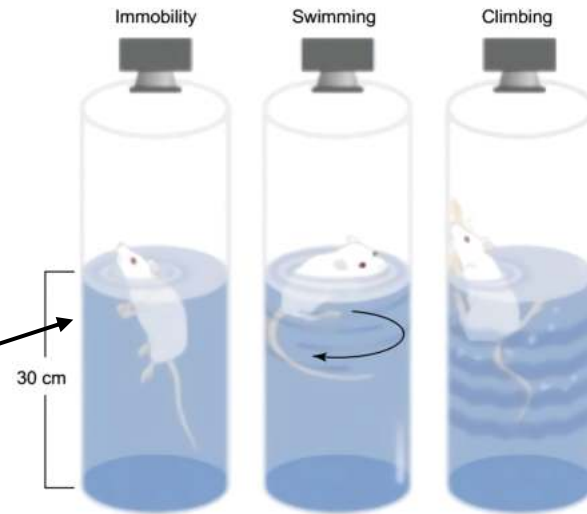
# Experimental methods for depressive behavior

- Reduced social behavior
- Loss of appetite
- Insufficient motivation
- Easy to despair

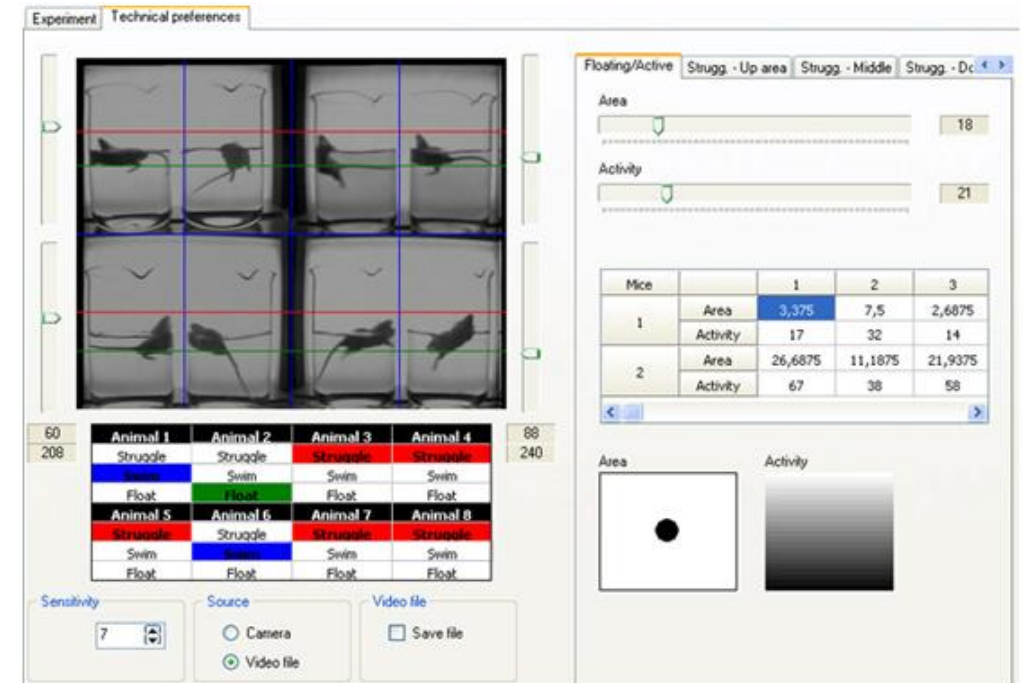
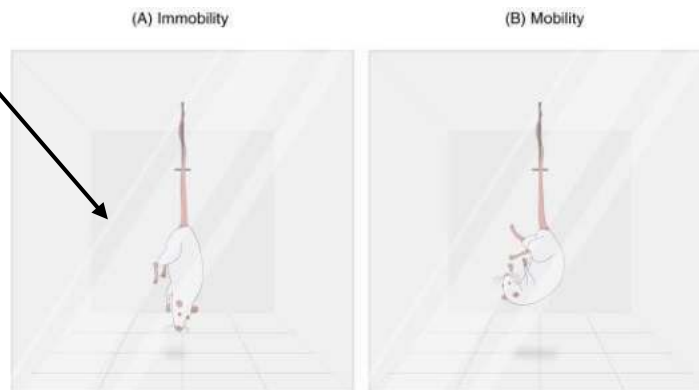


# Forced Swimming Test(FST) & Tail Suspension Test(TST)

Immobile Time  
Latency of Immobility



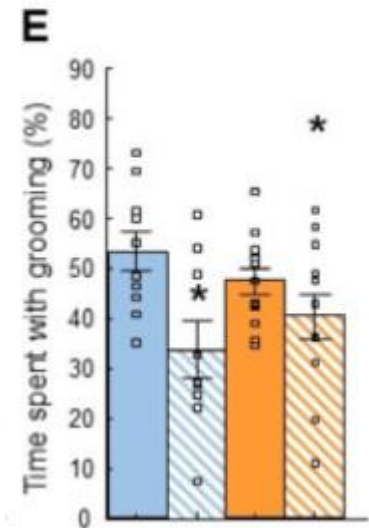
easy to despair



## Sucrose Preference Test(SPT) & Splash Test

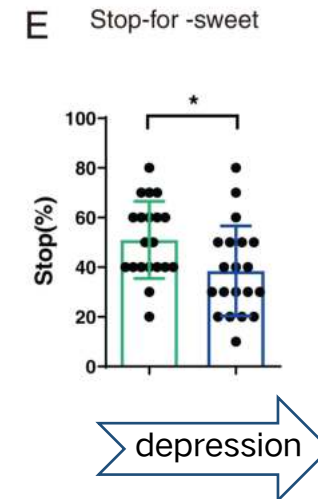
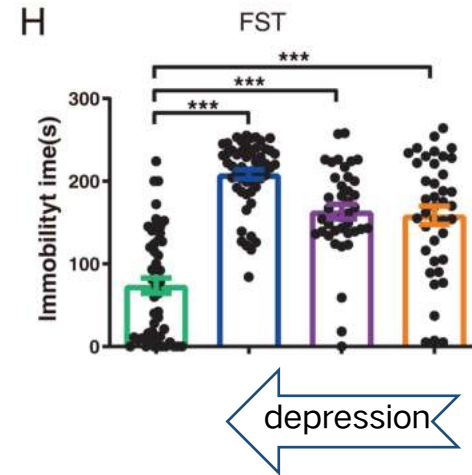
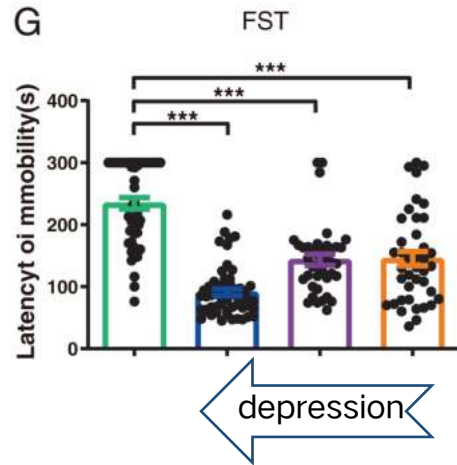
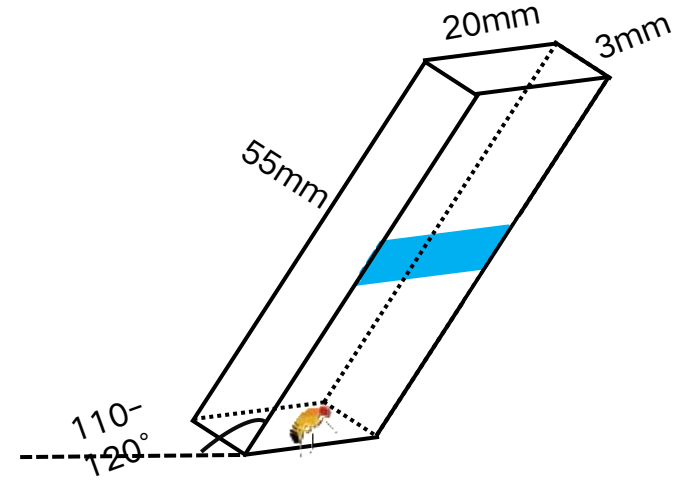
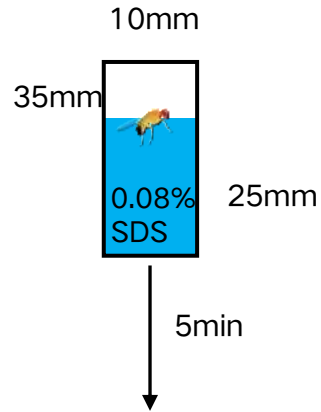


### C Splash test – 5 min



Várkonyi, D. et al., *Int. J. Mol. Sci.* 2022.

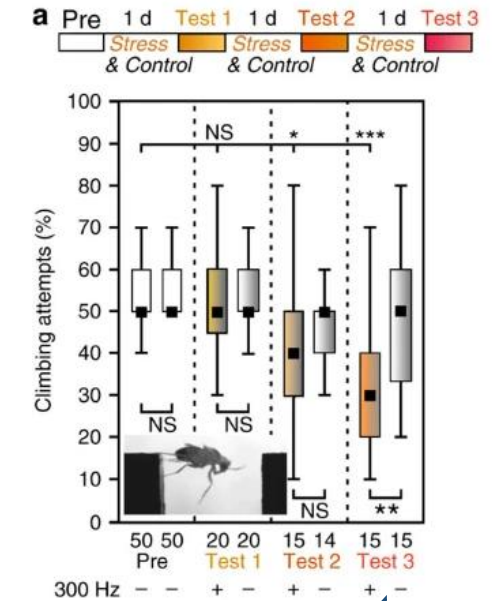
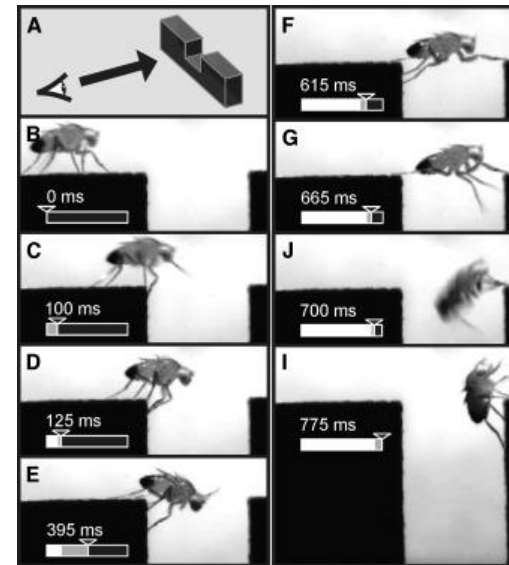
# Forced Swimming Test(FST) & Stop-for-sweet Assay of *Drosophila*



Jia, J. et al., *PNAS*, 2023.

# How to measure depression-like states in *Drosophila*?

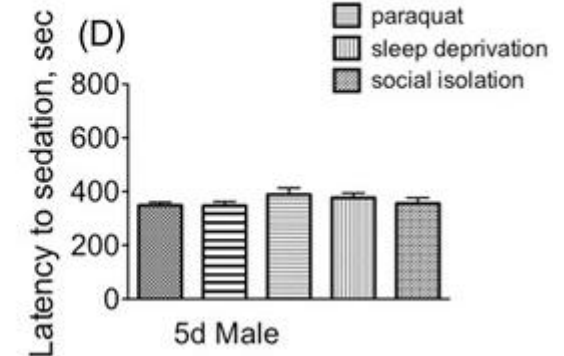
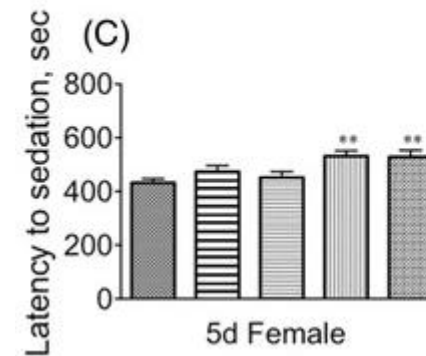
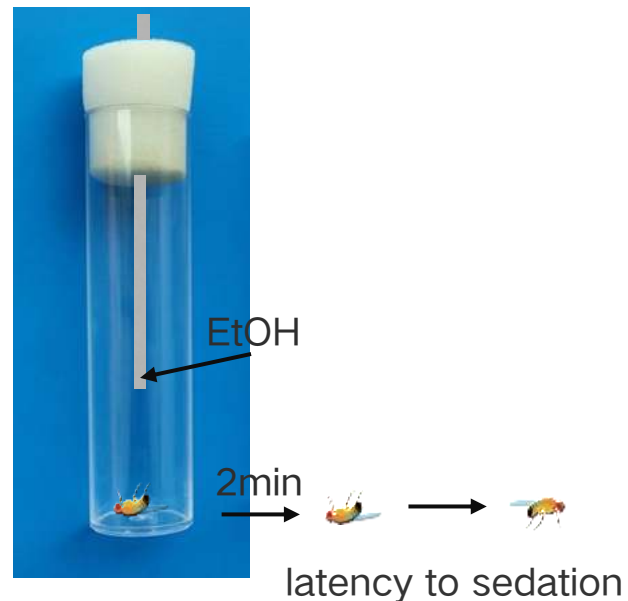
## Gap Climbing Assay



Ries, AS. *et al.*, *Nat Commun*, 2017.

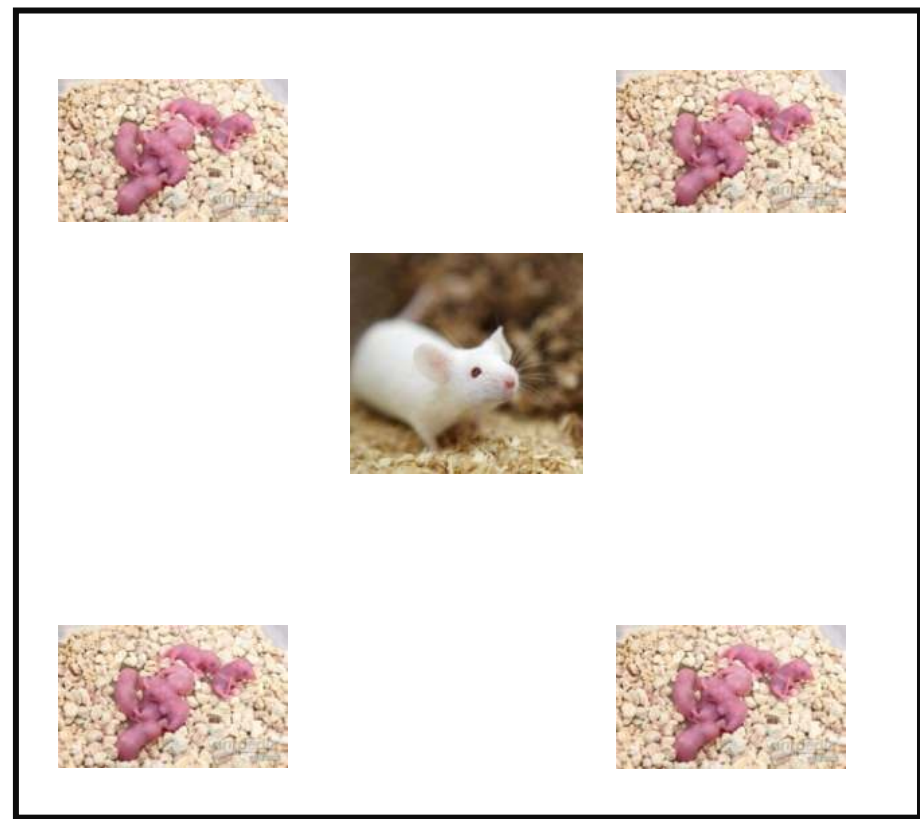
depression

## Ethanol sedation



Neckameyer WS, Nieto-Romero AR., *Stress*, 2015

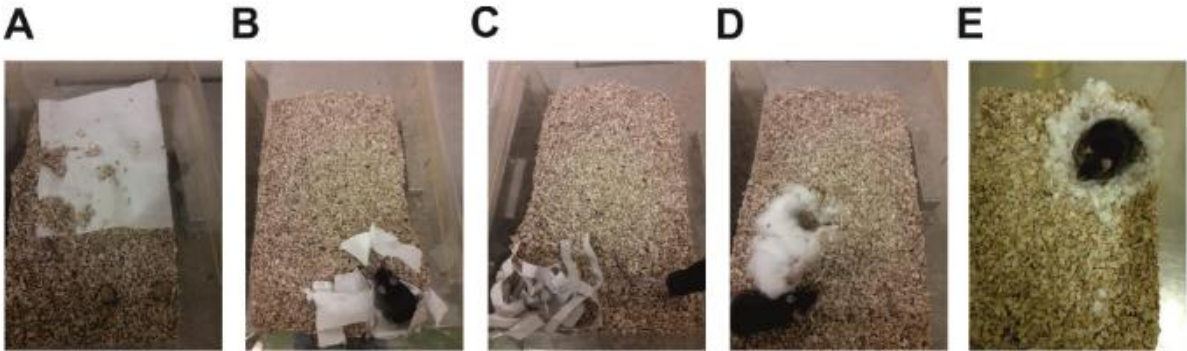
# Maternal care behavior testing for offspring& Nest Building Test(NBT)



Take care or Negative behavior  
Positive behavior

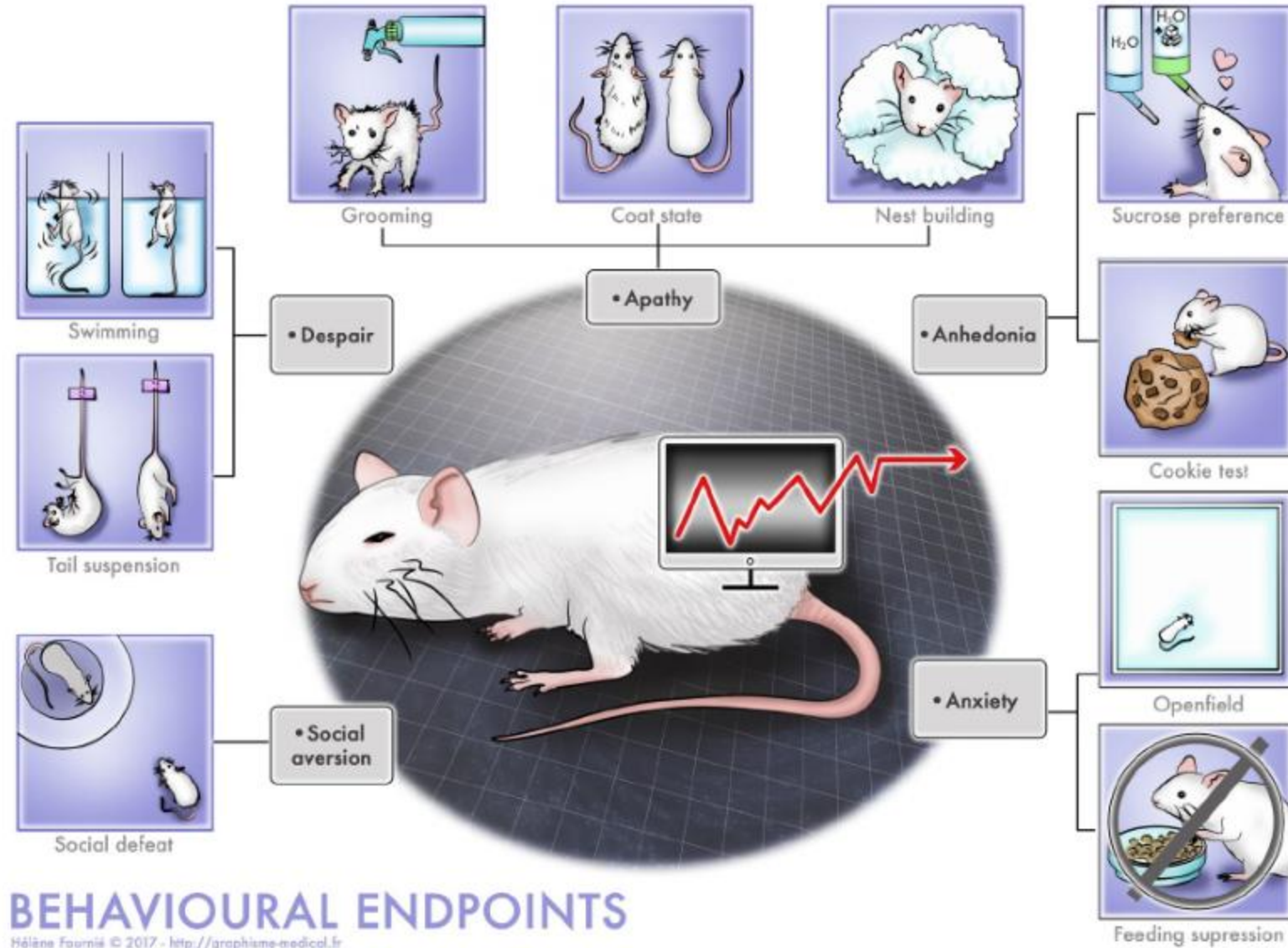
Table 1. Scoring scheme for assessment of nests, as described by Deacon, 2006.  
Note that grading steps of 0.5 can be assigned for more exact evaluation.

Score	Description
1	Nestlet (mostly) untouched
2	Parts of the nestlet shredded; 50% or more remain intact
3	Nestlet mostly shredded but material often dispersed with no delimited nest site
4	Identifiable but flat nest with most of the nestlet shredded
5	Nestlet fully shredded to form a crater-like, delimited nest



Dorninger F et al., *Bio Protoc.*, 2020.

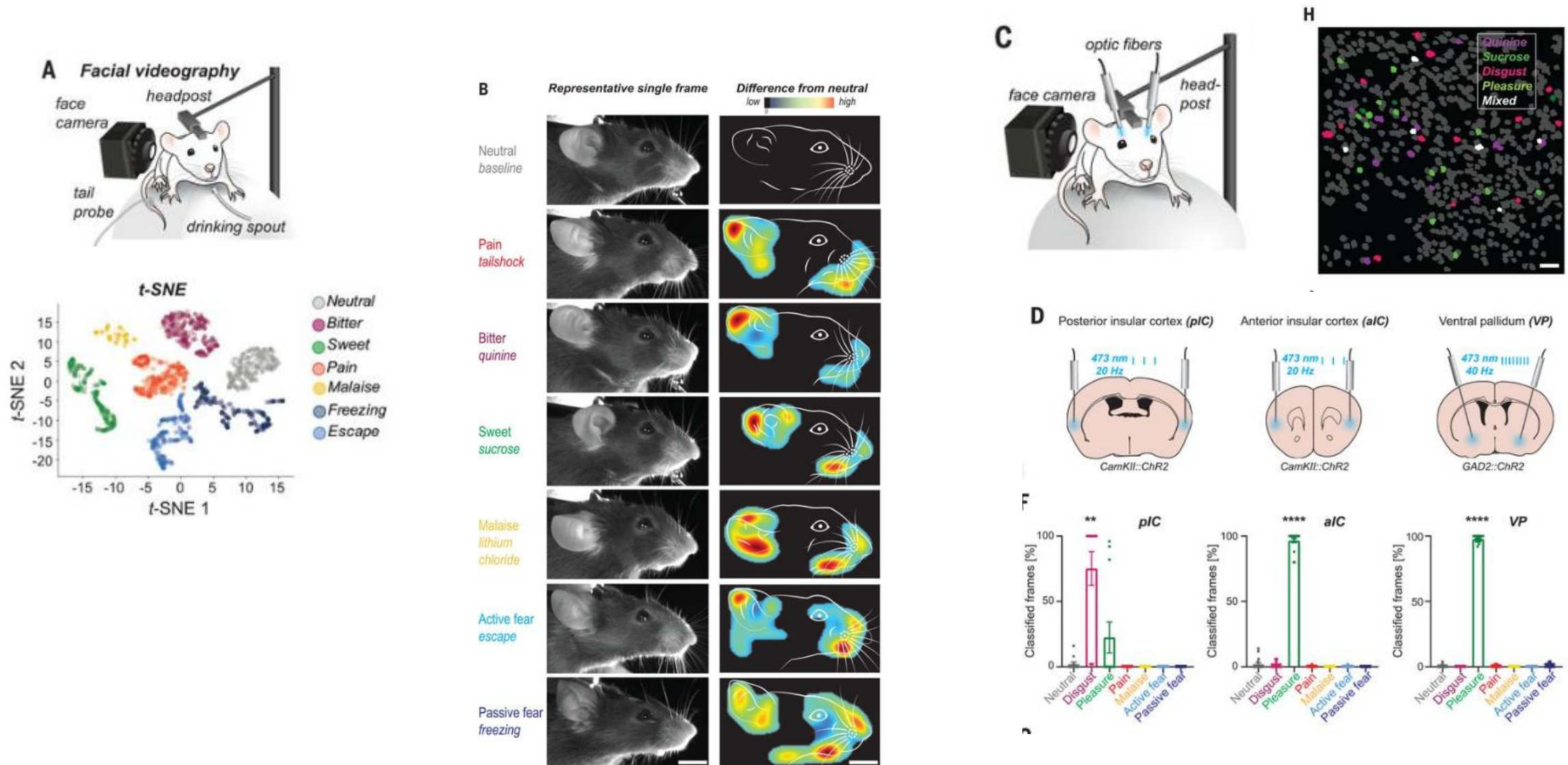
# Summary



The emotion-like behavior is regulated by biogenic amines in *Drosophila*



# Facial expressions should have neuronal correlates in emotion-relevant brain regions



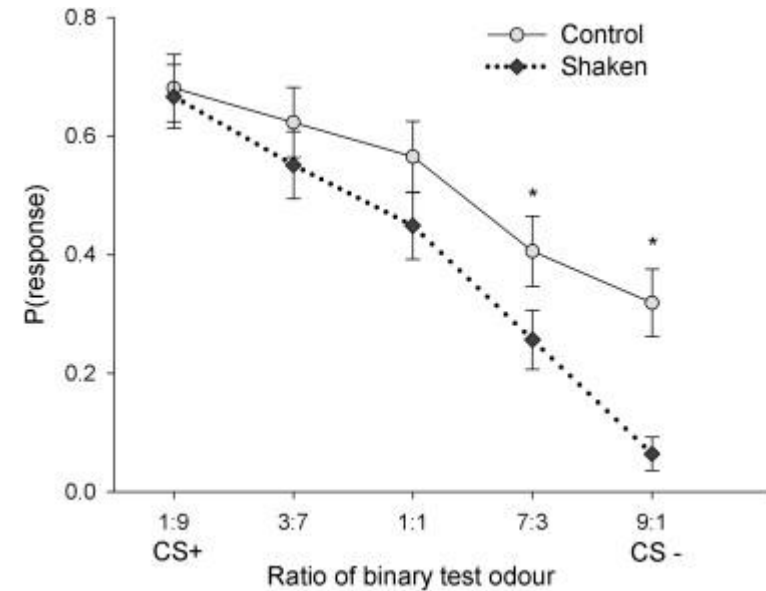
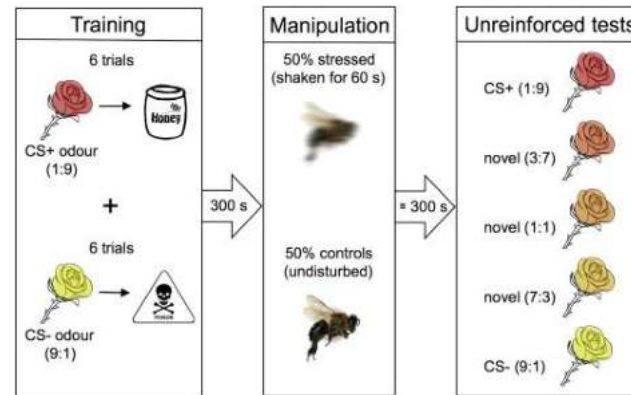
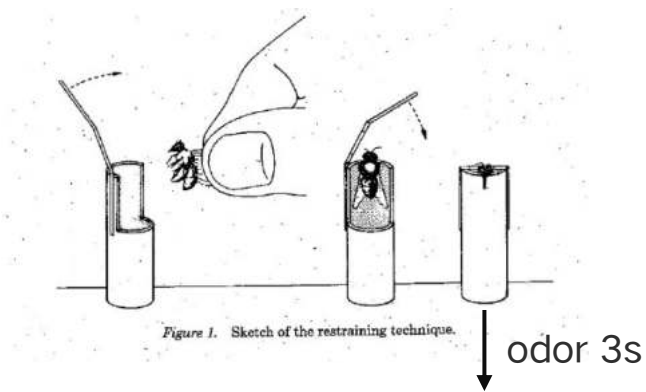
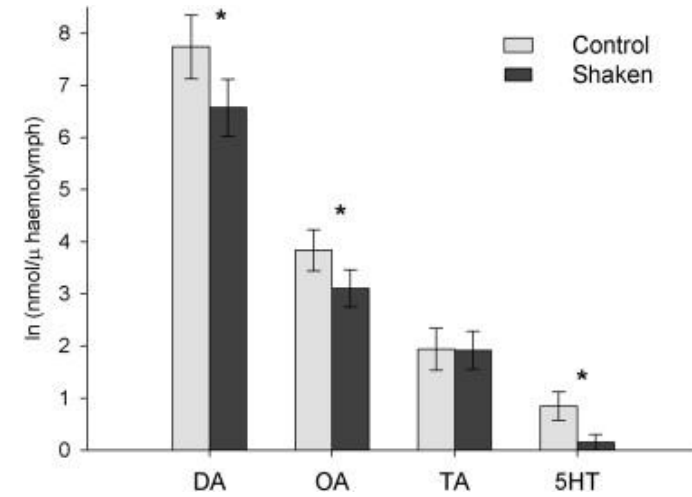
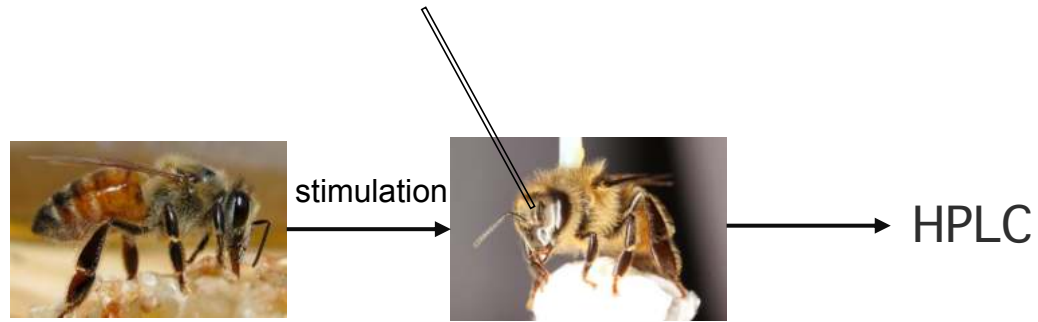
## Take home messages

- The comprehensive judgment of emotions based on changes in physiology and behavior is a reasonable way
- Learning ability are also related to emotions
- The regulation of emotions is neuron specific

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# Emotional state can be inferred using physiological, cognitive measures in Honeybees

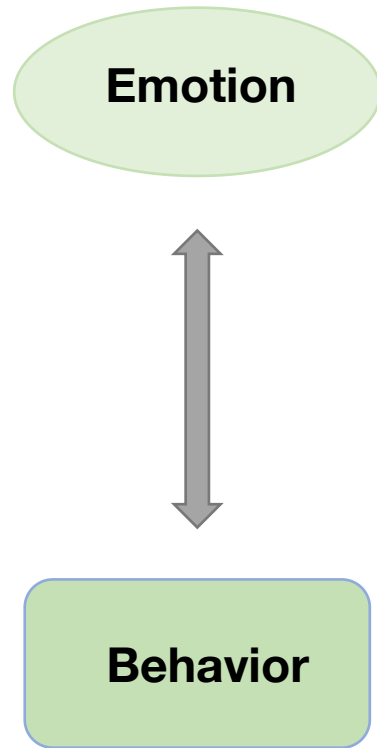


## PART3:

Impact of animal emotions on behaviors

XLM

Some emotions can be intuitively expressed through behavior



# Some questions

- Is there a direct link between emotion and behavior?
- What controls happiness?
- Are there conservative neural circuits and transmitters that control emotion related behaviors?
- Can emotions really be infected?

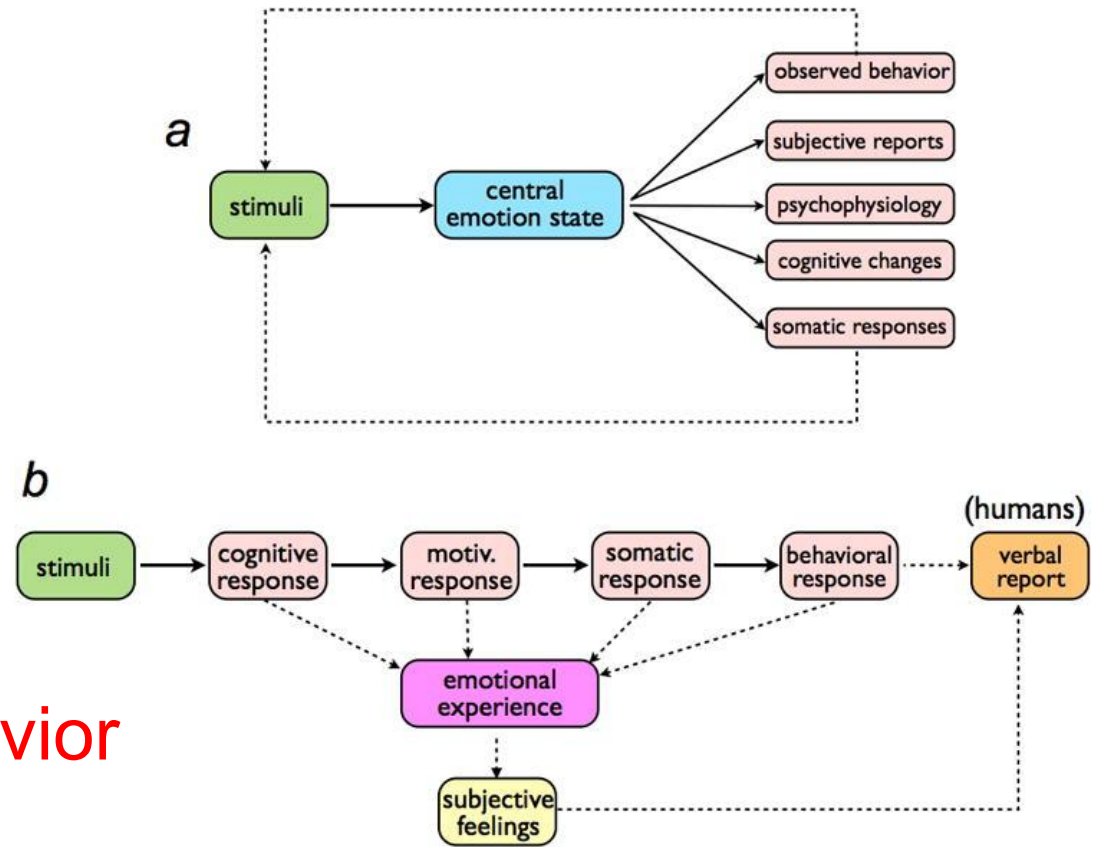
# The relationship between emotion states and observable behavior

## 情绪的不同理论：

- 詹姆士-朗格理论
- 坎农-巴德丘脑学说
- 阿诺德的“评定 - 兴奋”说
- 沙赫特-辛格的激活归因理论
- 拉扎勒斯的认知 - 评价理论
- 伊扎德的情绪动机 - 分化理论
- .....

It is more or less accepted that:

**emotions are expressed through behavior**



# Jaak Panksepp: Pioneer of Affective Neuroscience



1. seeking/expectancy,
2. rage/anger,
3. fear/anxiety,
4. lust,
5. care/nurturing,
6. panic/sadness,
7. play/social joy

“Affective Neuroscience” (AN):  
today being accepted as a unique research  
area in cross-species brain science.



and more...

Klaus-Peter Lesch [Edit Profile](#)

psychiatrist, university professor



Klaus-Peter Lesch is a clinical psychiatrist who has been investigating the neurobiological foundation of personality traits.

## Career

His 1996 paper on the association between the 5-HTTLPR polymorphism in the serotonin transporter gene and the personality trait neuroticism has been highly cited and was one of the first papers in personality genetics. He is professor at the University of Würzburg. Among his coauthors has been Peter Riederer.

[Comparative Study](#) > [J Neural Transm Gen Sect.](#) 1993;91(1):67-72. doi: 10.1007/BF01244919.

## Isolation of a cDNA encoding the human brain serotonin transporter

[K P Lesch<sup>1</sup>](#), [B L Wolozin](#), [H C Estler](#), [D L Murphy](#), [P Riederer](#)

[Affiliations](#) + [expand](#)

[PMID: 8452685](#) [DOI: 10.1007/BF01244919](#)

## Abstract

A cDNA encoding a serotonin transporter (5-HTT) in the human dorsal raphe nucleus was isolated and sequenced using cross-species amplification of human 5-HTT partial cDNA by the polymerase chain reaction (PCR) and the RACE-PCR procedure, designed for rapid amplification of 3' and 5' cDNA

[J Neural Transm \(1996\) 103: 957–965](#)

— **Journal of** —  
**Neural**  
**Transmission**

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Printed in Austria

## Identification of serotonin transporter mRNA in rat platelets

**D. Hranilović<sup>1</sup>, K.-P. Lesch<sup>1</sup>, D. Ugarković<sup>2</sup>, L. Čičin-Šain<sup>1</sup>, and B. Jernej<sup>1</sup>**



and generate a lot of vocal activity  
并产生大量的声乐活动

Last generation of anti-inflammatory drugs!



## What controls happiness?



### Natural Neural Projection Dynamics Underlying Social Behavior

Lisa A. Gunaydin,<sup>1,5</sup> Logan Groseknick,<sup>1,2,5</sup> Joel C. Finkelstein,<sup>1,5</sup> Isaac V. Kauvar,<sup>1,5</sup> Lief E. Fenno,<sup>1,2</sup> Avishek Adhikari,<sup>1</sup> Stephan Lammel,<sup>3</sup> Julie J. Mirzabekov,<sup>1</sup> Raag D. Airan,<sup>1</sup> Kelly A. Zalocusky,<sup>1,2</sup> Kay M. Tye,<sup>1</sup> Polina Anikeeva,<sup>1</sup> Robert C. Malenka,<sup>3</sup> and Karl Deisseroth<sup>1,3,4,\*</sup>



### HHS Public Access

Author manuscript

*Science*. Author manuscript; available in PMC 2020 January 18.

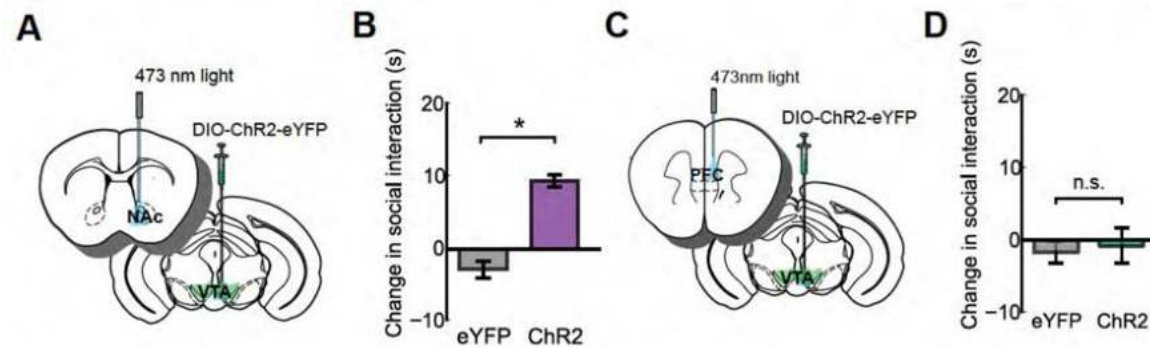
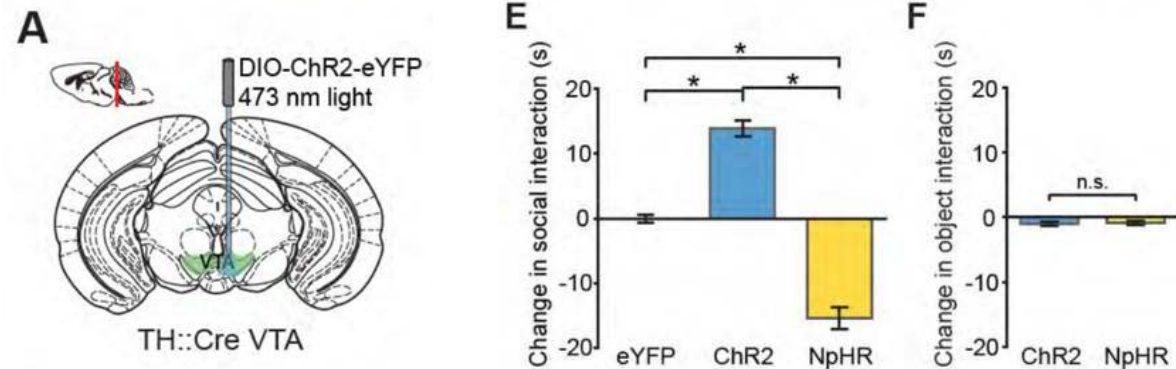
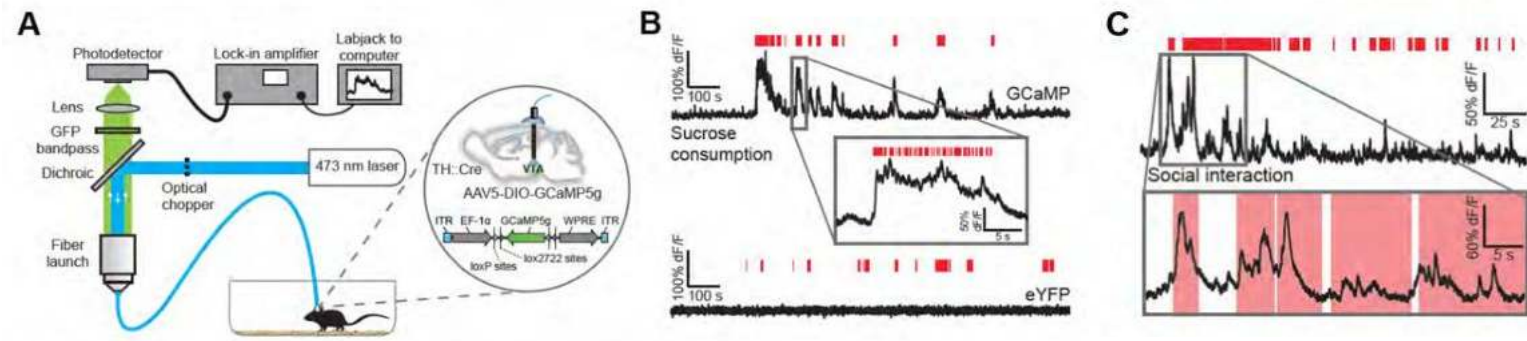
Published in final edited form as:

*Science*. 2019 January 18; 363(6424): . doi:10.1126/science.aav0581.

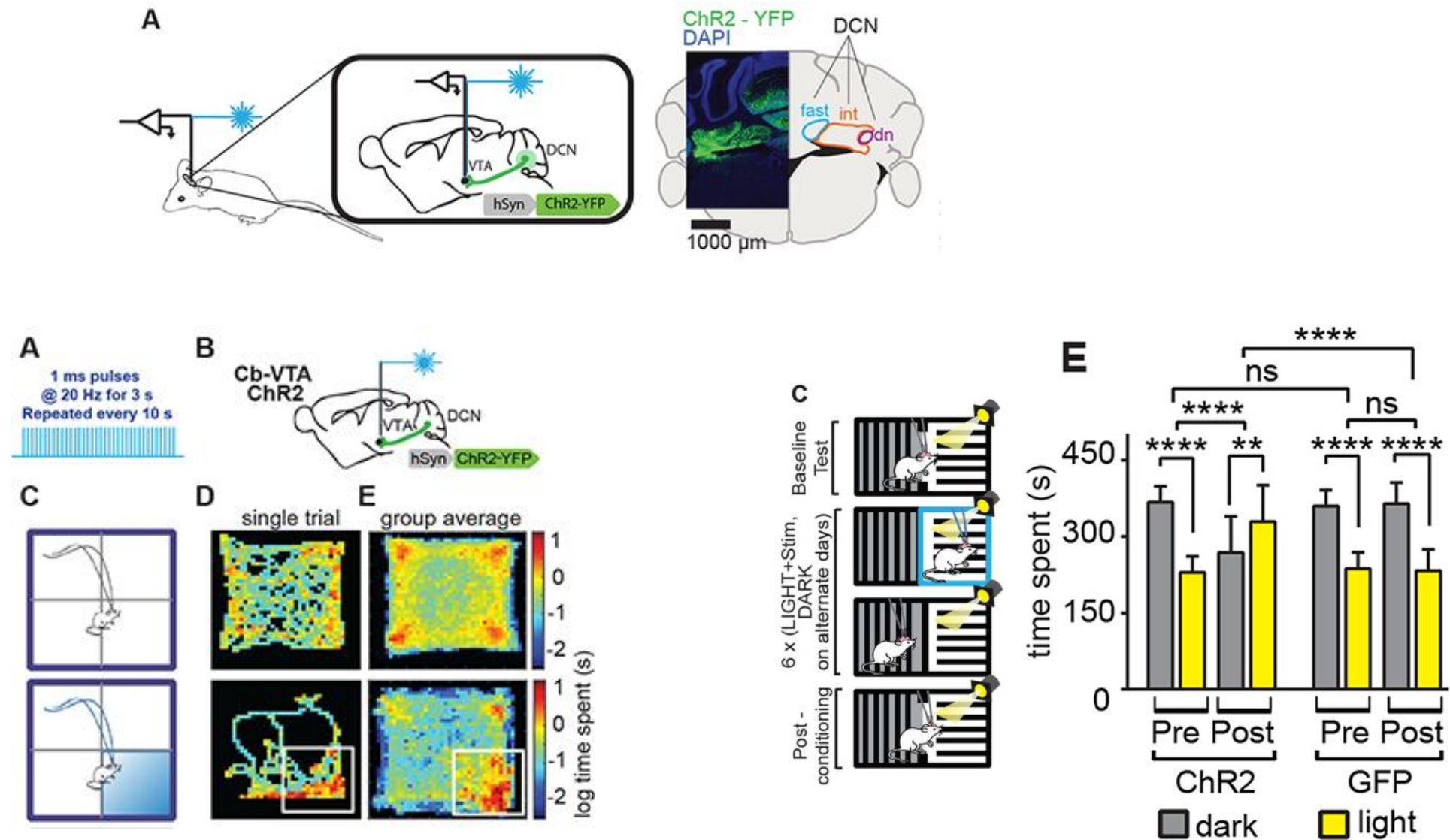
### Cerebellar Modulation of the Reward Circuitry and social behavior

Ilaria Carta<sup>\*,1</sup>, Christopher H Chen<sup>\*,1,4</sup>, Amanda Schott<sup>1</sup>, Schnaude Dorizan<sup>1</sup>, Kamran Khodakhah<sup>1,2,3,#</sup>

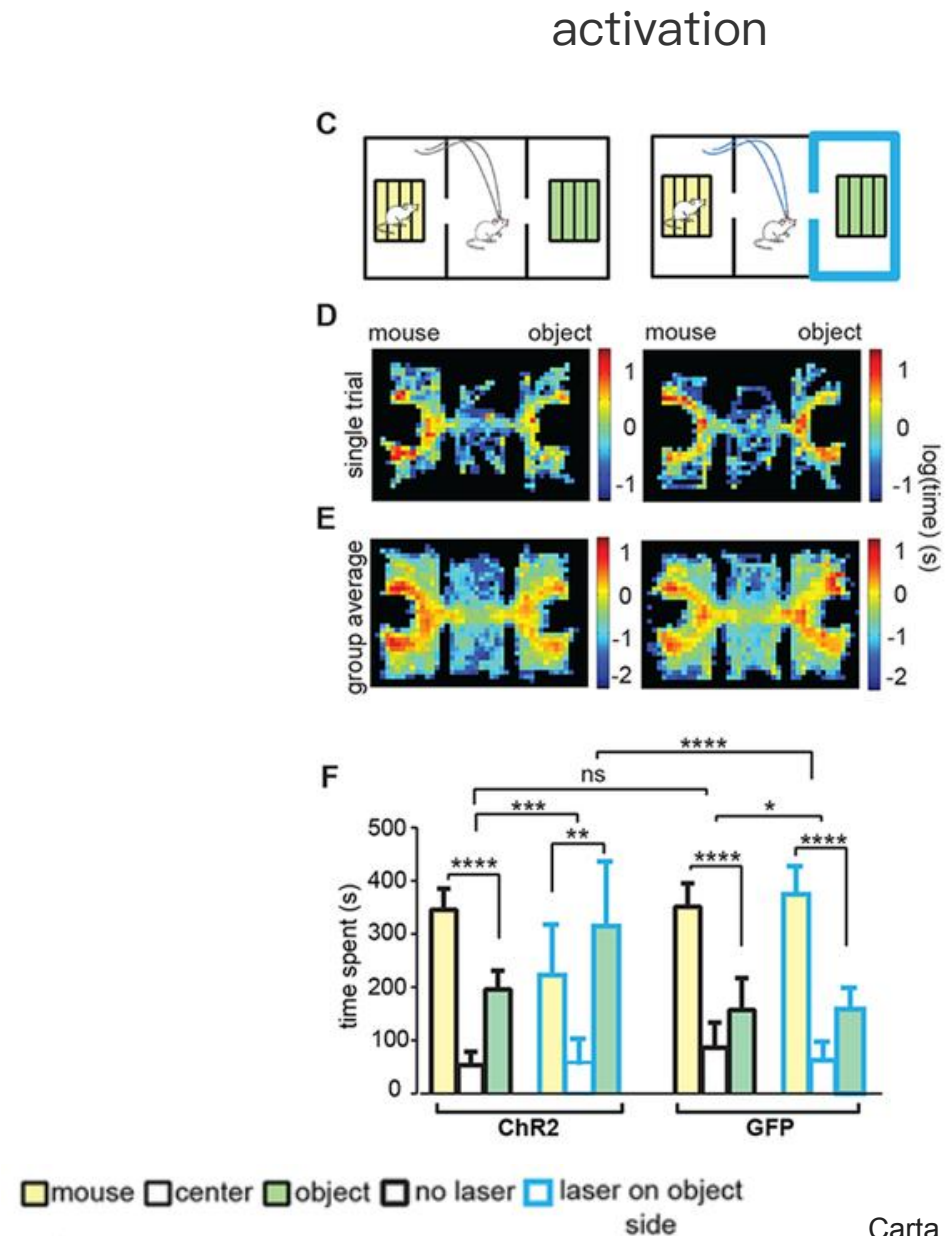
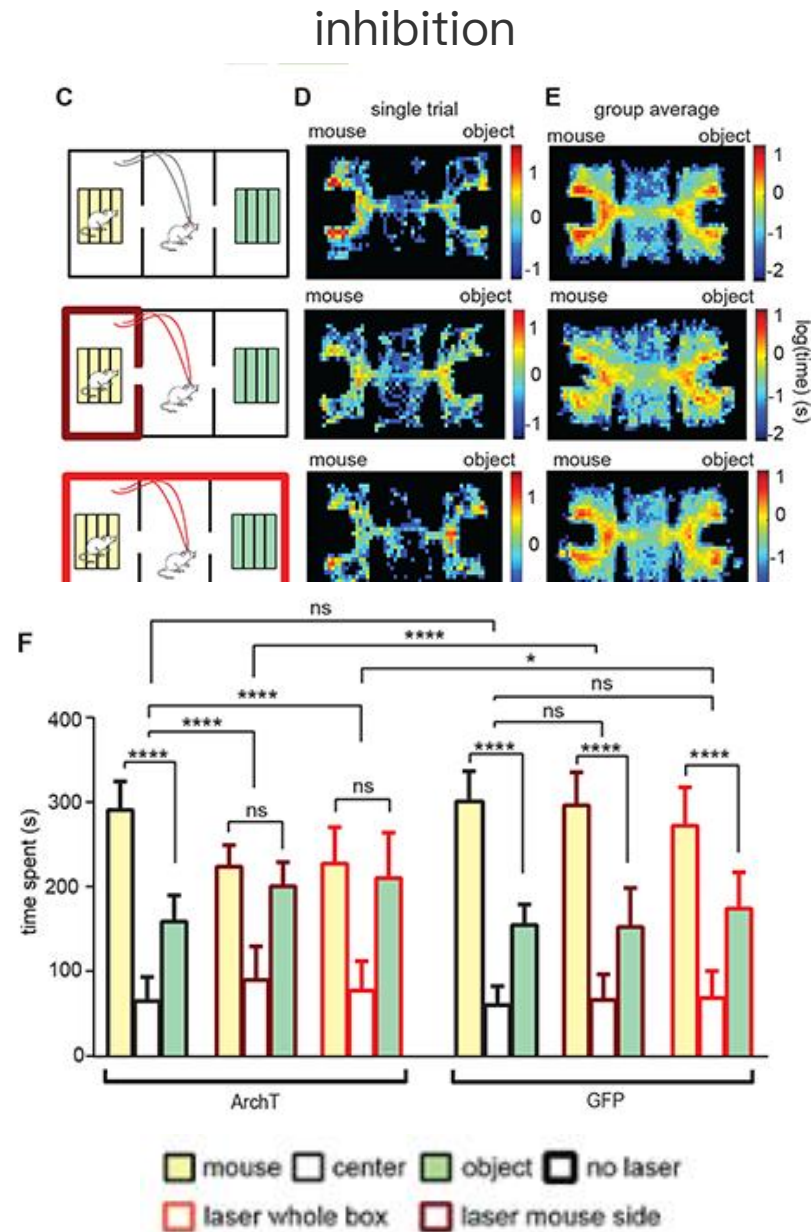
# VTA-DA-NAc actively regulates social behavior bidirectionally

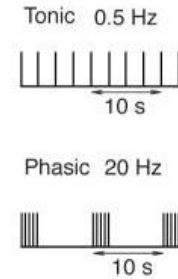


# Activation of cerebellar inputs to VTA promotes positive behavior



# The function of the cerebellar-VTA pathway in sociability and reward





## LETTER

doi:10.1038/nature11713

# Rapid regulation of depression-related behaviours by control of midbrain dopamine neurons

Dipesh Chaudhury<sup>1\*</sup>, Jessica J. Walsh<sup>1,2\*</sup>, Allyson K. Friedman<sup>1</sup>, Barbara Juarez<sup>1,2</sup>, Stacy M. Ku<sup>1,2</sup>, Ja Wook Koo<sup>2</sup>, Deveroux Ferguson<sup>2</sup>, Hsing-Chen Tsai<sup>3</sup>, Lisa Pomeranz<sup>4</sup>, Daniel J. Christoffel<sup>2</sup>, Alexander R. Nectow<sup>4</sup>, Mats Ekstrand<sup>4</sup>, Ana Domingos<sup>4</sup>, Michelle S. Mazei-Robison<sup>2</sup>, Ezekiel Mouzon<sup>2</sup>, Mary Kay Lobo<sup>2</sup>, Rachael L. Neve<sup>5</sup>, Jeffrey M. Friedman<sup>4</sup>, Scott J. Russo<sup>2</sup>, Karl Deisseroth<sup>3</sup>, Eric J. Nestler<sup>1,2</sup> & Ming-Hu Han<sup>1,2</sup>



## ARTICLE

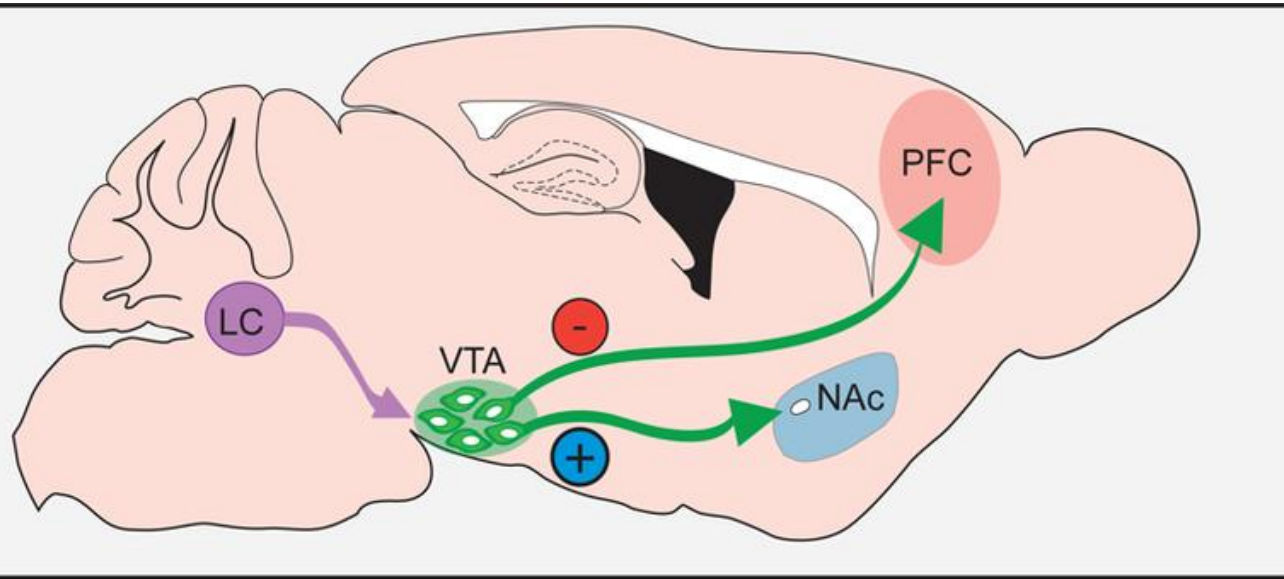
<https://doi.org/10.1038/s41467-022-29155-1>

OPEN

Check for updates

Midbrain projection to the basolateral amygdala encodes anxiety-like but not depression-like behaviors

Carole Morel<sup>1,2,8</sup>, Sarah E. Montgomery<sup>1,2,3</sup>, Long Li<sup>2,3</sup>, Romain Durand-de Cuttoli<sup>2,3</sup>, Emily M. Teichman<sup>1,2,3</sup>, Barbara Juarez<sup>1,2,3,4,5</sup>, Nikos Tzavaras<sup>3,6</sup>, Stacy M. Ku<sup>1,2,3</sup>, Meghan E. Flanigan<sup>2,3,7</sup>, Min Cai<sup>1,2</sup>, Jessica J. Walsh<sup>1,2,3,8,9</sup>, Scott J. Russo<sup>2,3</sup>, Eric J. Nestler<sup>1,2,3</sup>, Erin S. Calipari<sup>2,3,10</sup>, Allyson K. Friedman<sup>1,2,11</sup> & Ming-Hu Han<sup>1,2,12,13</sup>



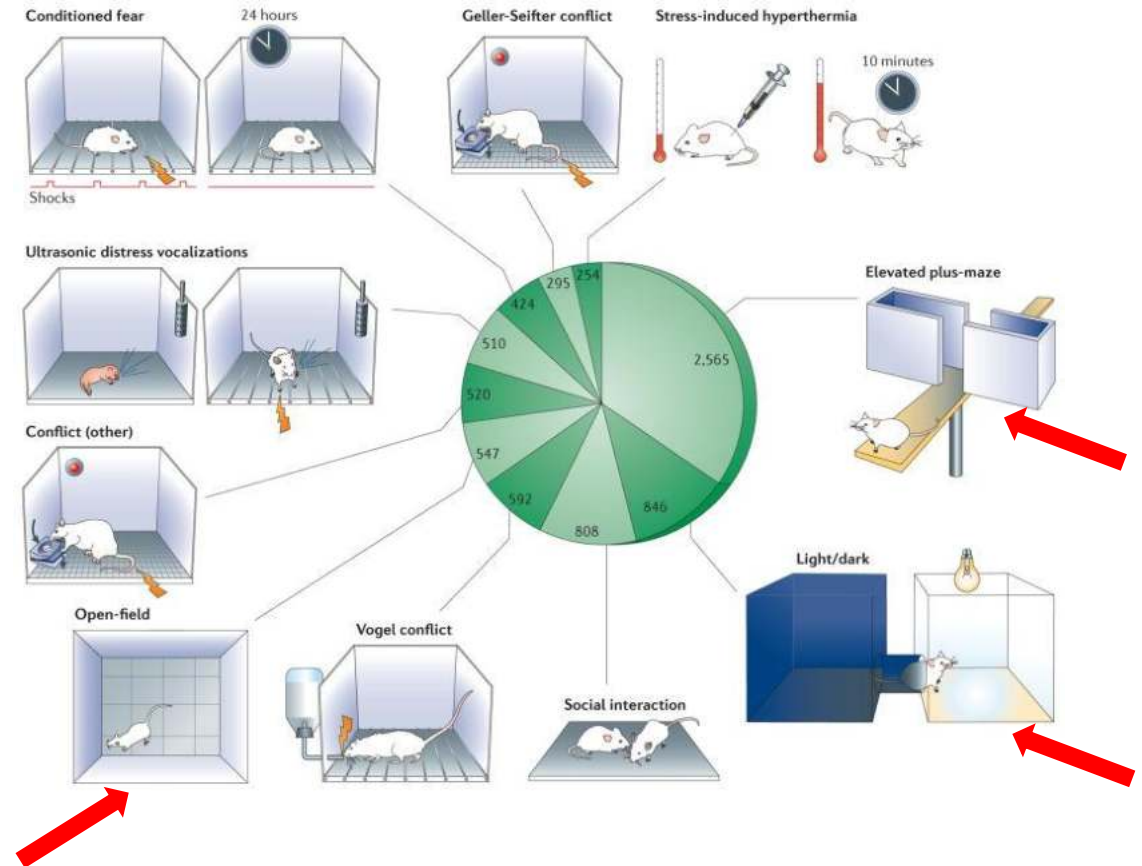
腹侧被盖区 (VTA)  
伏隔核 (NAc)  
内侧前额叶皮层 (mPFC)

# Bad moods have received much more attention than happy ones

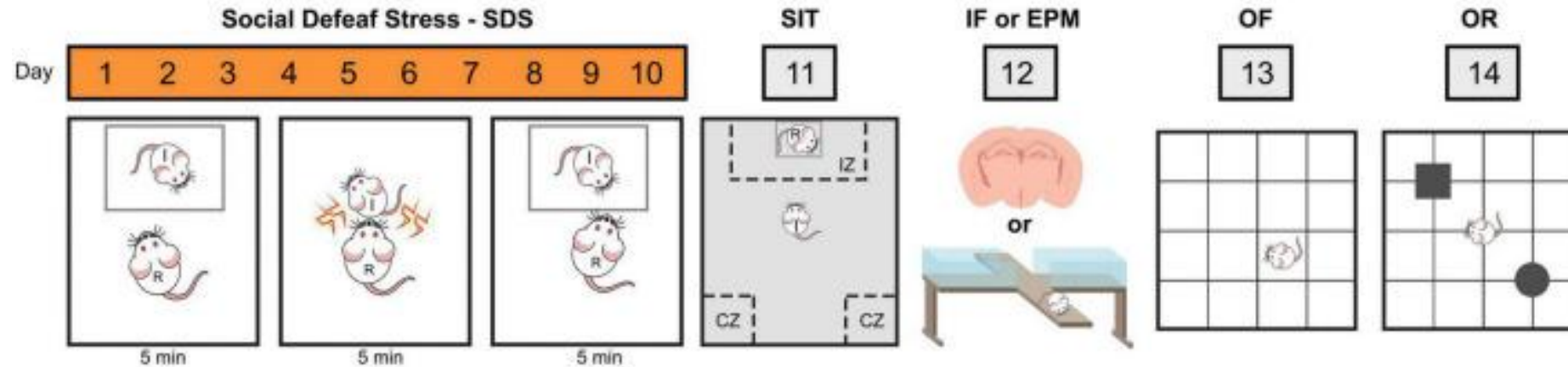
- ◆ Anxiety-like behavior
- ◆ Depression-like behavior



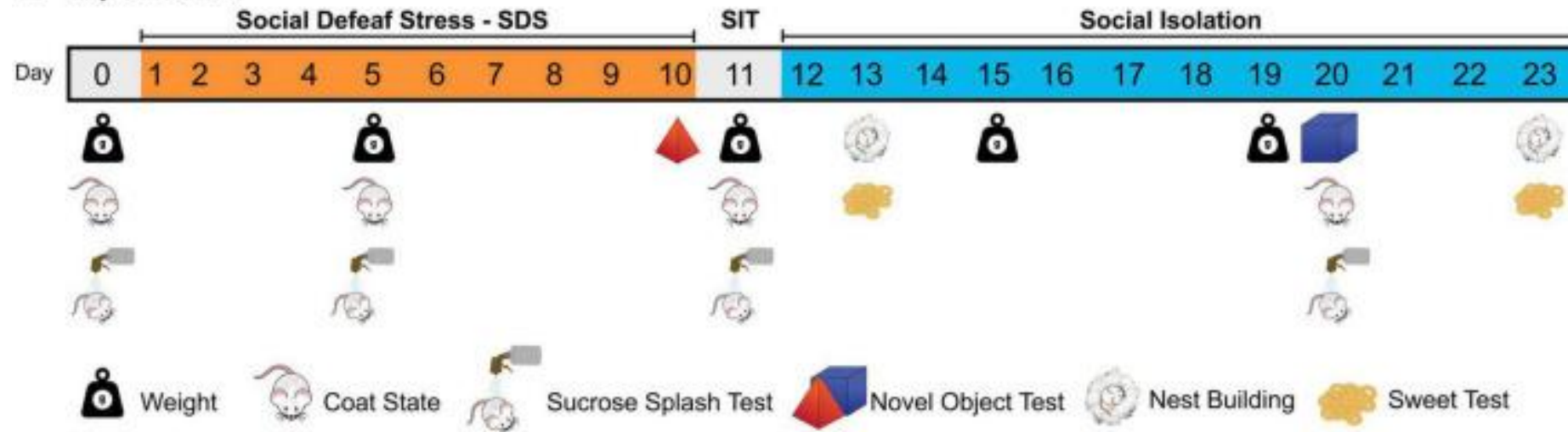
- ◆ Injury
- ◆ Conflict
- ◆ Death
- ◆ ...



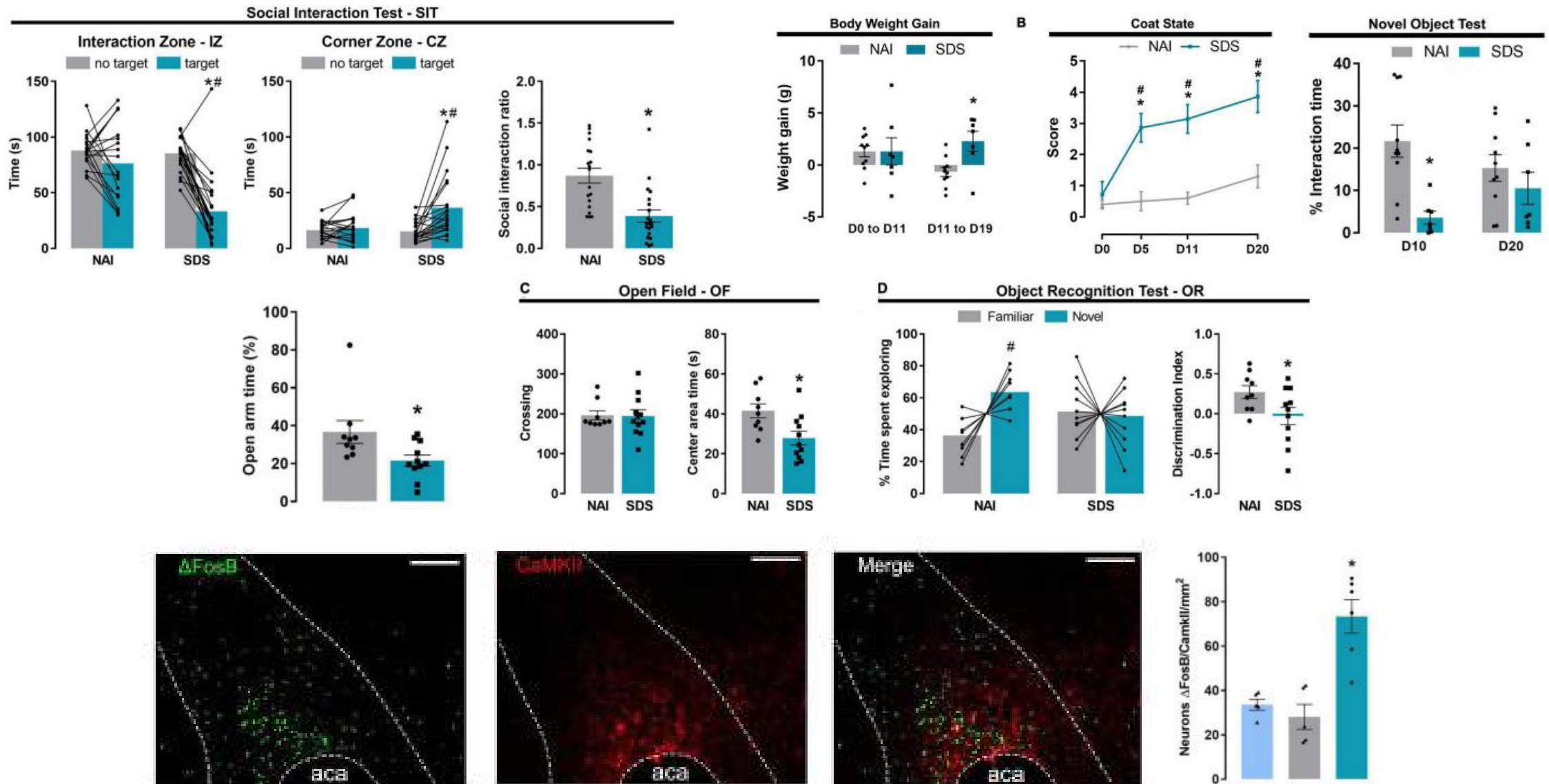
## A Experiment 1



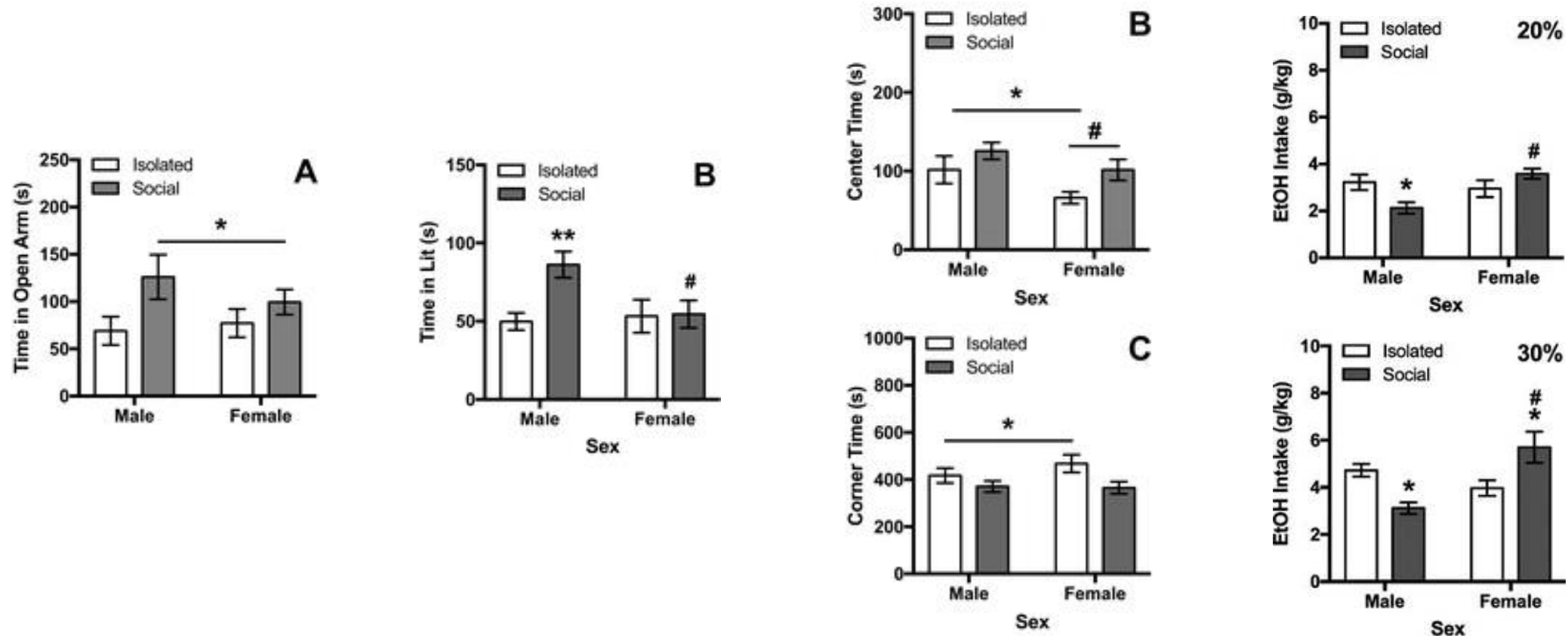
## B Experiment 2



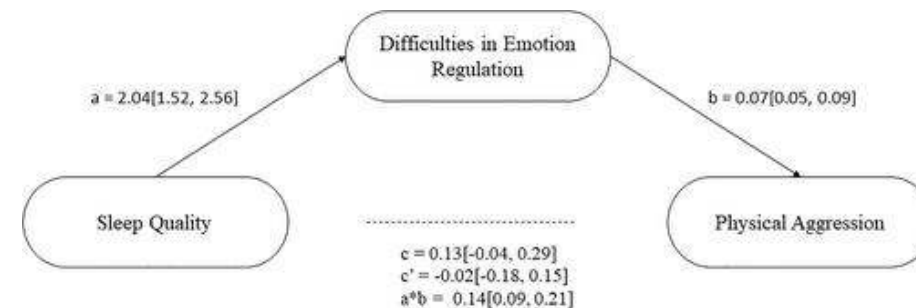
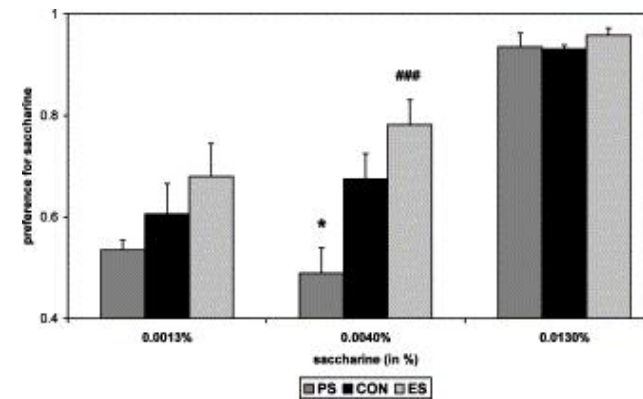
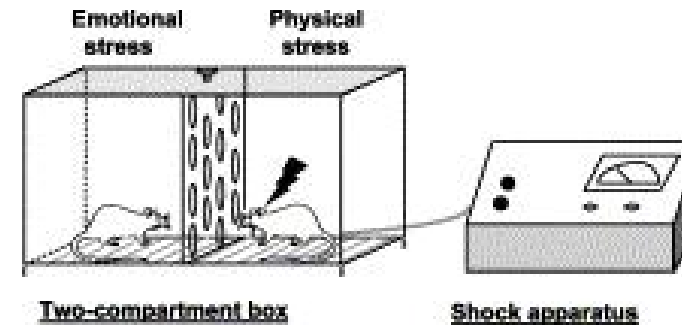
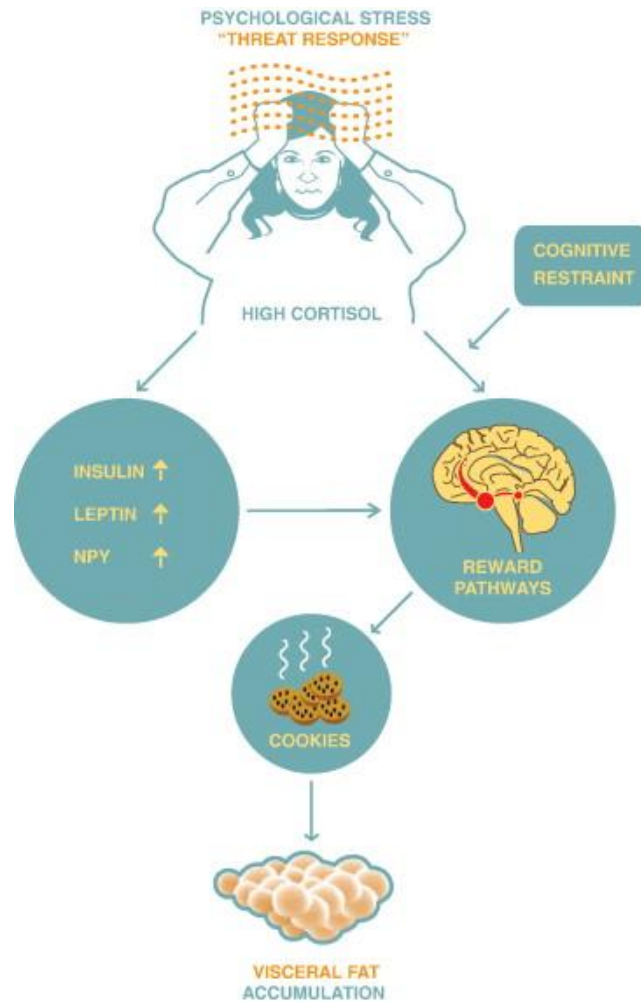
# Emotional-like responses induced by social defeat stress in male mice are modulated by the BNST, amygdala, and hippocampus



# Anxiety-associated behavior can be induced by social isolation and produce sex-dependent changes in EtOH consumption



# Emotional stress also affects many behaviors in many ways

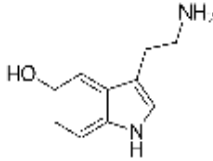


Jahng JW. *Horm Behav.* 2011

Pijlman FT, et al. *Behav Brain Res.* 2003

# The “star molecule” of depression research

## Serotonin: 5-HT



### Crystalline Serotonin<sup>1</sup>

MAURICE M. RAPPORT, ARDA ALDEN GREEN,  
and IRVINE H. PAGE

Research Division, Cleveland Clinic Foundation,  
Cleveland, Ohio

SCIENCE, September 24, 1948, Vol. 108

## 5-HT Transporter: 5-HTT

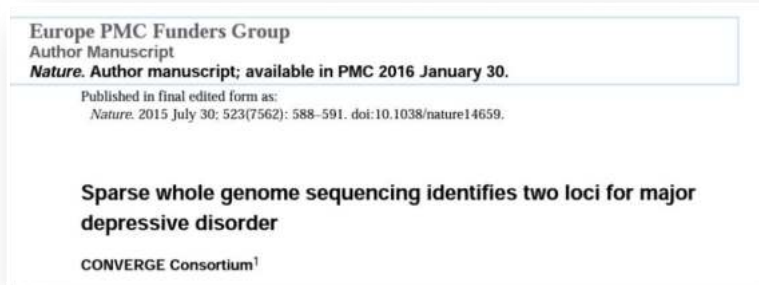
J Neural Transm [Gen Sect] (1993) 91: 67–72

— *Journal of* —  
*Neural*  
*Transmission*  
© Springer-Verlag 1993  
Printed in Austria

Isolation of a cDNA encoding the human brain serotonin transporter

Rapid Communication

K.-P. Lesch<sup>1</sup>, B. L. Wolozin<sup>2</sup>, H. C. Estler<sup>1</sup>, D. L. Murphy<sup>2</sup>, and P. Riederer<sup>1</sup>



## Controversial voice

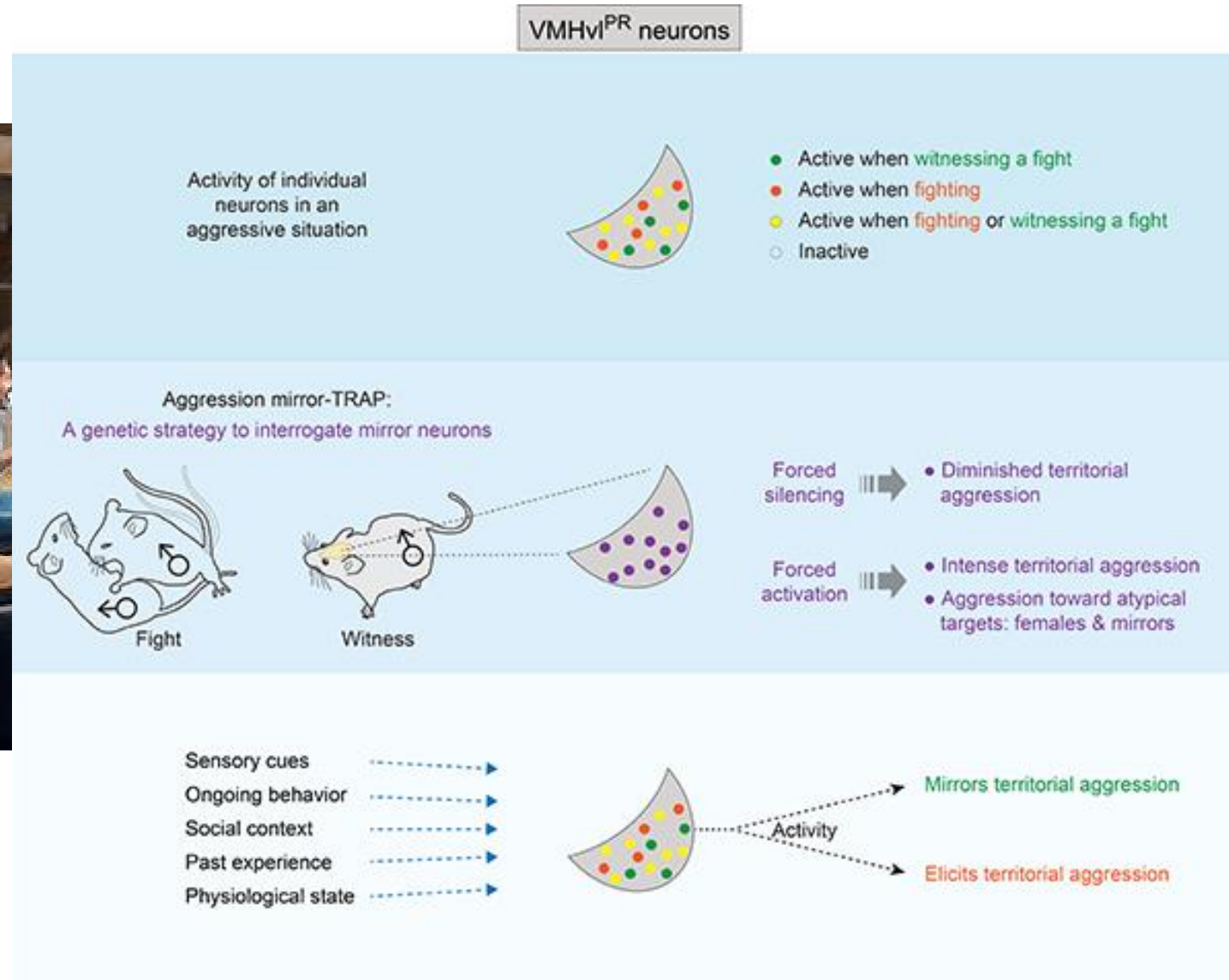
2019

### No Support for Historical Candidate Gene or Candidate Gene-by-Interaction Hypotheses for Major Depression Across Multiple Large Samples

Richard Border, M.A., Emma C. Johnson, Ph.D., Luke M. Evans, Ph.D., Andrew Smolen, Ph.D., Noah Berley, Patrick E. Sullivan, M.D., Matthew C. Keller, Ph.D.



# How do emotions infect each other?



11.2023.01.022.

ession

Landayan<sup>1</sup>, Ivo M. Marcelo<sup>6,7</sup>,  
Shaul Druckmann<sup>1,2</sup>, Nirao M.

VMHvl<sup>PR</sup> neurons evoke aggression in a social context-sensitive manner

# Studying the link between emotion and behavior: from vertebrates to insects

Invert Neurosci (2012) 12:81–92  
DOI 10.1007/s10158-012-0140-y

REVIEW

## Serotonin circuits and anxiety: what can invertebrates teach us?

Kevin P. Curran · Sreekanth H. Chalasani

*J. Neurogenetics*, 23: 136–146  
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ISSN: 0167-7063 print/1563-5260 online  
DOI: 10.1080/01677060802471650

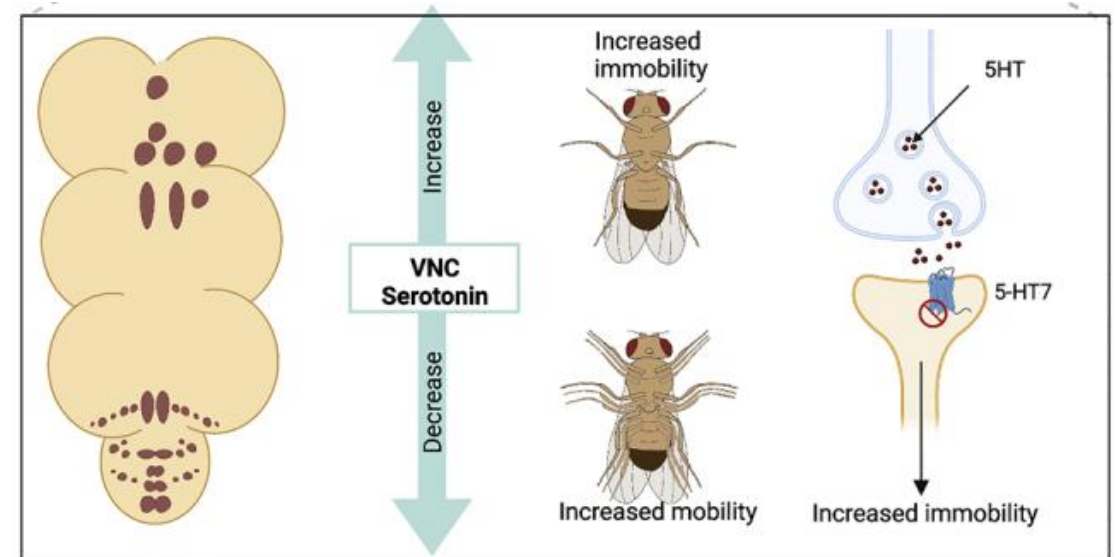
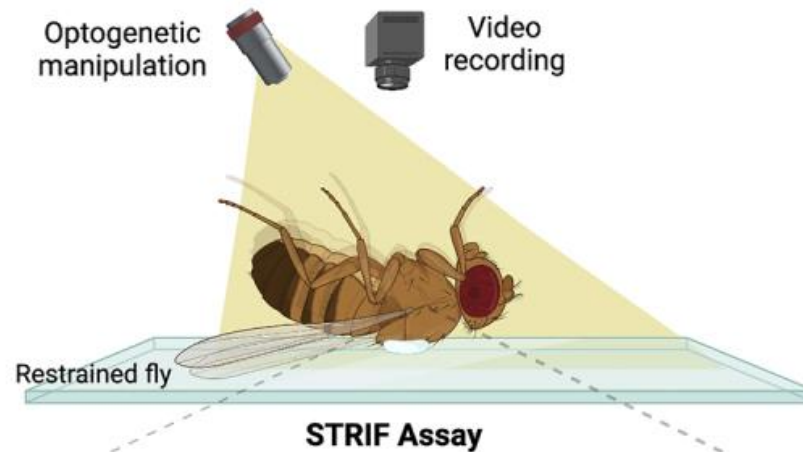
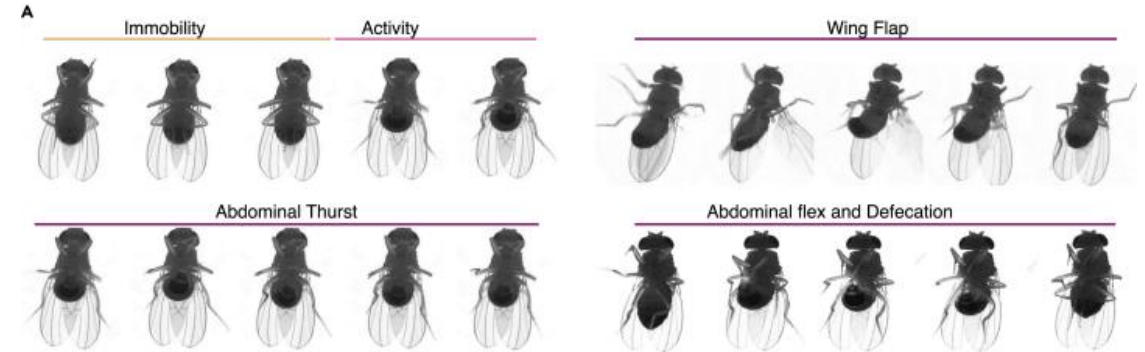
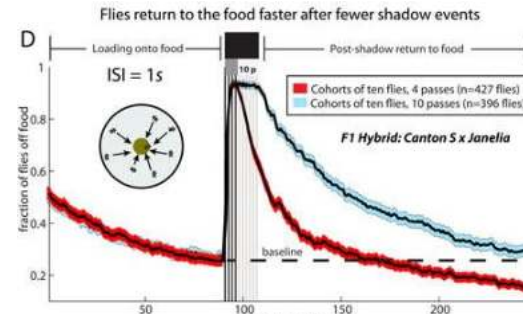
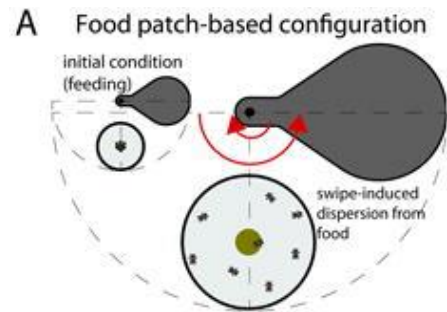
**informa**  
healthcare

## The Genetic Basis of Emotional Behavior: Has the Time Come for a *Drosophila* Model?

**Konstantin G. Iliadi**

Program in Developmental and Stem Cell Biology, The Hospital for Sick Children, Toronto, Ontario, Canada

# Flies' "fear" response similar to mammals, which mediated by serotonin through 5-HT7 receptors in the VNC

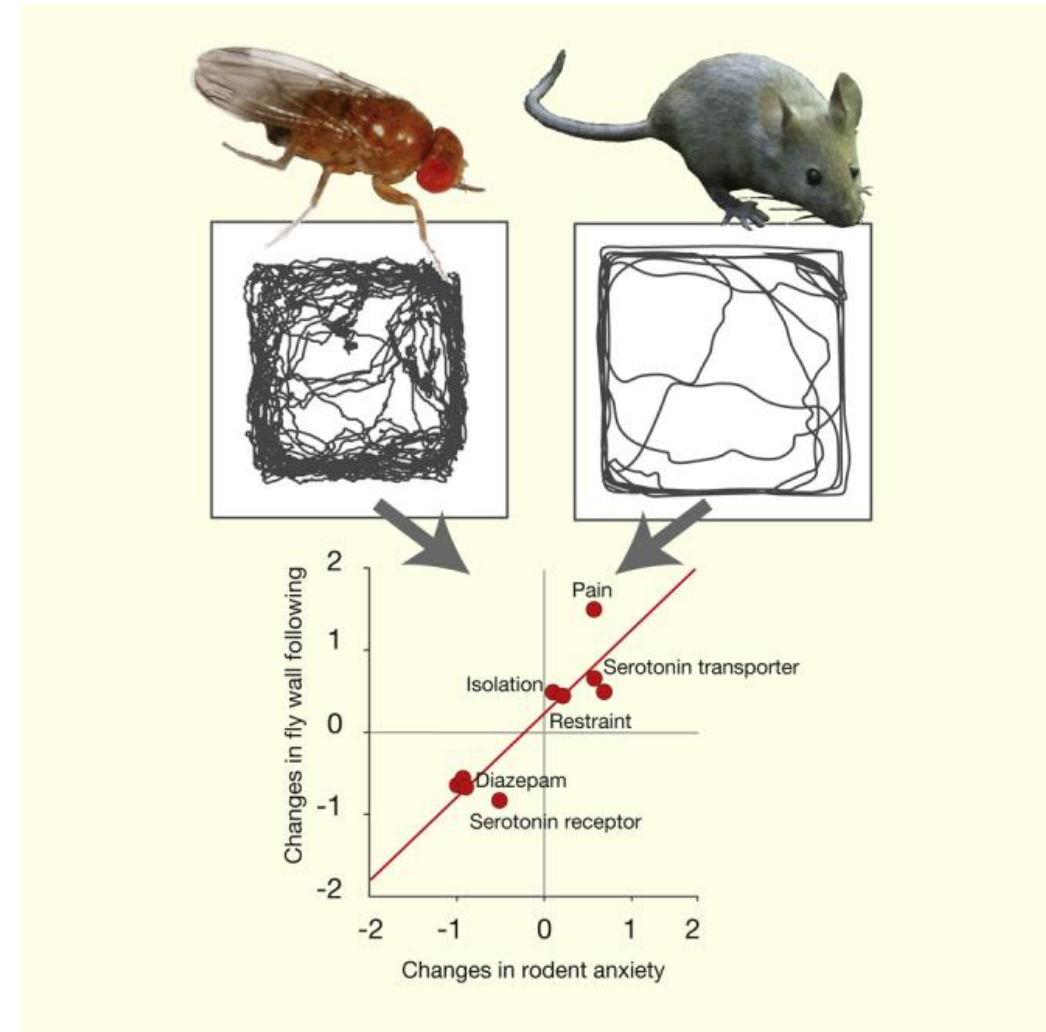
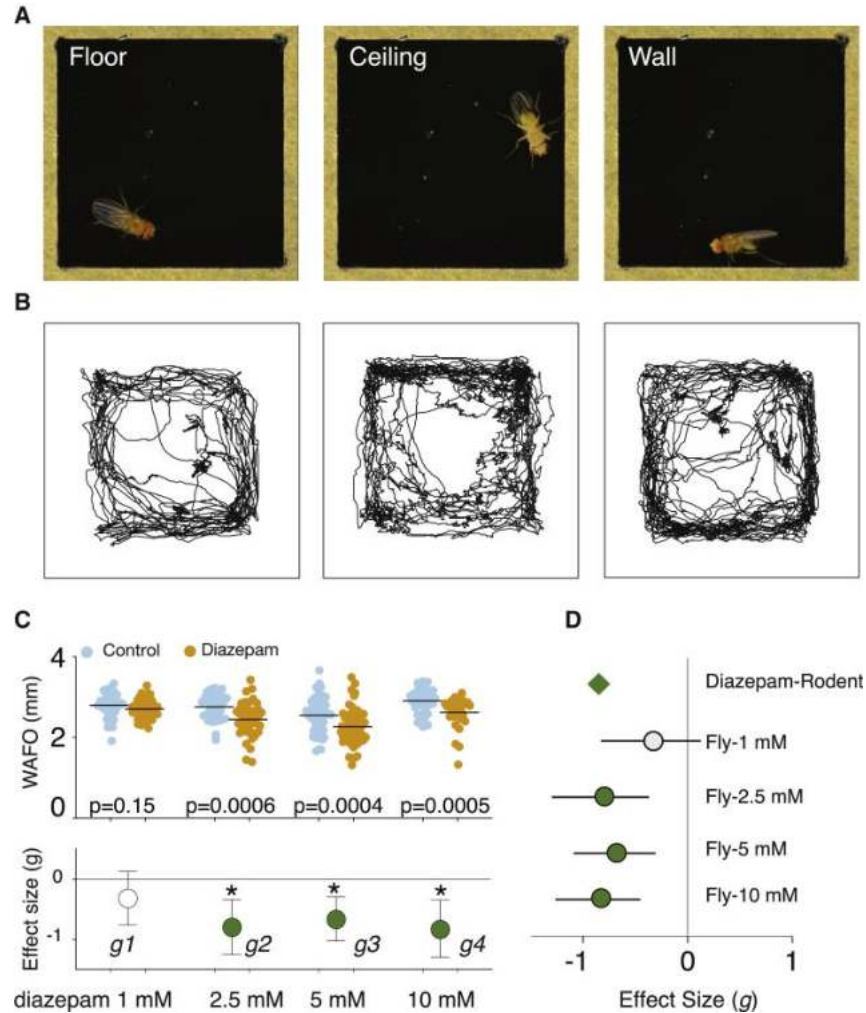


Gibson WT, *et al. Curr Biol.* 2015

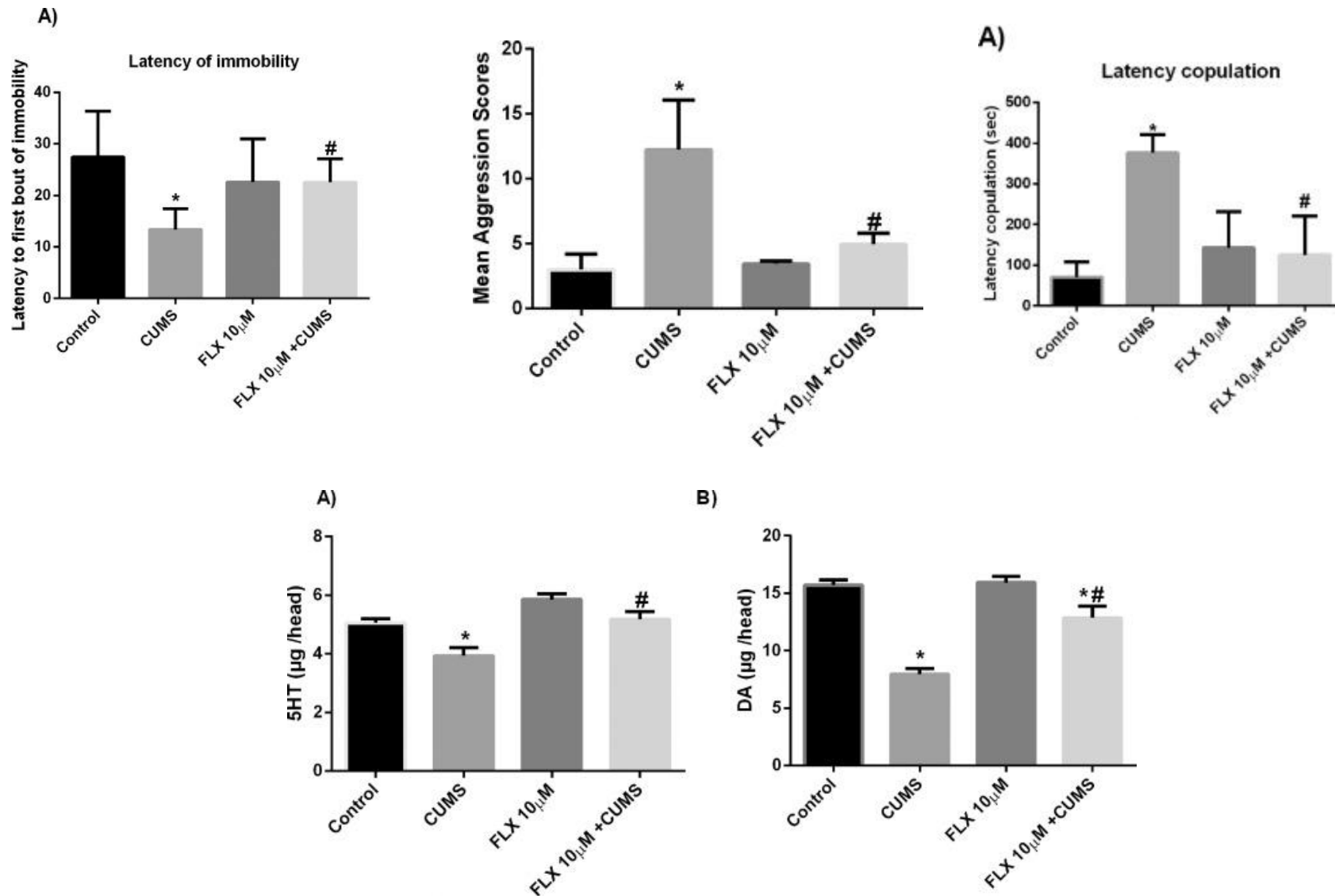
Gowda SBM., *et al. iScience.* 2022

# Ancient anxiety pathways influence defense behaviors in *Drosophila*

“wall following” (WAFO)



# Chronic stress induces depression-like behavior in fruit flies by modulating 5-HT

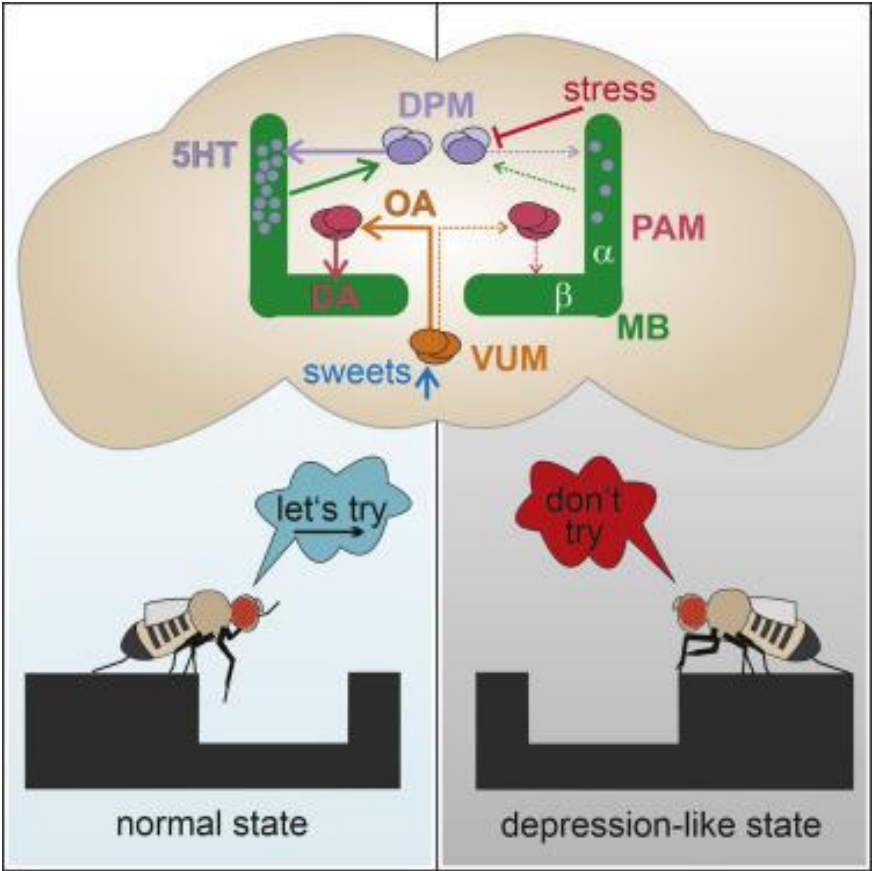
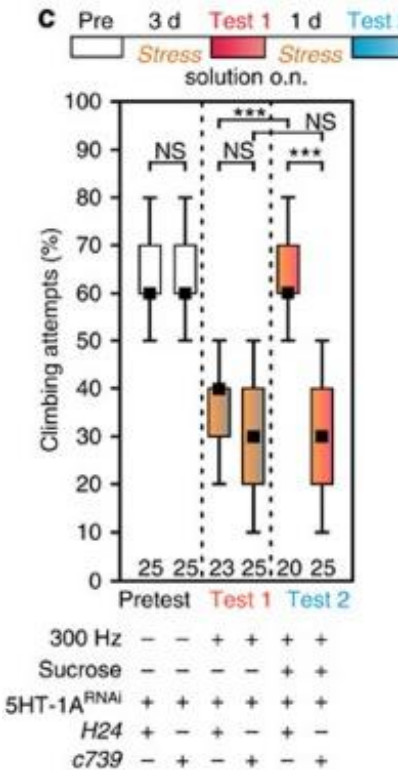
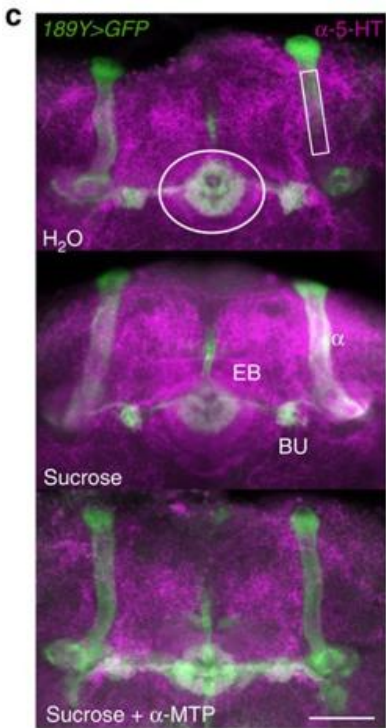
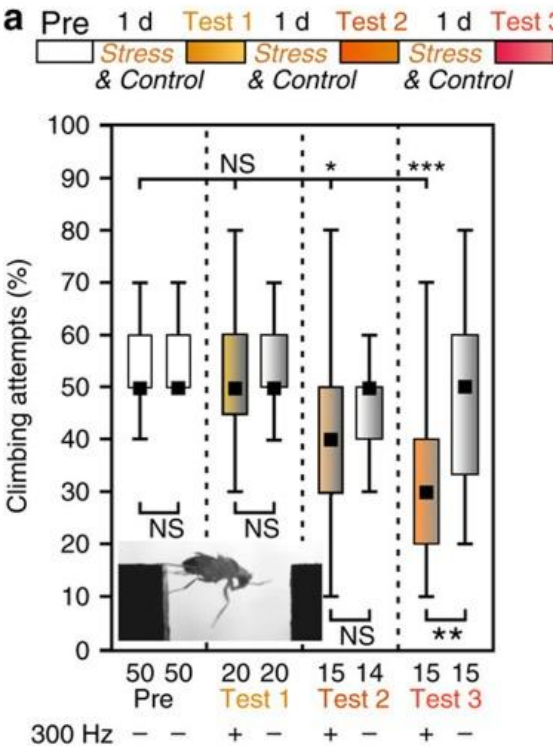


# Mushroom bodies are regulated by 5-HT and OA to regulate depression-like behavior in *Drosophila*

Prof. Dr. Roland Strauss

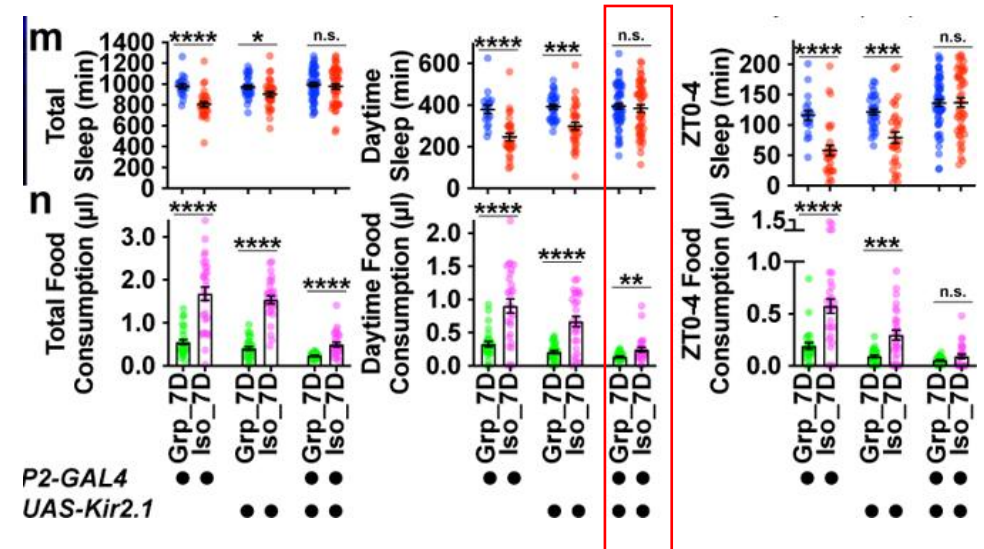
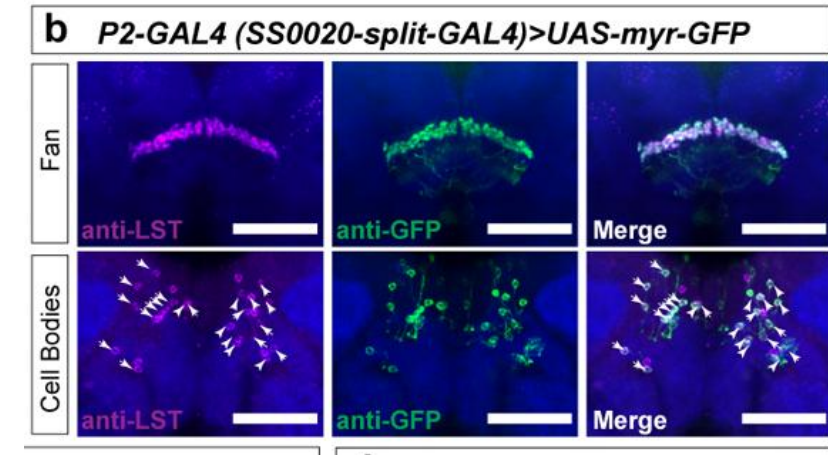
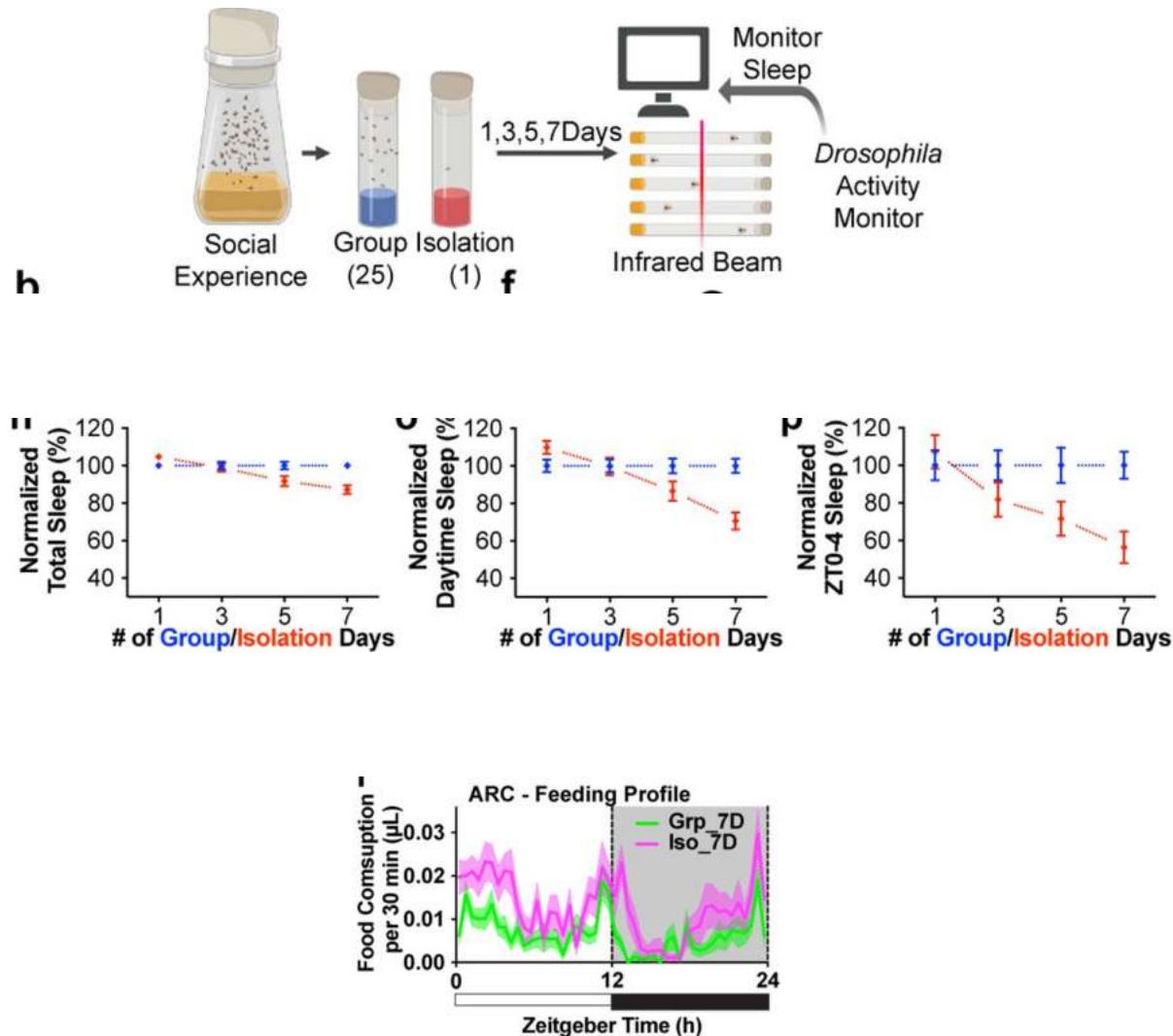


Foto: Peter Pulkowski



Ries AS., et al. *Nat Com.* 2017  
 Tim Hermanns., et al. *Curr bio.* 2022

# Chronic social isolation signals starvation and reduces sleep in *Drosophila*



# Conclusions

- Emotions can be expressed through behavior
- VTA is known to be an emotional center in mice and involved in a variety of emotion-related behaviors such as reward and anxiety-like behaviors.
- *Drosophila* can be used for studying emotions as model animals, due to its behavioral phenotype and highly homologous neuropeptides.

	Mammals/insects	Neuron/neuropeptide
Joy	Courtship, sugar-feeding	DA
Fear	Freezing; running	5-HT
Anger	aggression	VMHvl <sup>PR</sup> (mouse), 5-HT
Anxiety	Wall following; social-interaction; sleep; grooming; feeding	5-HT, 5-HTT, NPF

THANK YOU!

