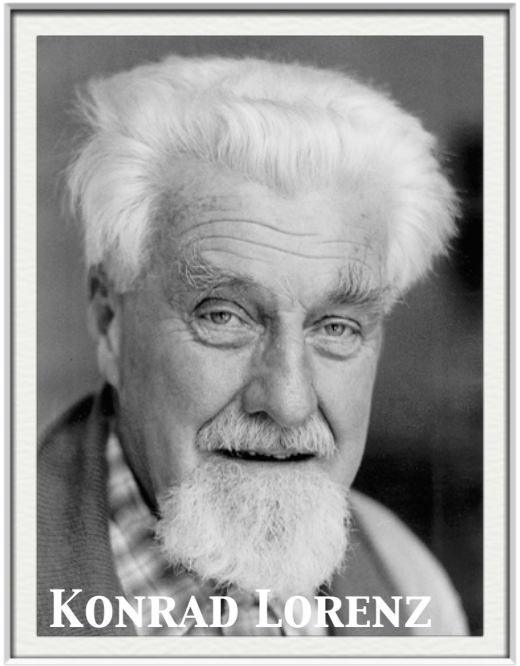
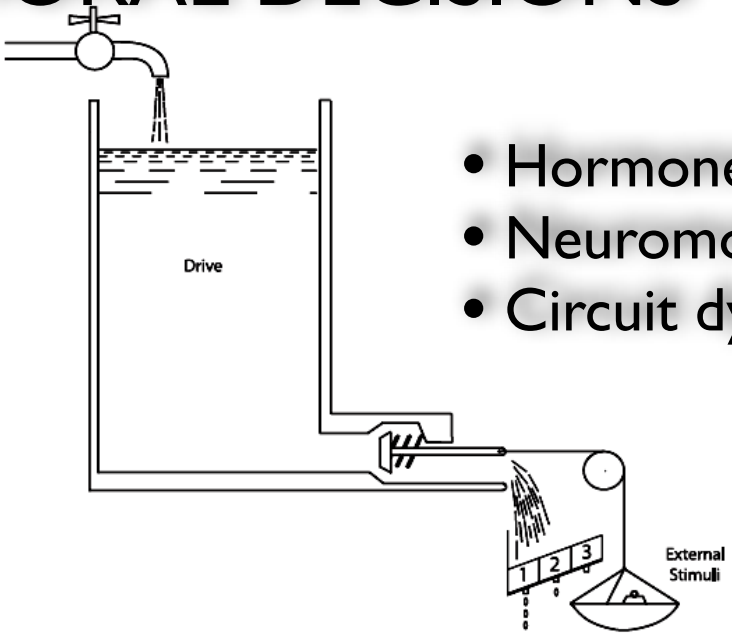
INTERNAL STATES AND BEHAVIORAL DECISIONS: MATING VS. AGGRESSION

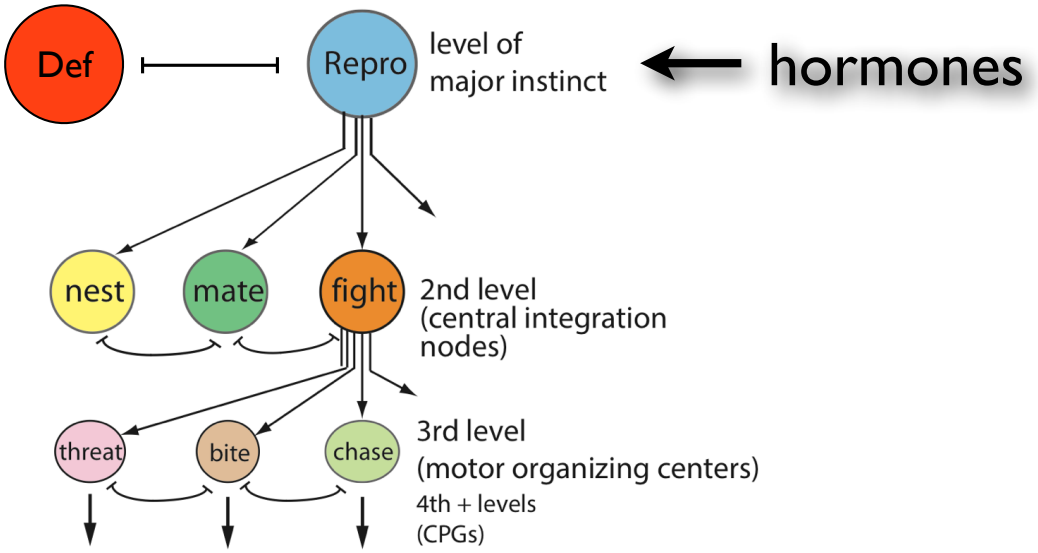
EARLY MODELS OF INTERNAL STATES AND BEHAVIORAL DECISIONS





- Hormones
- Neuromodulators
- Circuit dynamics?

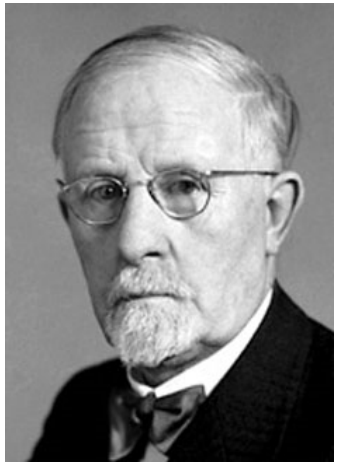
Berridge (2014) after Lorenz and Leyhausen (1973)

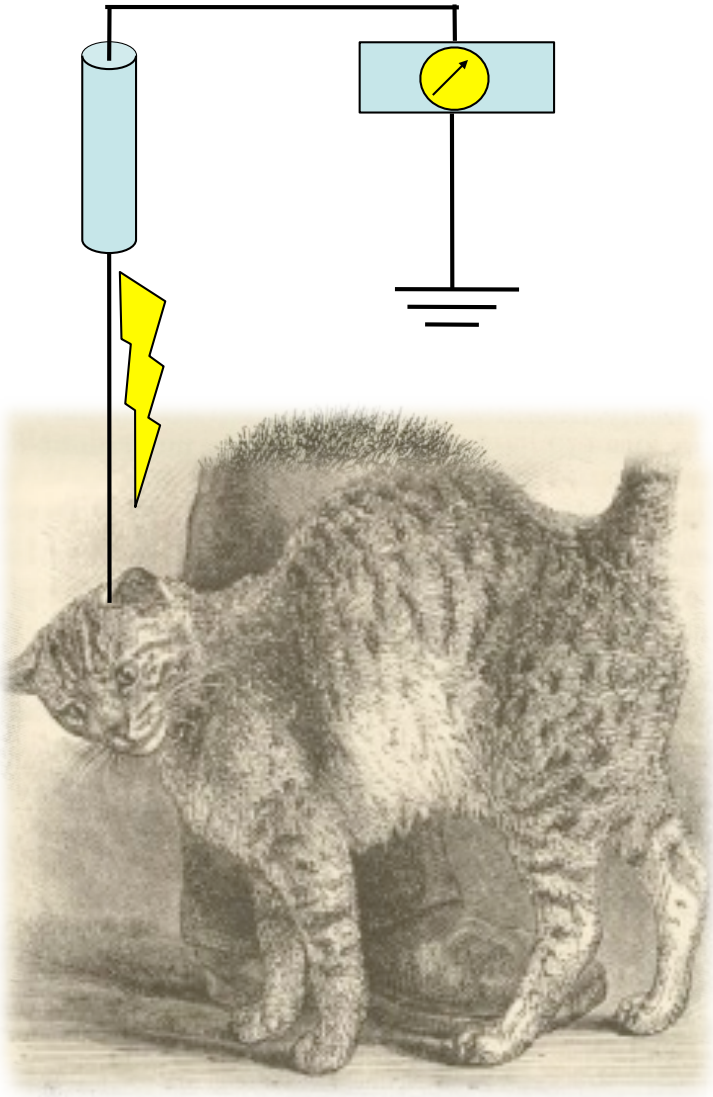


Anderson (2012) after Tinbergen (1951)

BRAIN STIMULATION EXPERIMENTS IDENTIFY AGGRESSION CENTERS IN THE HYPOTHALAMUS

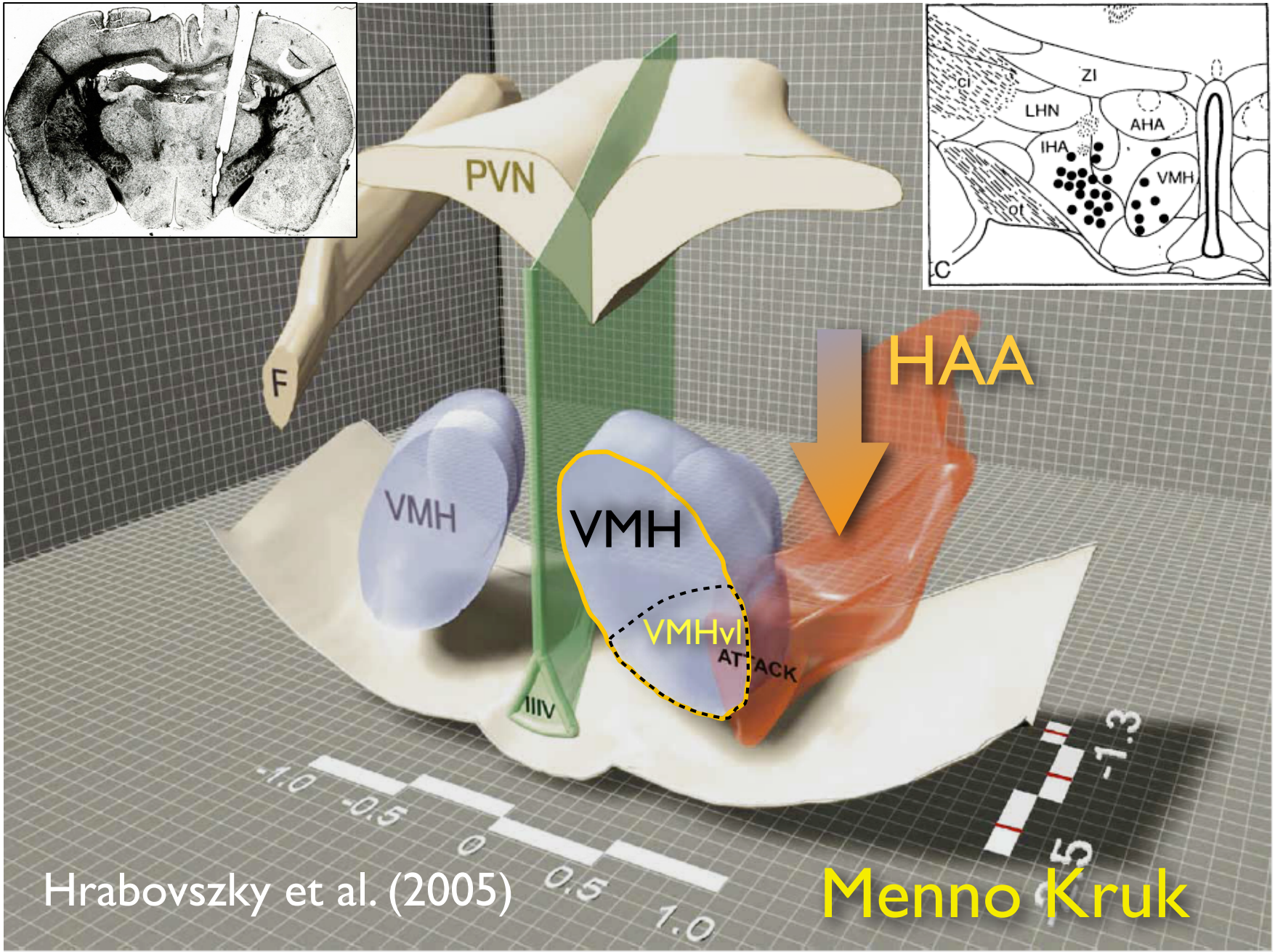
Walter Rudolf Hess (1943)



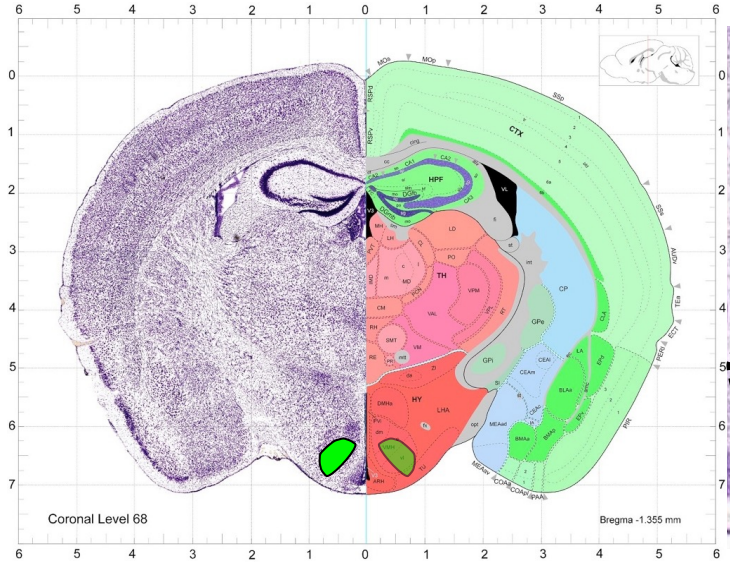


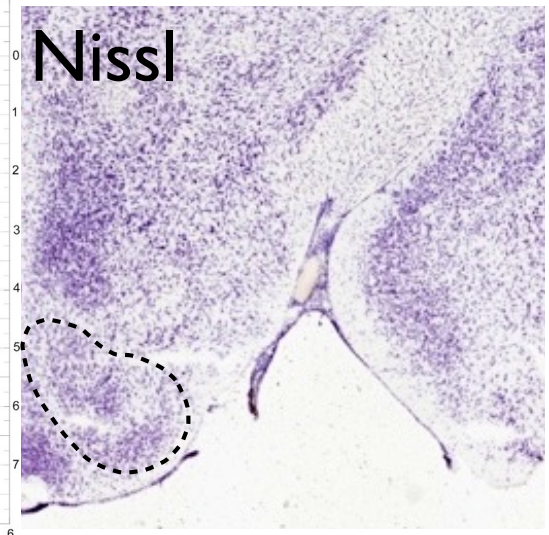
Hess, W.R. (1928) Physiologie *42*: 554-555

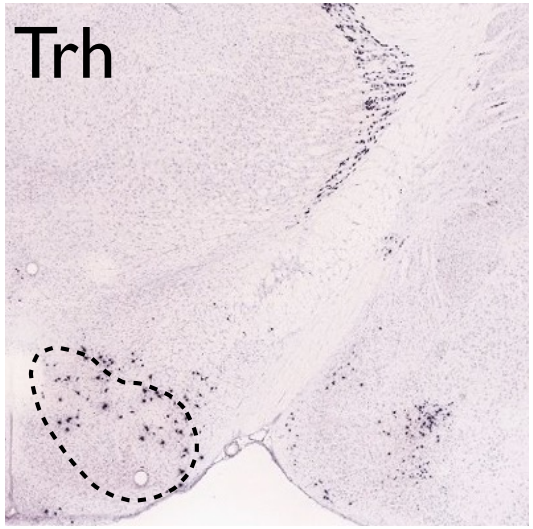
STIMULATION MAPPING OF THE "HYPOTHALAMIC ATTACK AREA" IN RAT

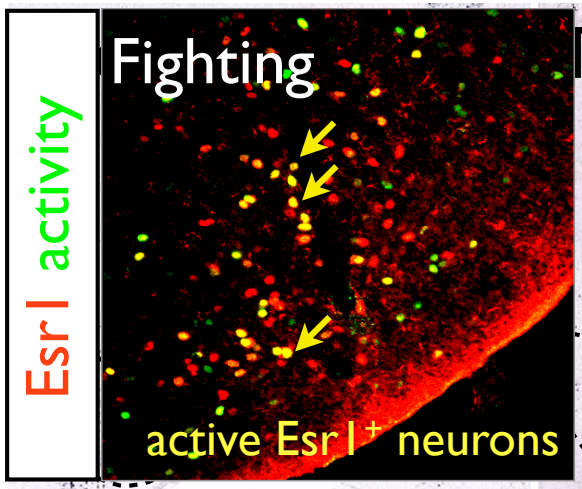


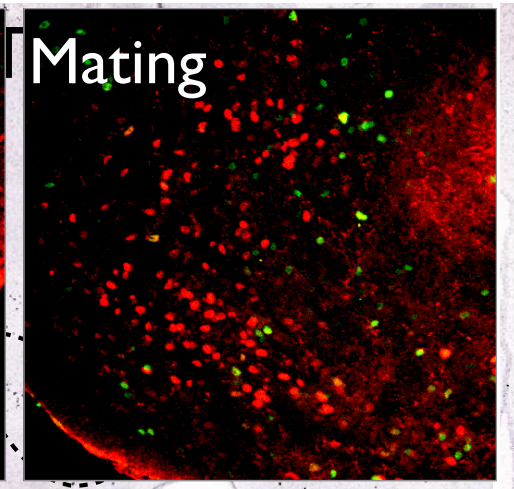
FINDING GENE MARKERS FOR AGGRESSION NEURONS IN MICE

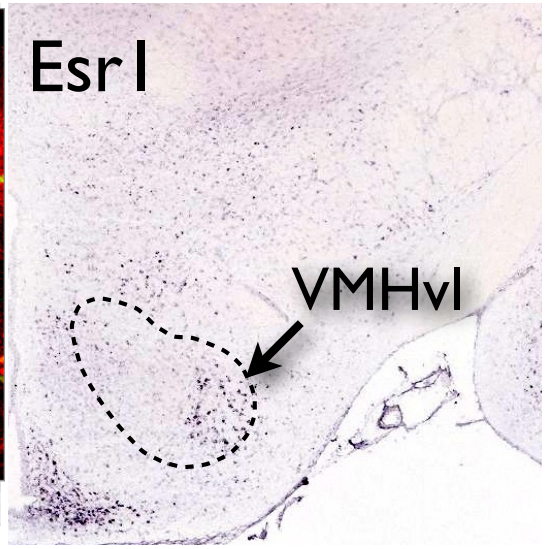






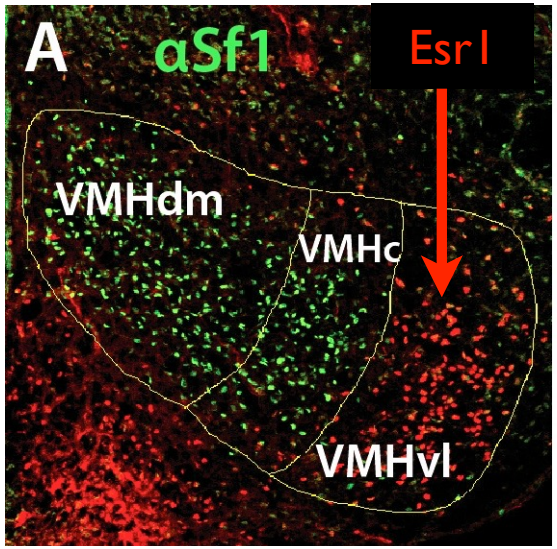




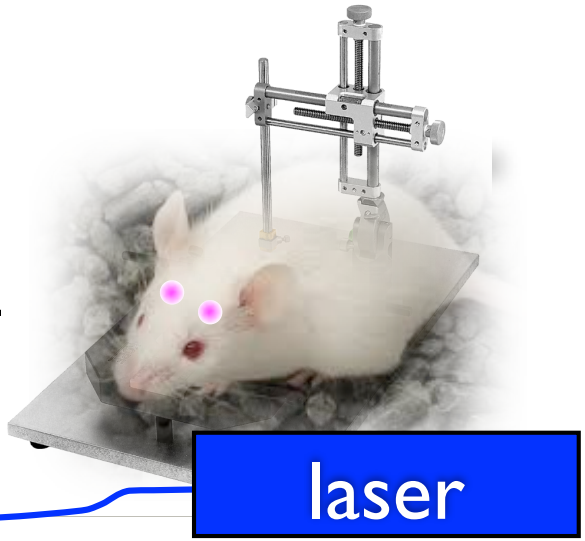


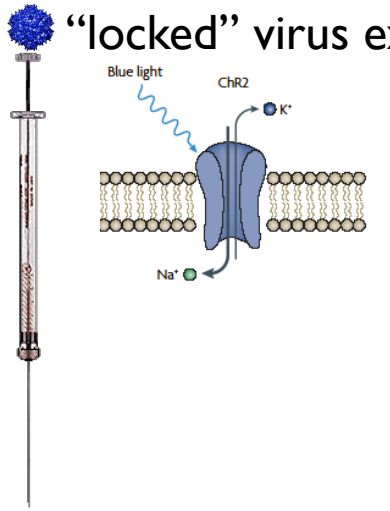
Allen Brain Atlas www.brain-map.org

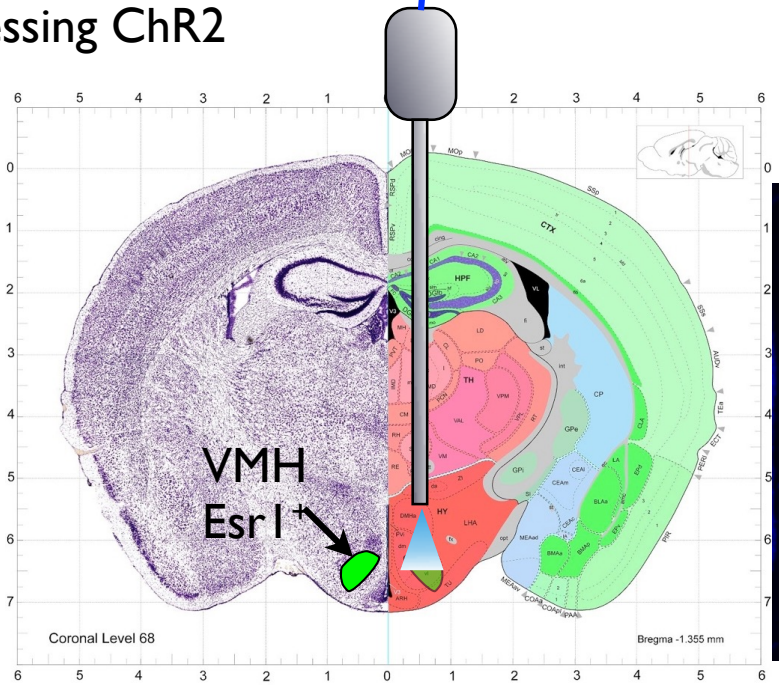
BUILDING MICE TO MANIPULATE Esr1^{+} NEURONS

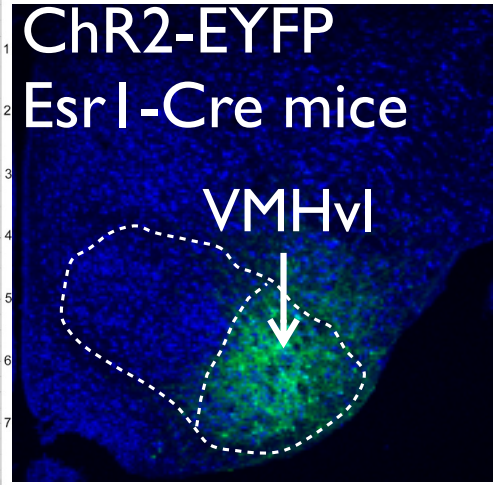


embryonic stem cells
with modified *Esr1* gene



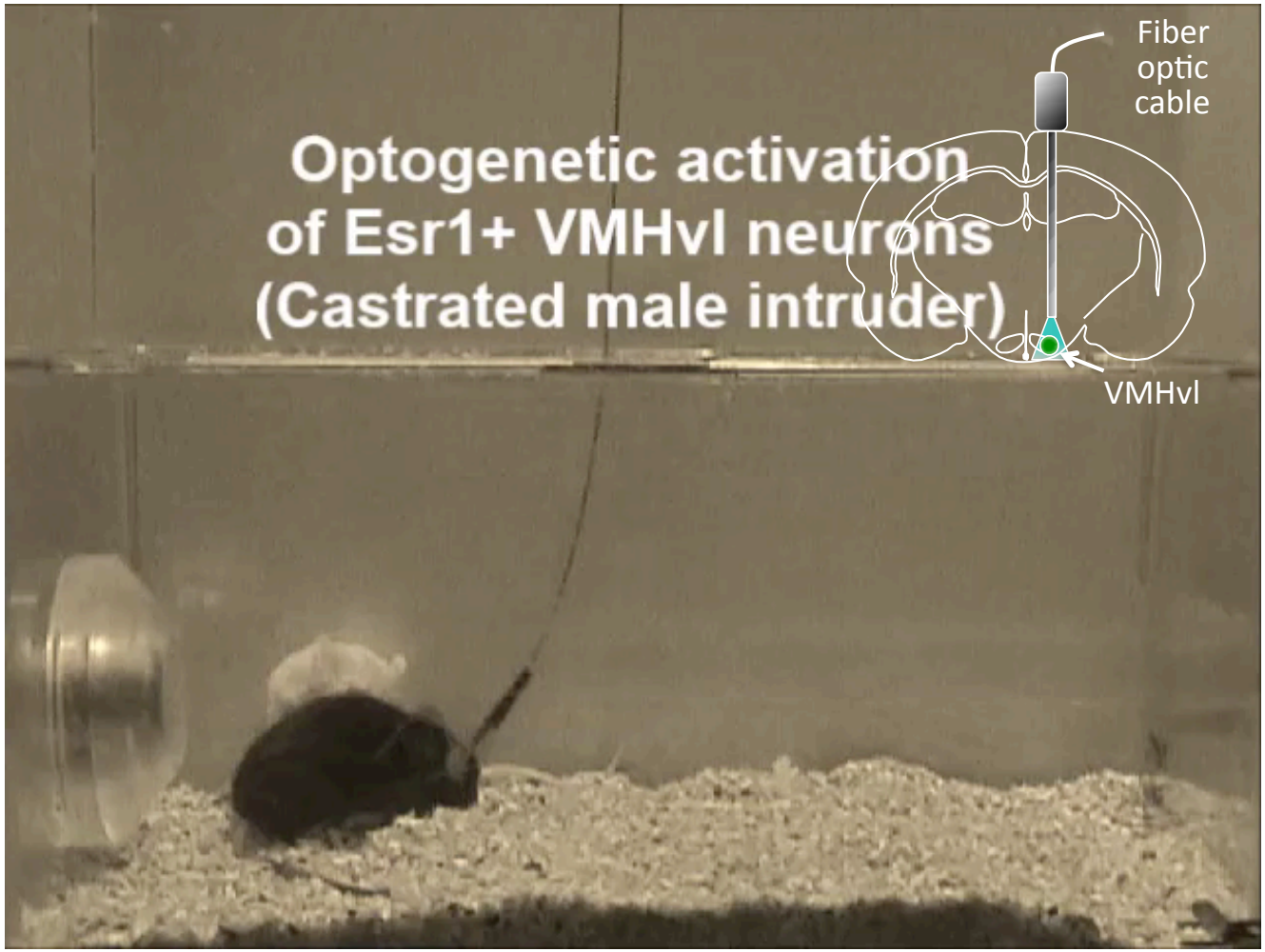


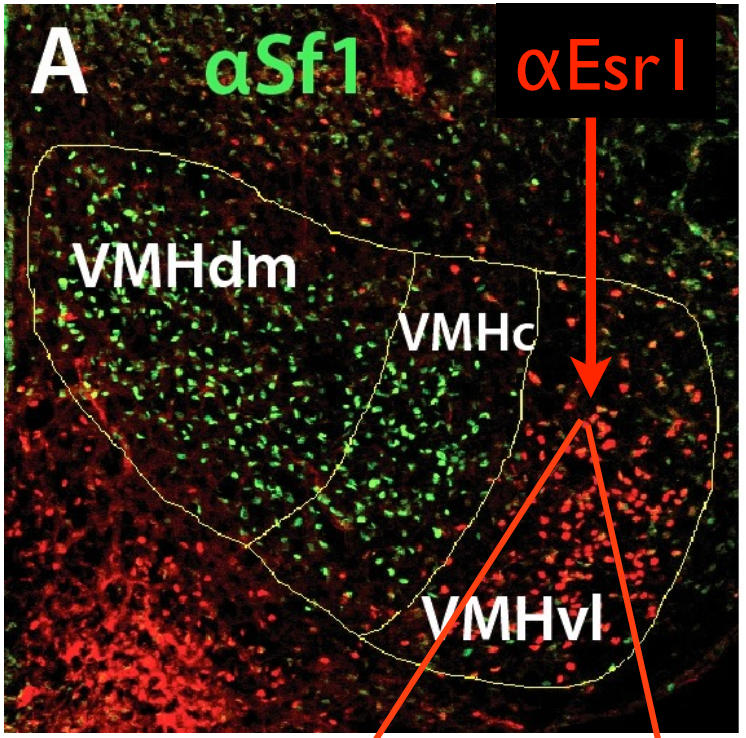


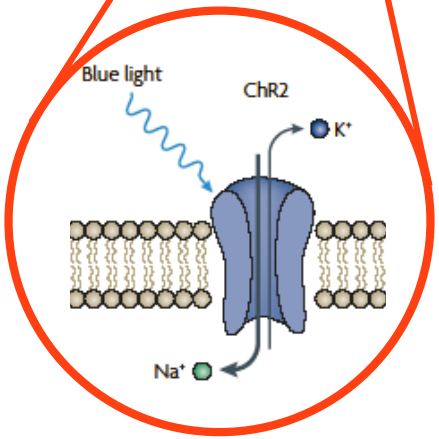


Lee et al. *Nature* (2014) *509*: 627-632

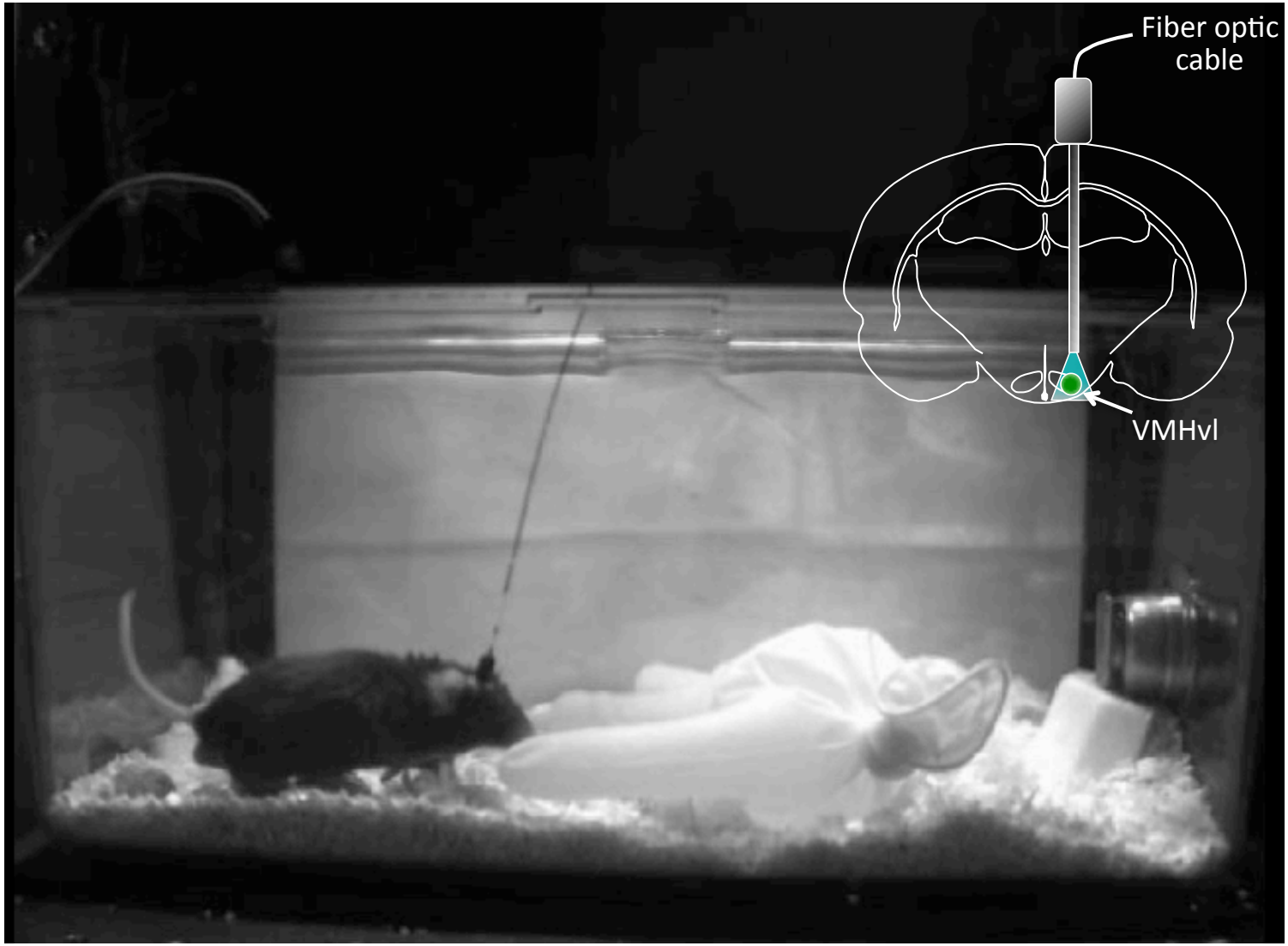
OPTOGENETIC ACTIVATION OF Esr1^{+} NEURONS IN VMHvl PROMOTES ATTACK







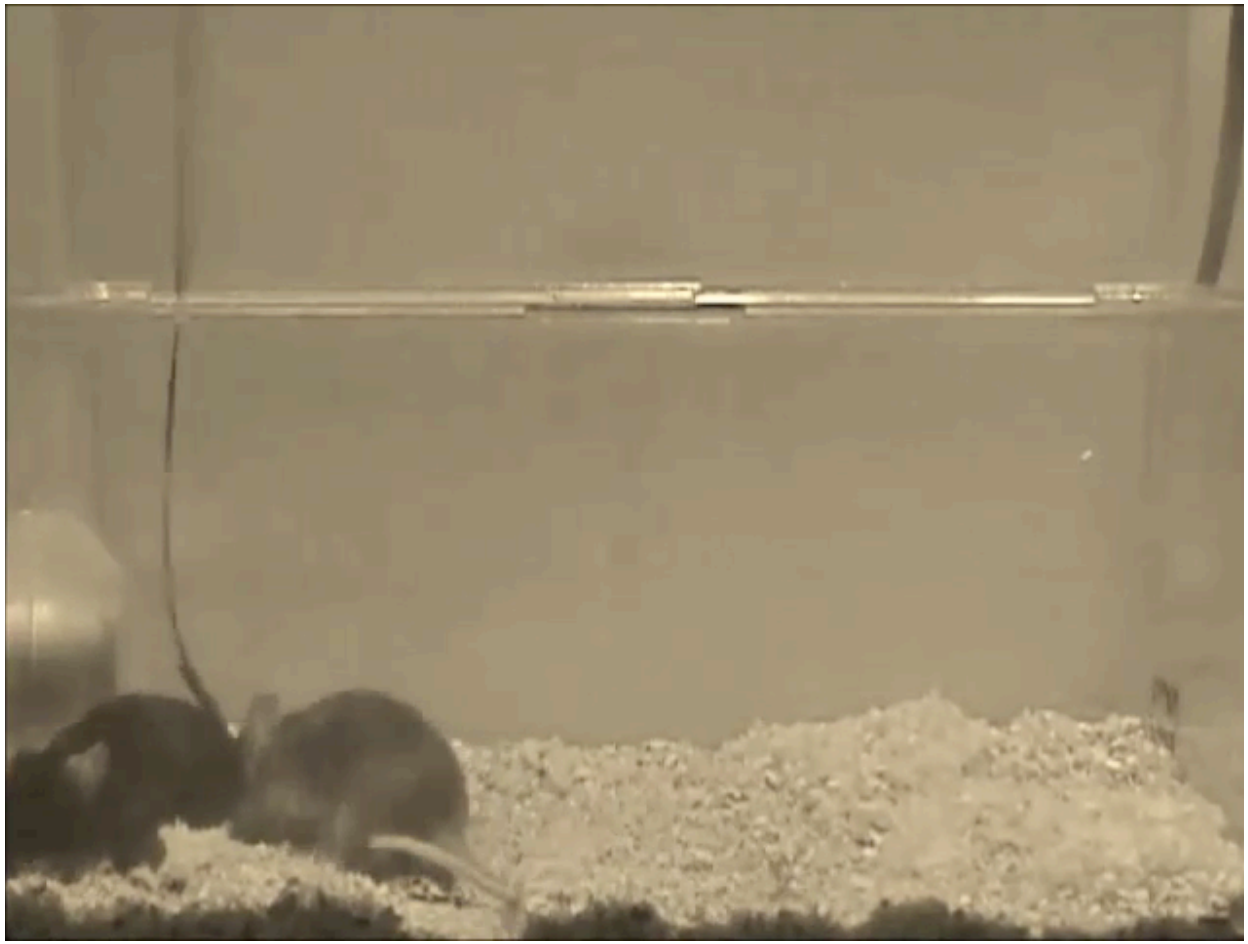
VMHvl ACTIVATION PROMOTES AGGRESSION, NOT SEX MIS-IDENTIFICATION

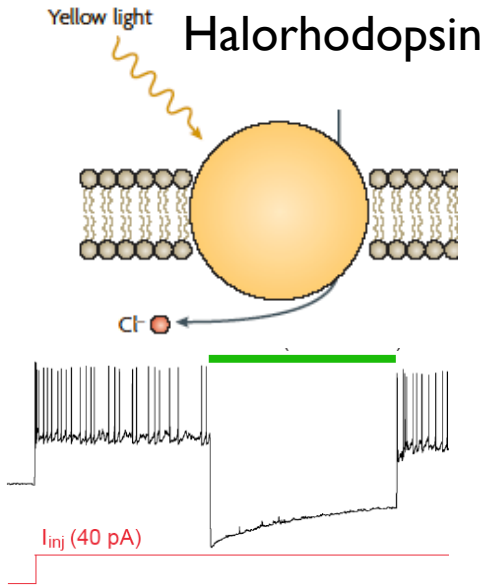


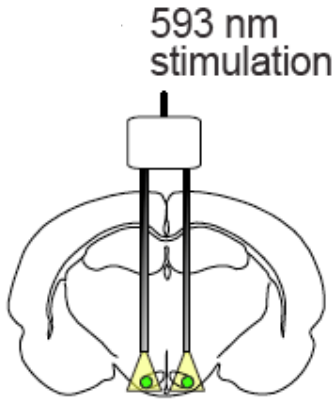
Lin et al. (2011) *Nature*

Falkner et al (2016)

OPTOGENETIC INHIBITION OF VMHvl Esr1^{+} NEURONS INTERRUPTS ATTACK





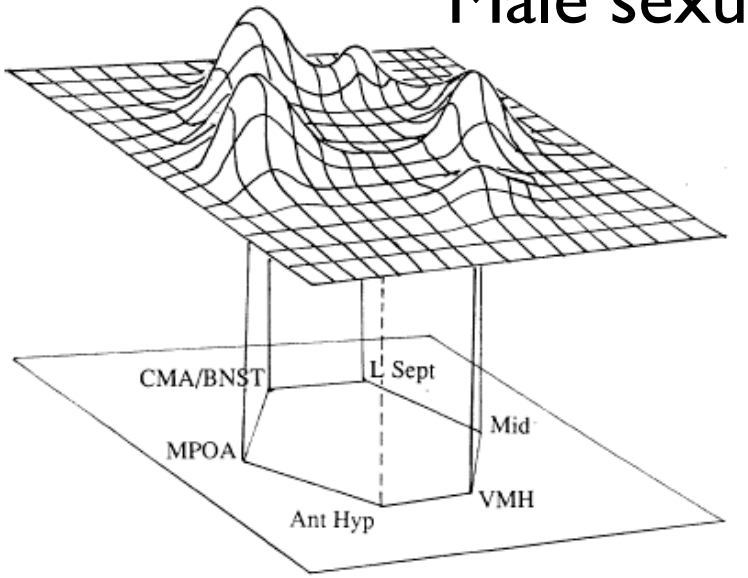


Lee et al., *Nature* (2014)

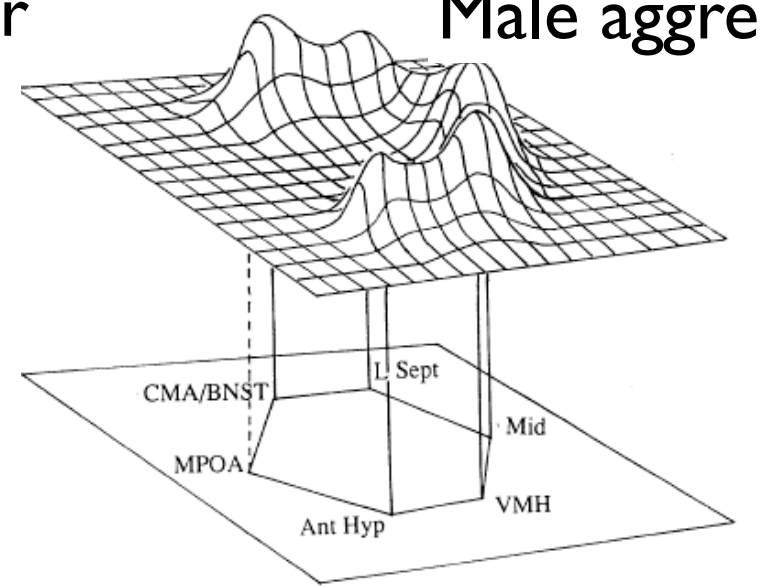
Shah, Ogawa

WHAT IS THE RELATIONSHIP BETWEEN MATING AND AGGRESSION CIRCUITS?

Male sexual behavior



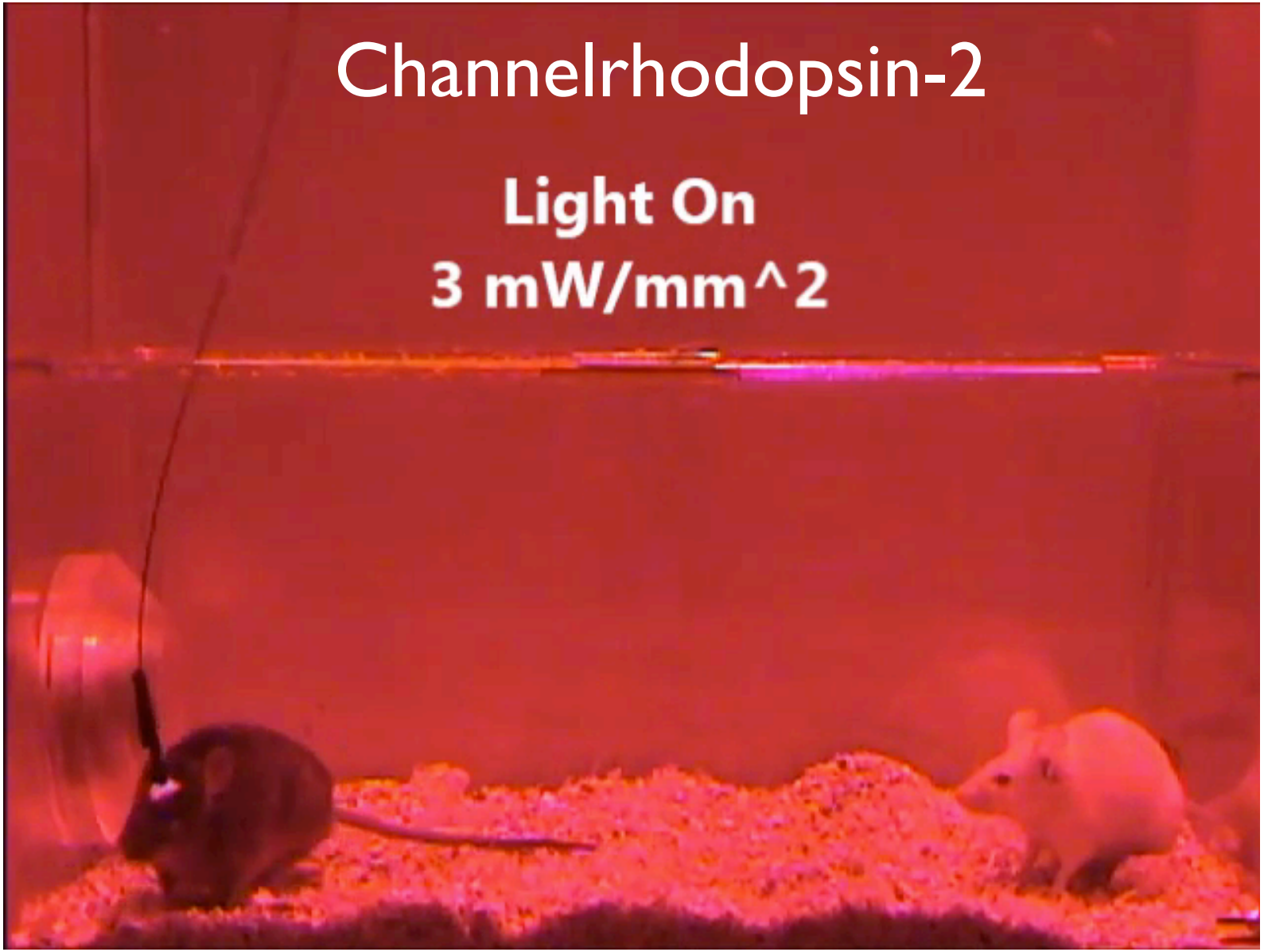
Male aggression

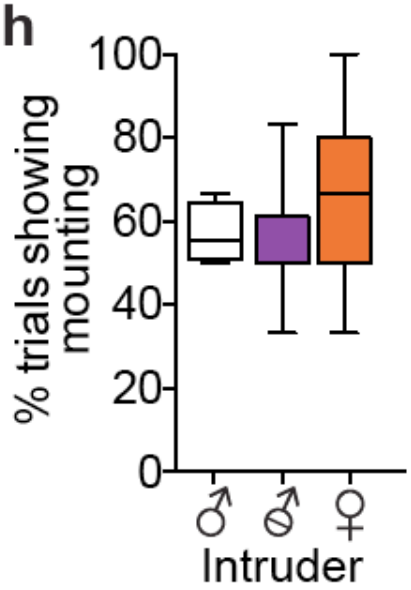


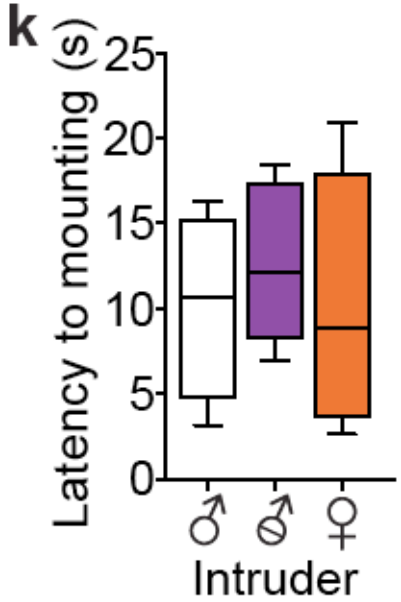
➡ Same regions/same neurons, or same regions/different neurons?

Newman, S.W. (1999) Ann. NY Acad. Sci. 877:242

CLOSE INVESTIGATION AND MOUNTING TRIGGERED BY LOW-INTENSITY ACTIVATION OF Esr1^{+} NEURONS



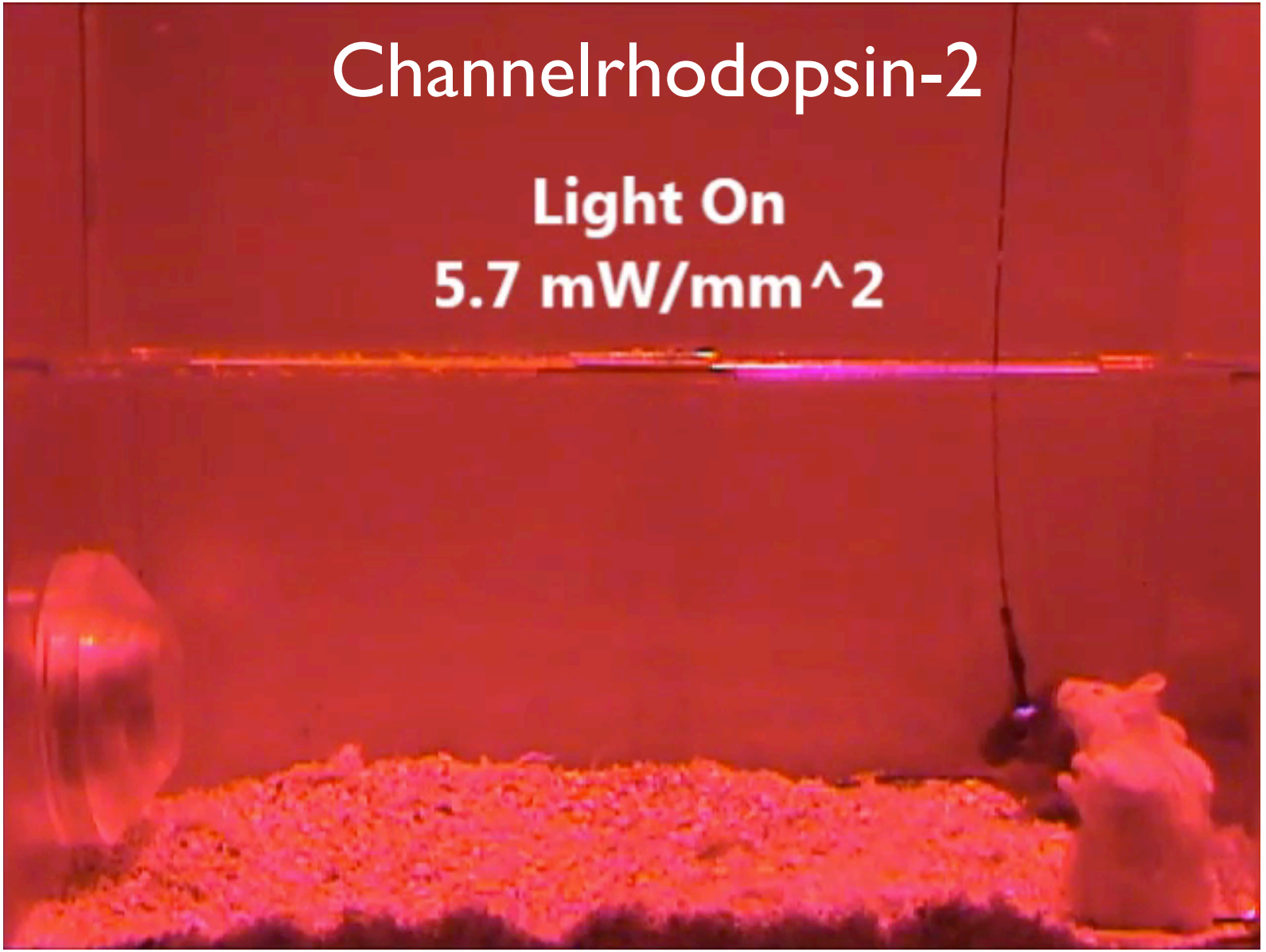


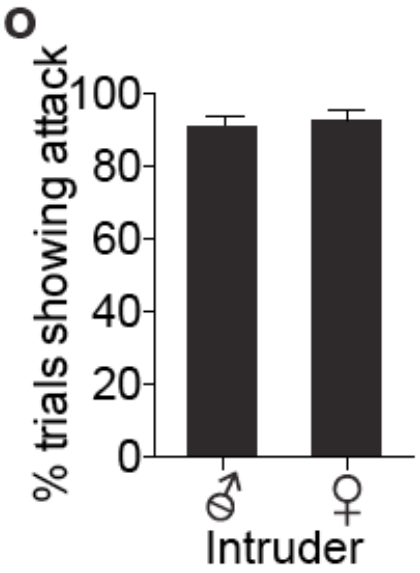


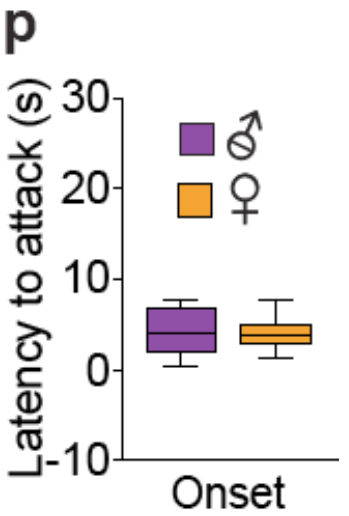
Lee et al. *Nature* (2014) *509*: 627-632

Shah, Ogawa

TRANSITION FROM MOUNTING TO ATTACK AT HIGHER LIGHT INTENSITIES

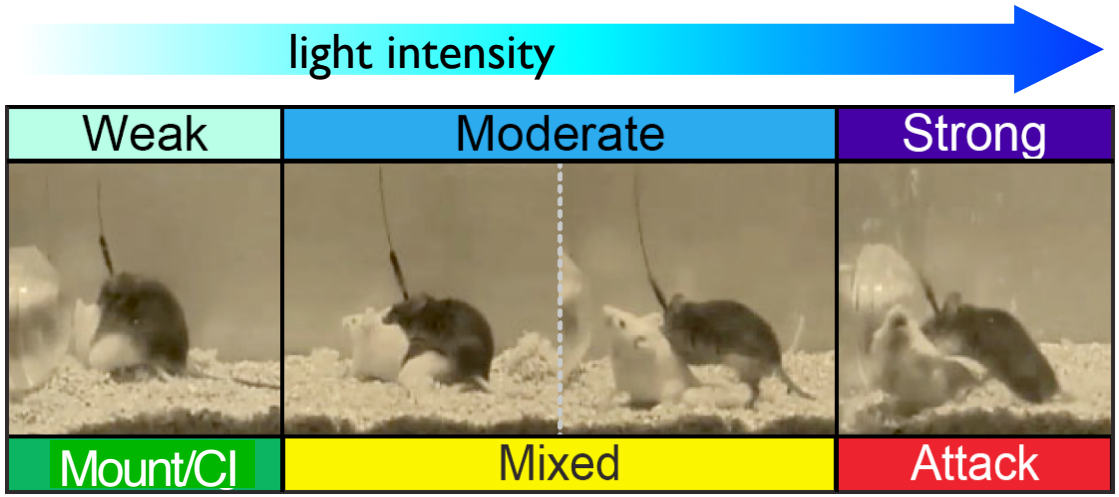


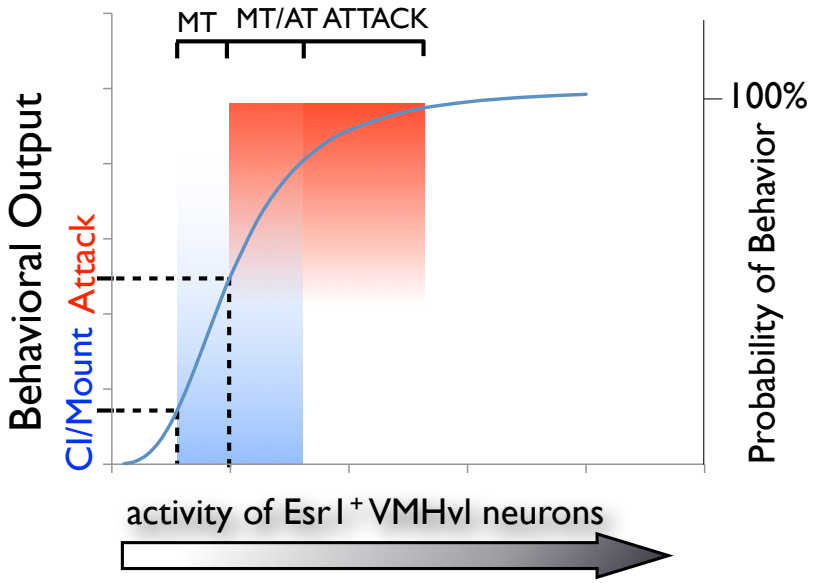


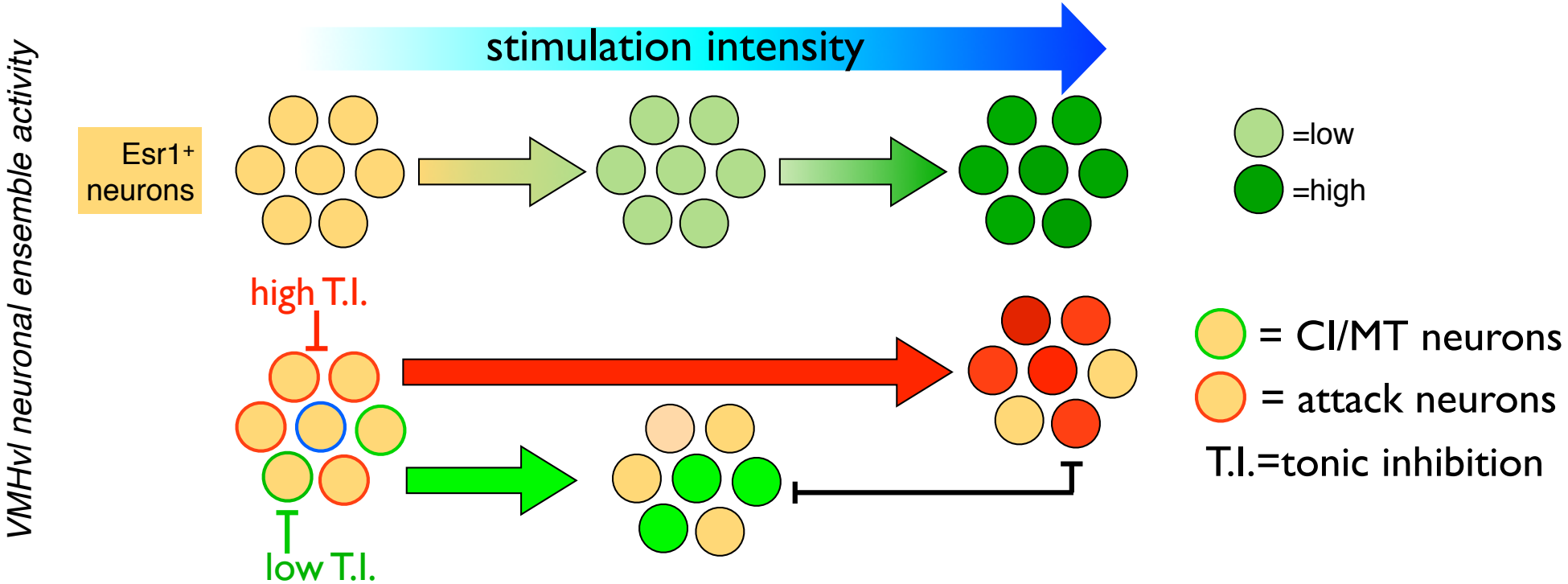


Lee et al. *Nature* (2014) *509*: 627-632

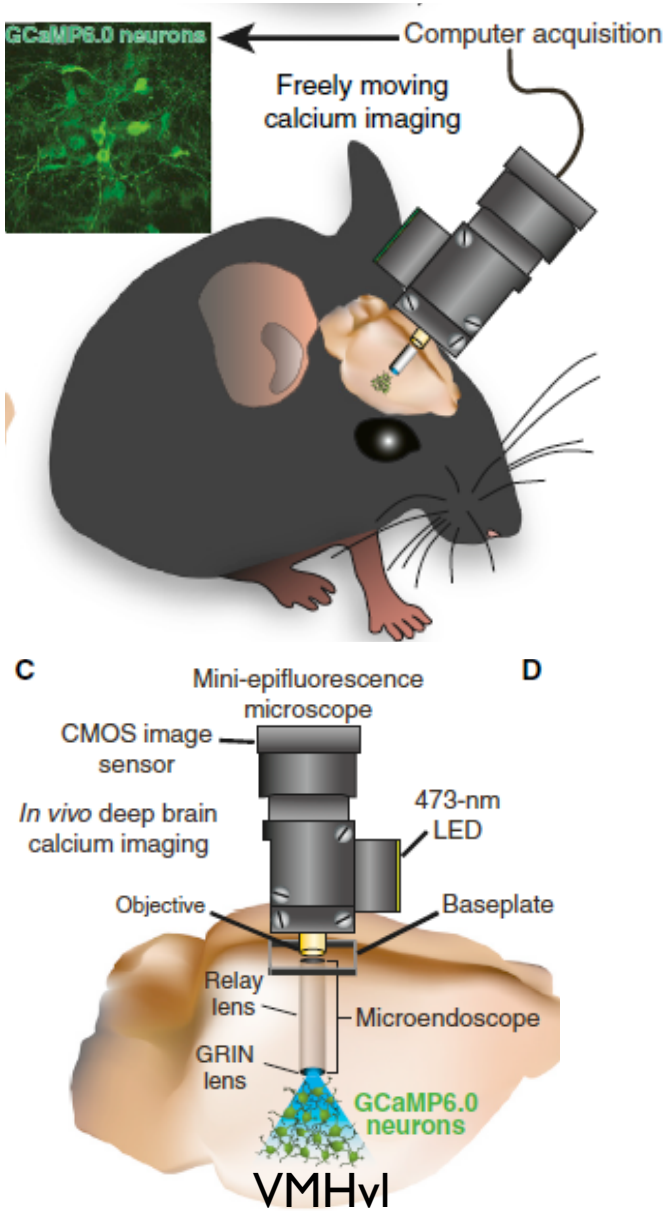
Esr1$^+$ NEURONS CONTROL SOCIAL BEHAVIOR IN A SCALABLE MANNER

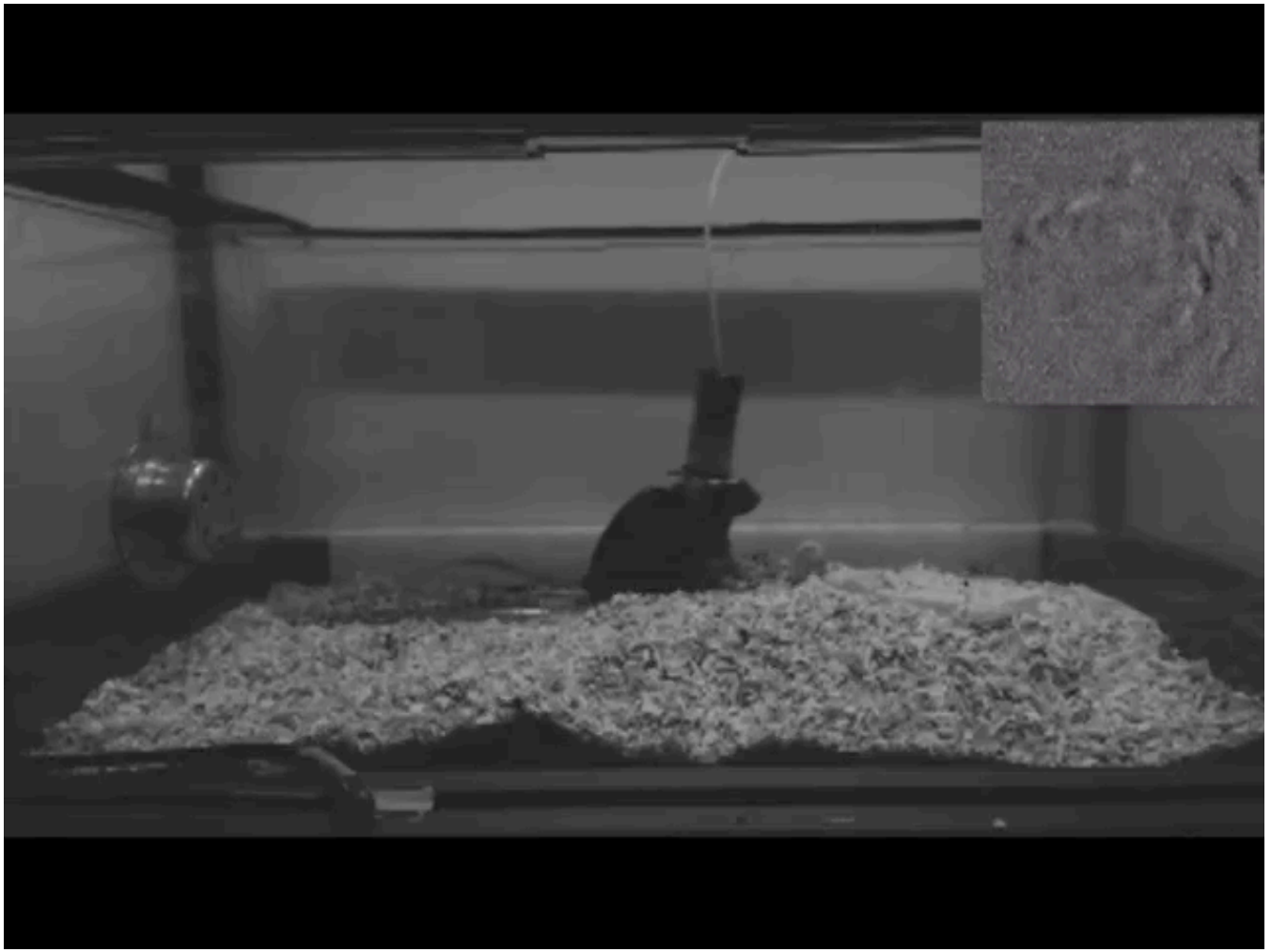






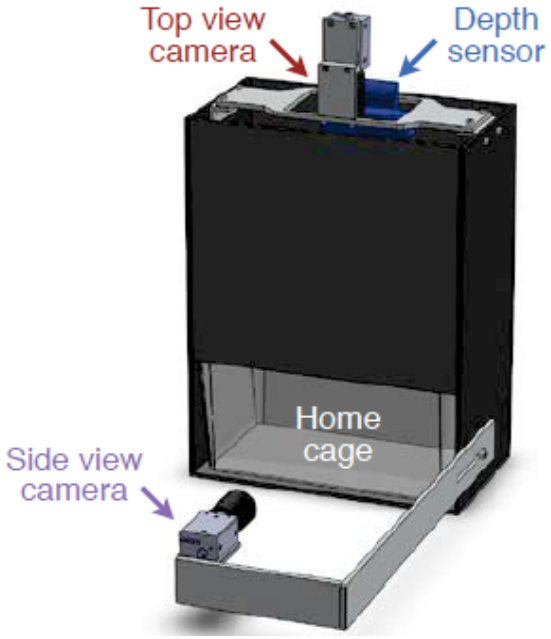
MICROENDOSCOPIC CALCIUM IMAGING FROM ESR1^{+} NEURONS DURING SOCIAL BEHAVIOR

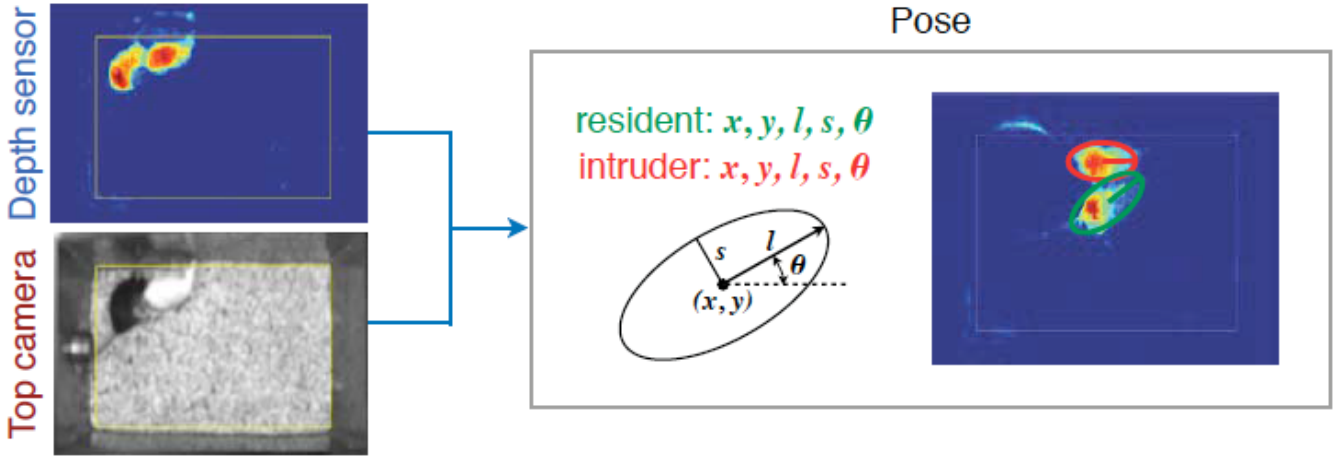


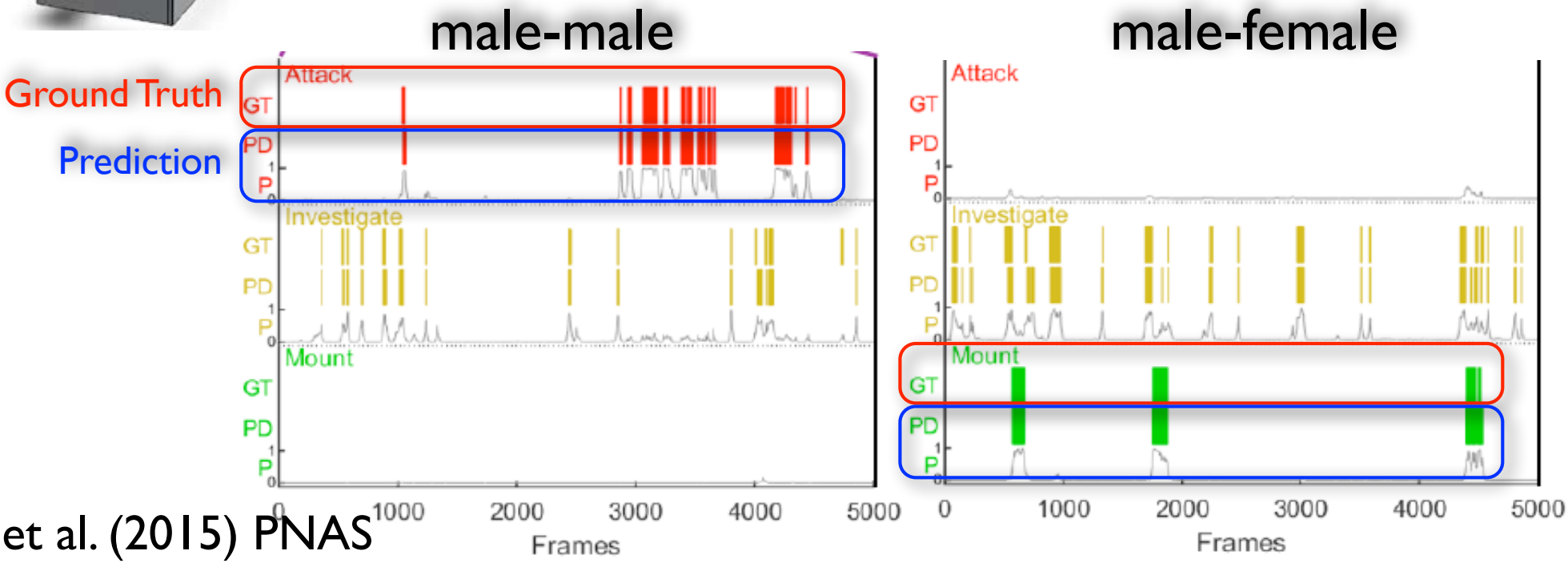


Ryan Remedios (Caltech); Benni Grewe, Mark Schnitzer (Stanford)

AUTOMATED MEASUREMENT OF SOCIAL BEHAVIORS

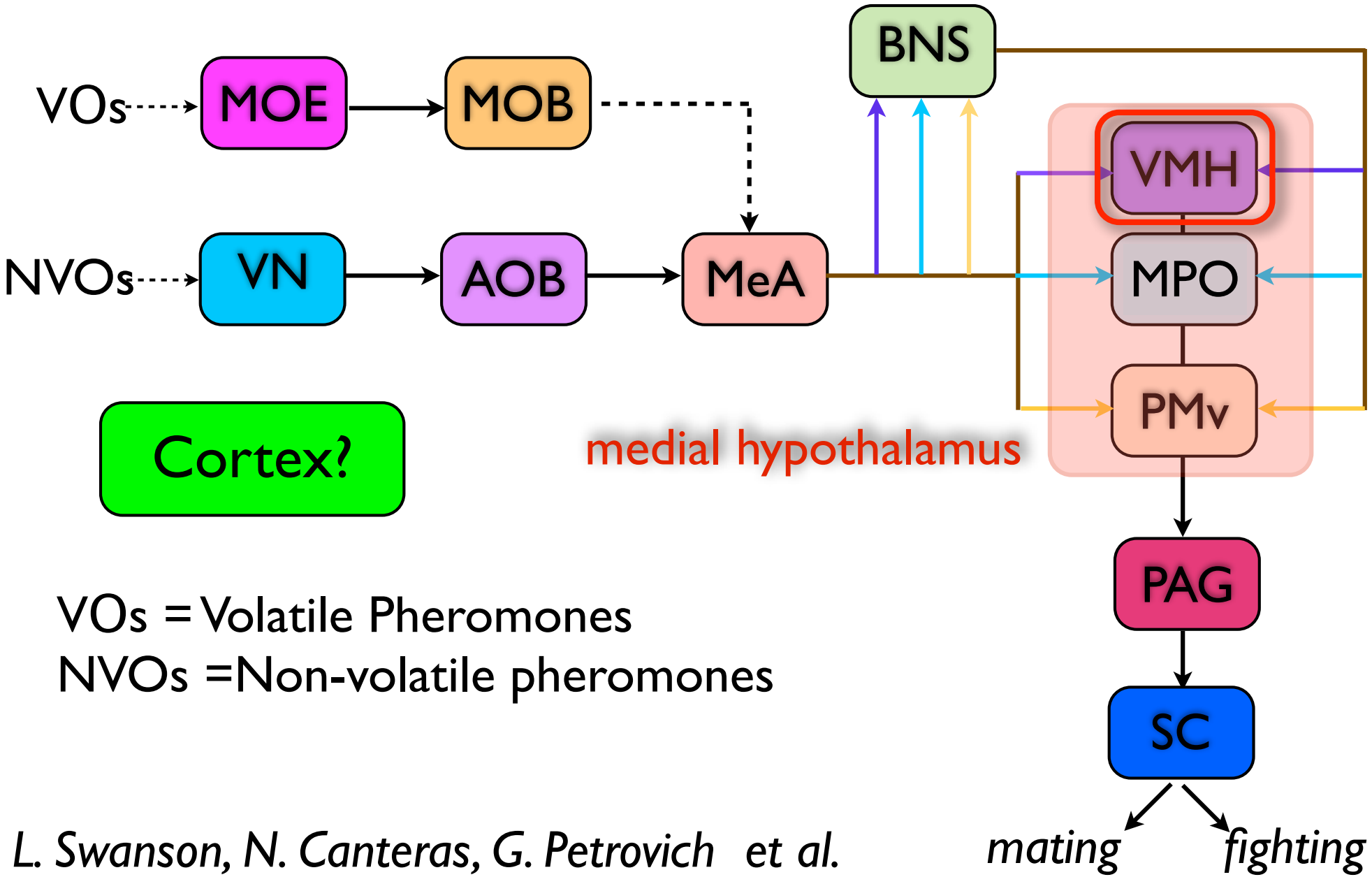






Hong et al. (2015) PNAS

INNATE BEHAVIOR PROCESSING PATHWAYS IN RODENTS



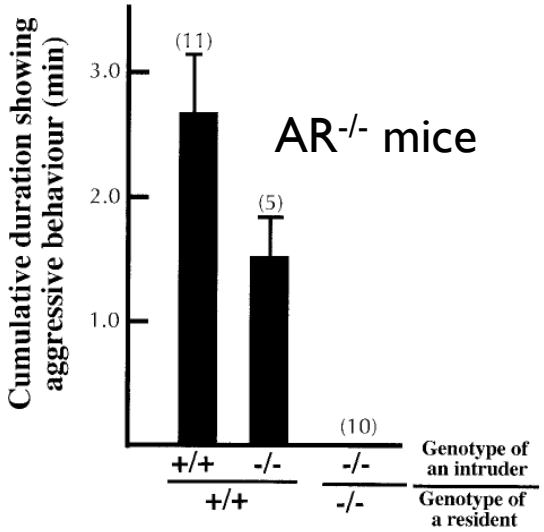
VOs = Volatile Pheromones
NVOs =Non-volatile pheromones

L. Swanson, N. Canteras, G. Petrovich et al.

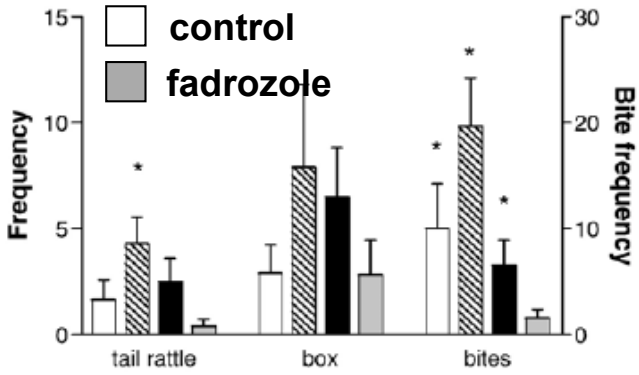
TAKE-HOME MESSAGE

- Genetic identification of hypothalamic attack neurons (Esr1^{+})
- Intermingled neurons control attack and sniffing/mounting
- VMHvl Esr1^{+} neurons may transform sensory signals into a representation of internal state
- Intensity-coding and thresholds may link internal states to behavioral decisions

TRANSLATIONAL APPLICATIONS: A NEW APPROACH TO TREATMENT OF AGGRESSIVENESS IN PTSD?



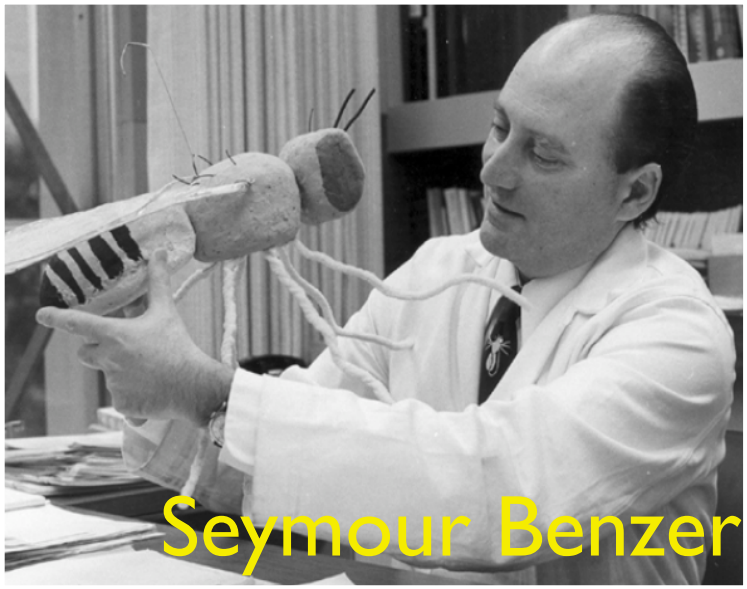
Toda et al. (2001)



Trainor et al. (2006)

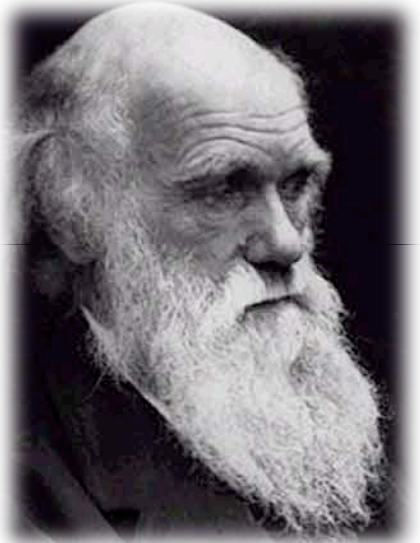
Balthazart, Ball, Marler, Shah

DROSOPHILA AS A MODEL FOR STUDYING CIRCUIT CONTROL OF INTERNAL STATES AND BEHAVIORAL DECISIONS



aggression

courtship

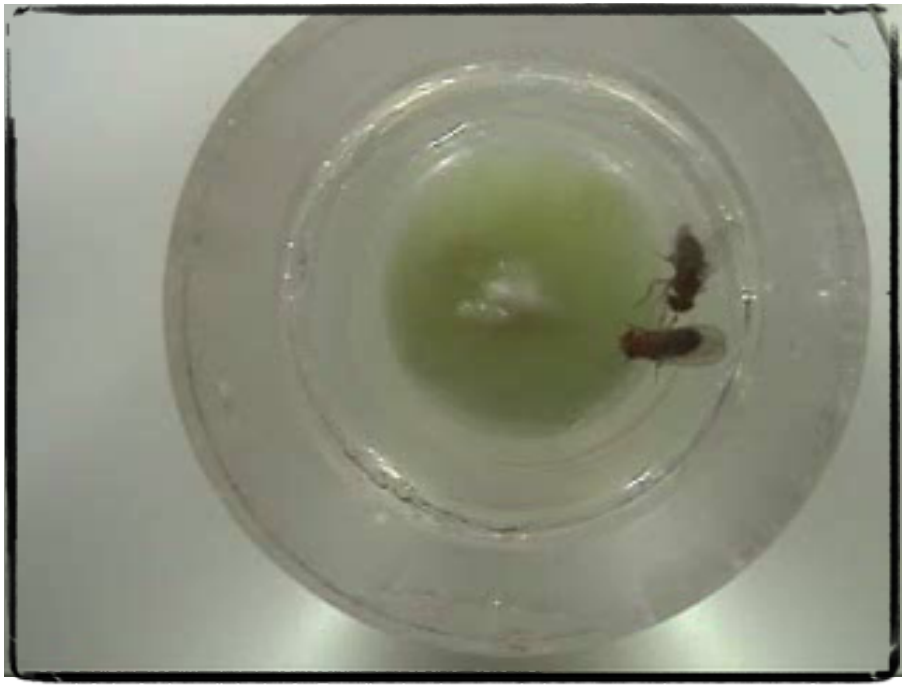


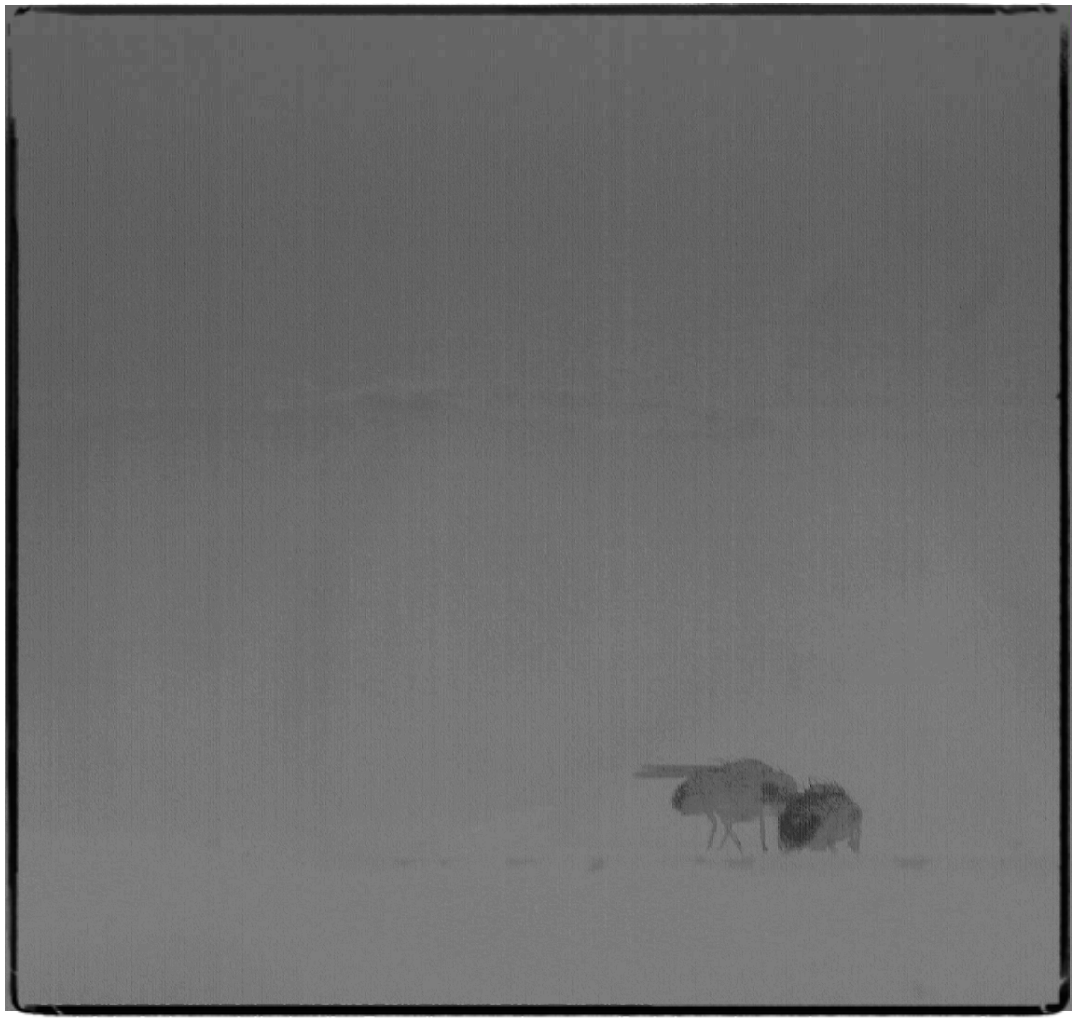
"Even insects *express* anger, terror, jealousy and love by their stridulation."

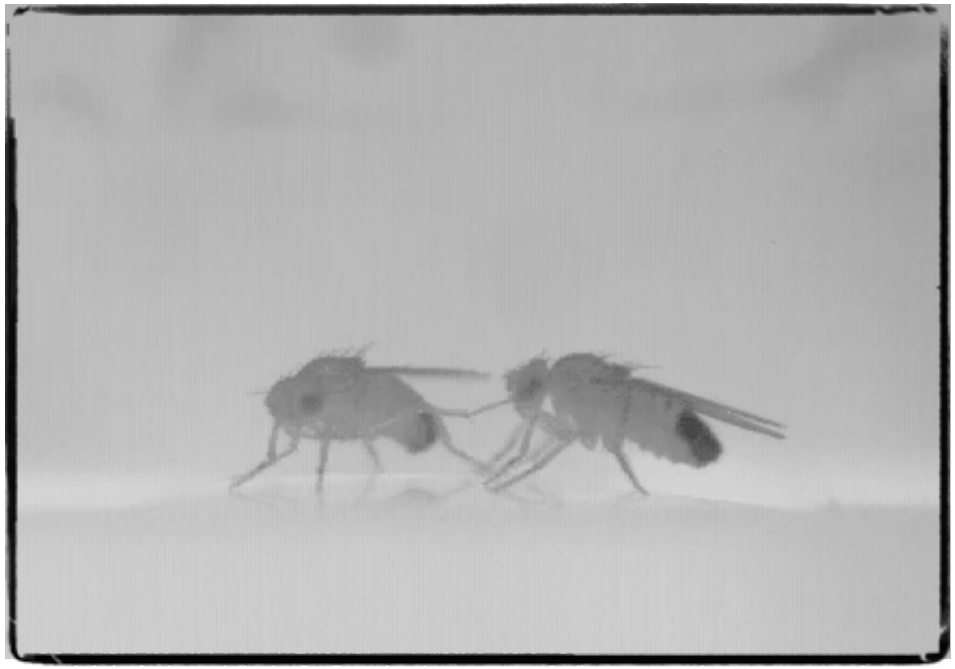
-Darwin, C.R. (1872) *The Expression of the Emotions in Man and Animals*, p.349

Hoffmann, Heisenberg, Greenspan, Brembs, Dickson

AGGRESSION IN *Drosophila*

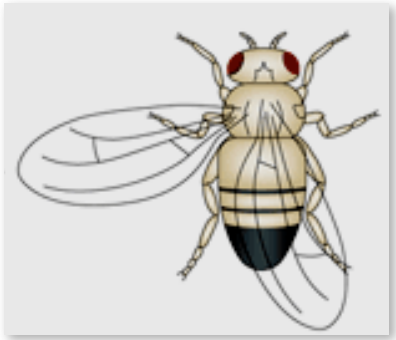


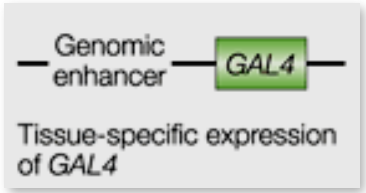




Hoyer et al. (2008) Curr. Biol.

FINDING AGGRESSION NEURONS IN THE FLY





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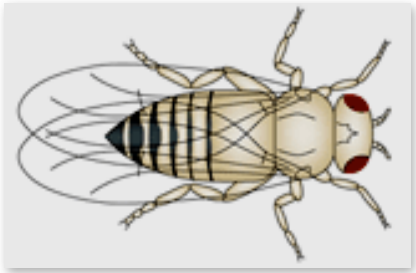
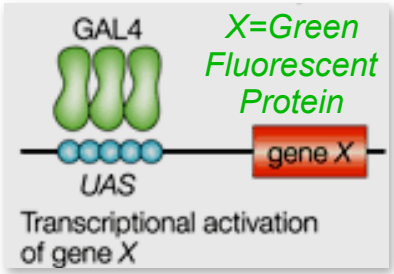
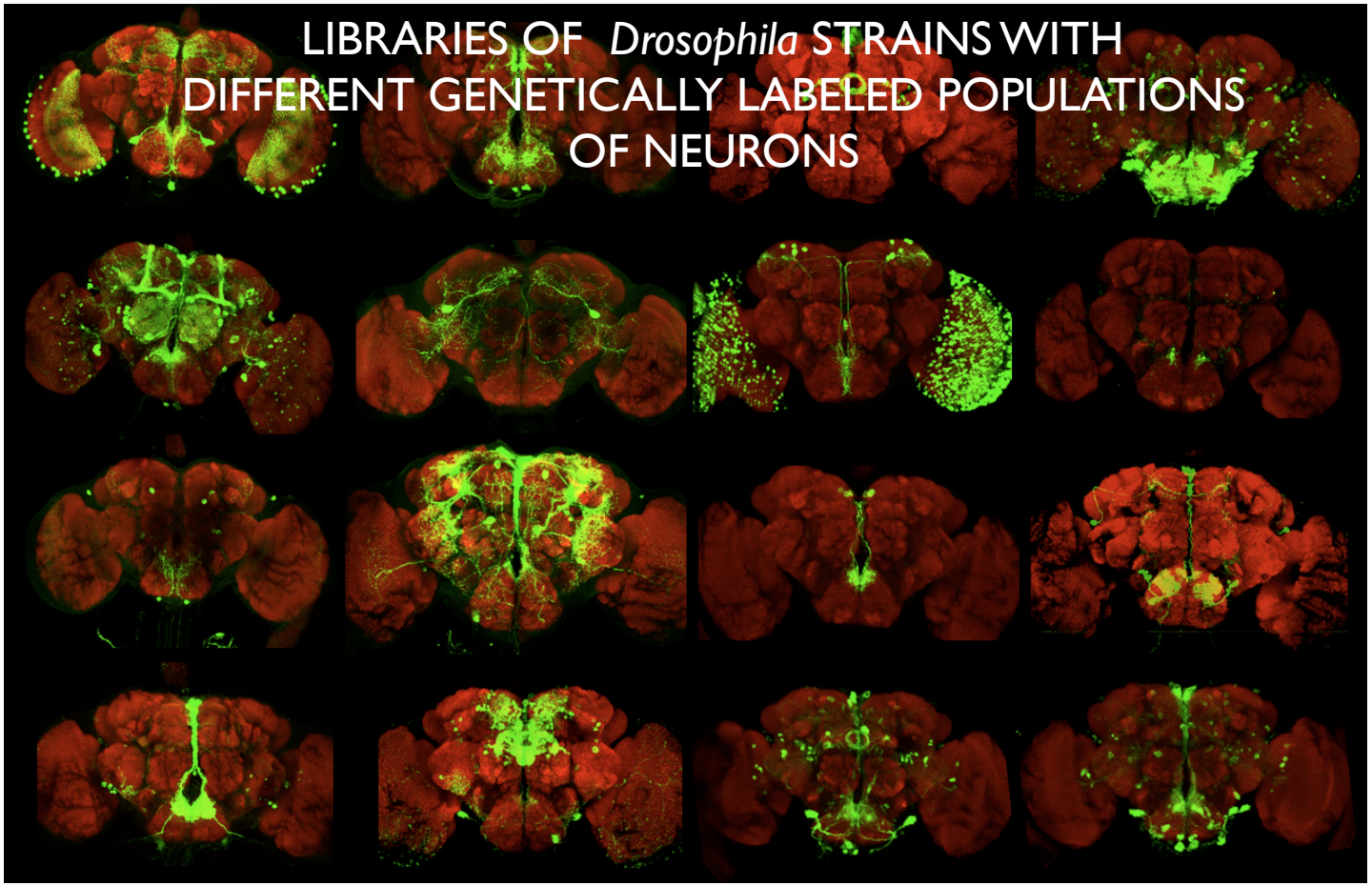
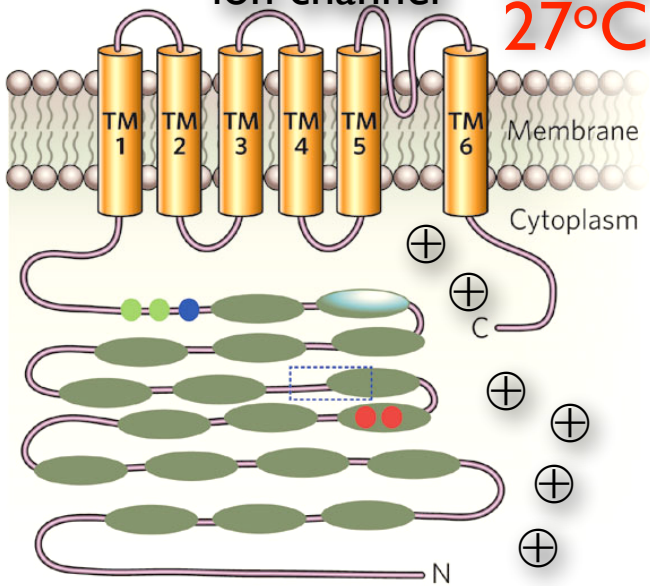






warmth-sensitive ion channel

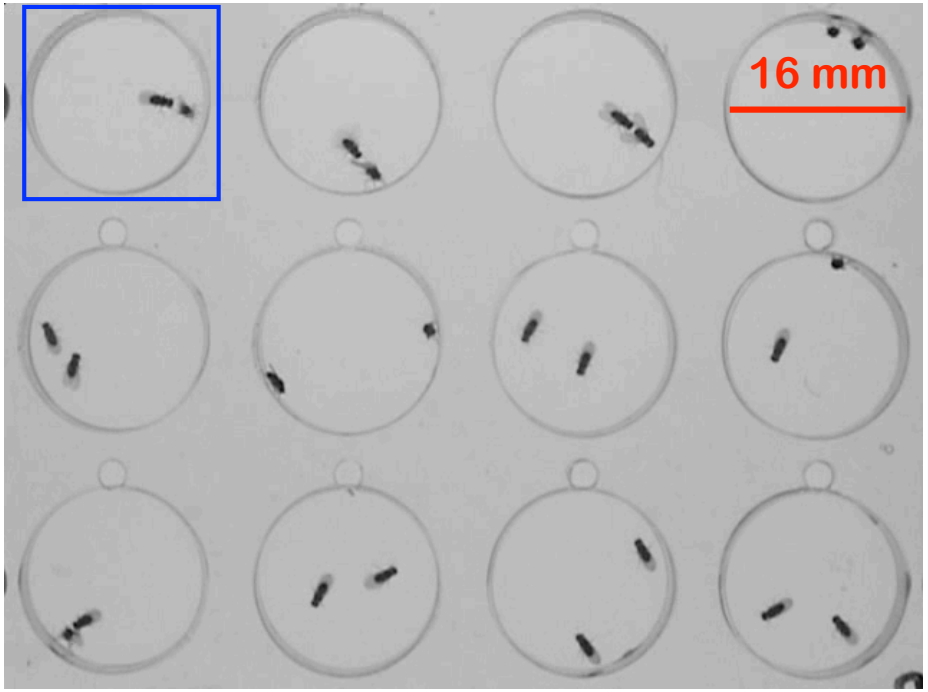
27°C



hyperaggressive?

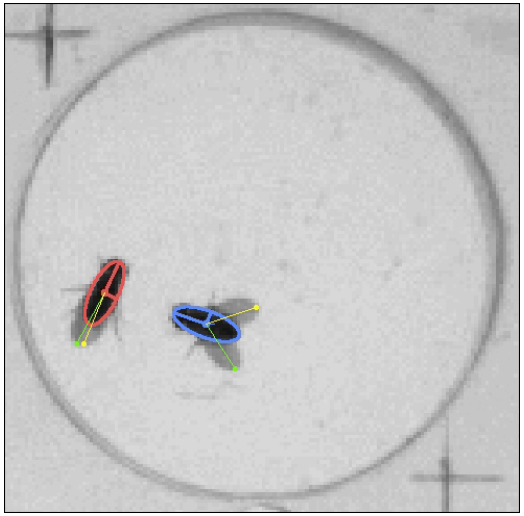
HIGH-THROUGHPUT BEHAVIORAL SCREENING IN DROSOPHILA

12 chamber arena

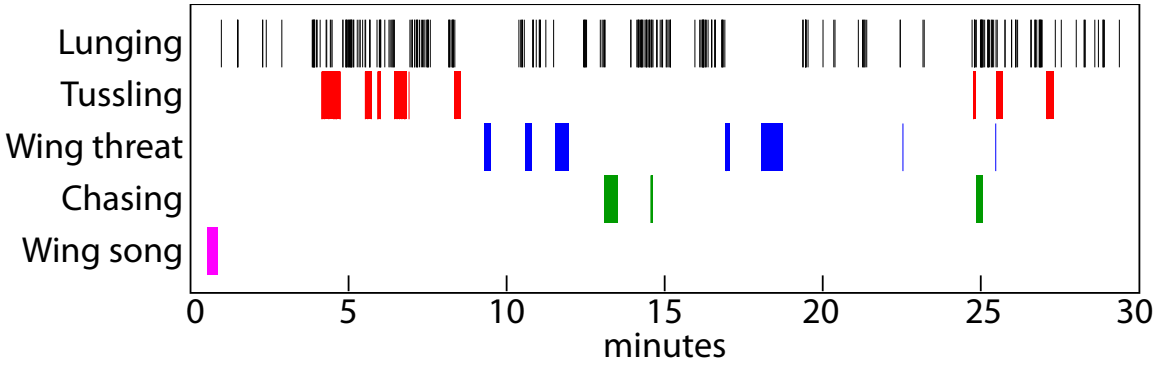


Tracking & Behavior Scoring

Dankert et al., Nat Methods (2009)

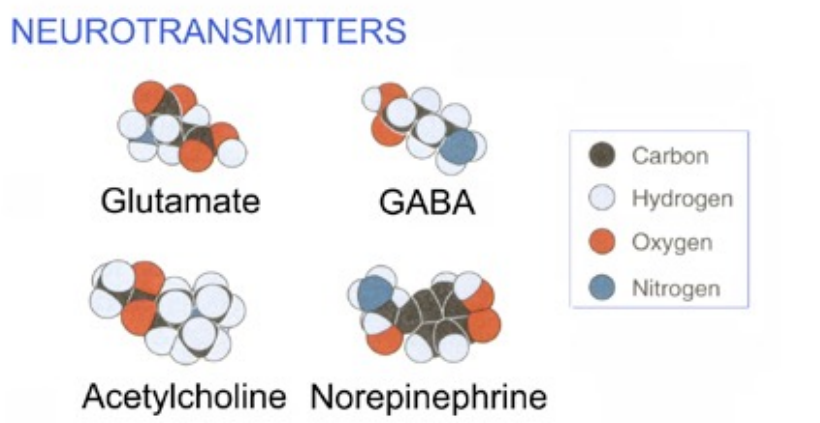


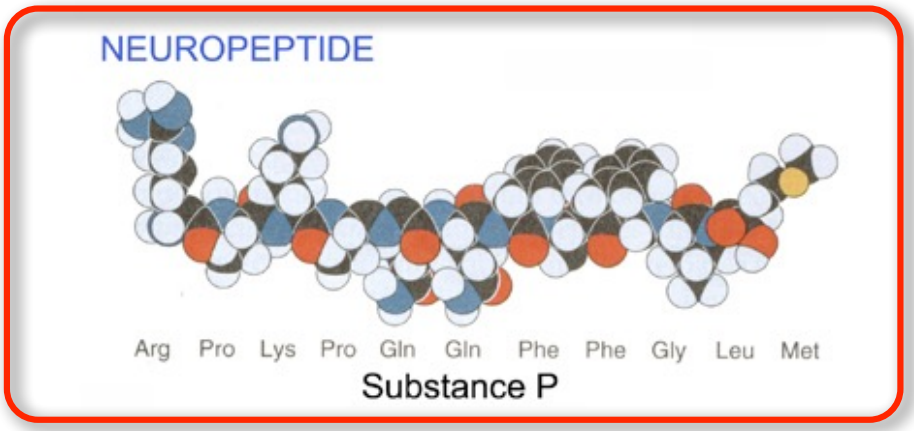
Time series of behaviors for each pair

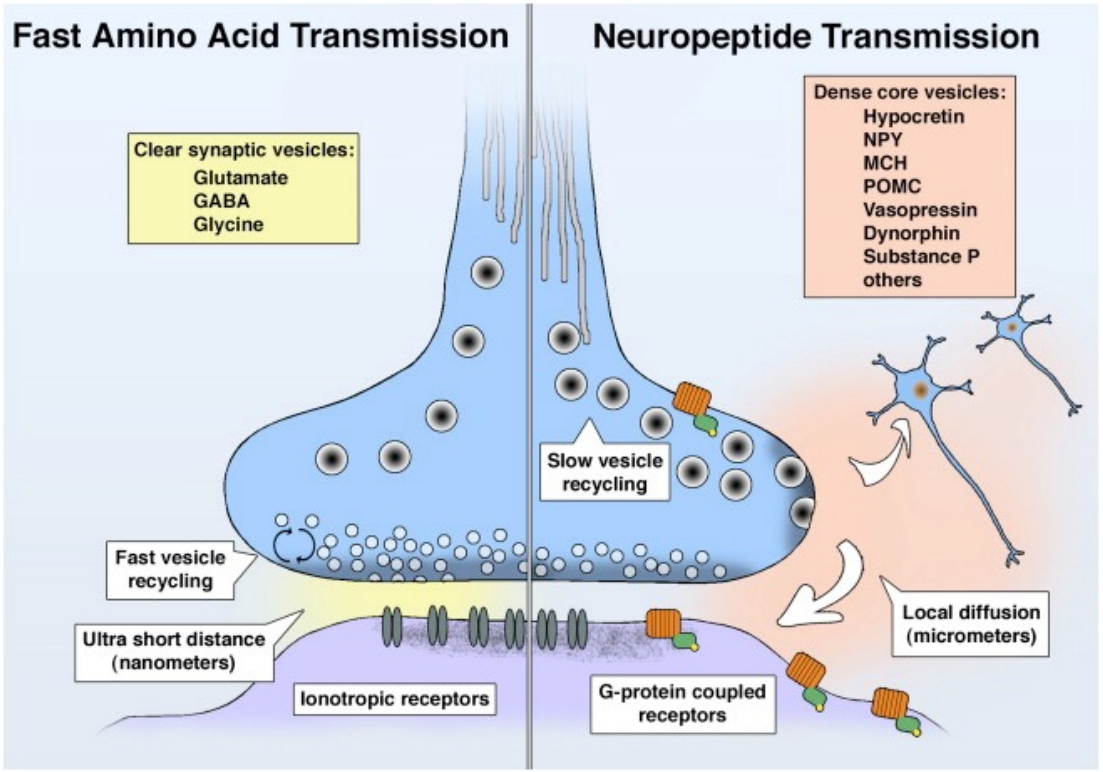


Eric Hoopfer

NEUROPEPTIDES CONTROL EVOLUTIONARILY CONSERVED SURVIVAL BEHAVIORS





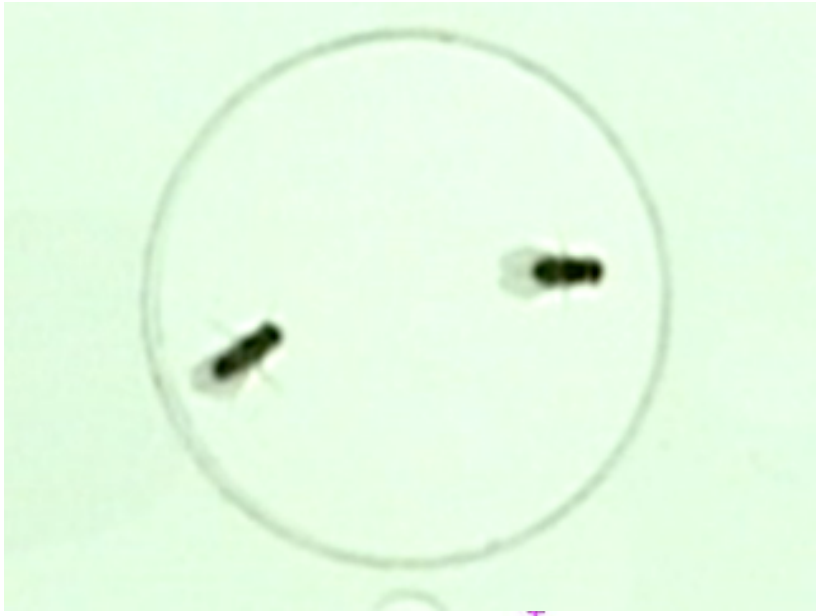


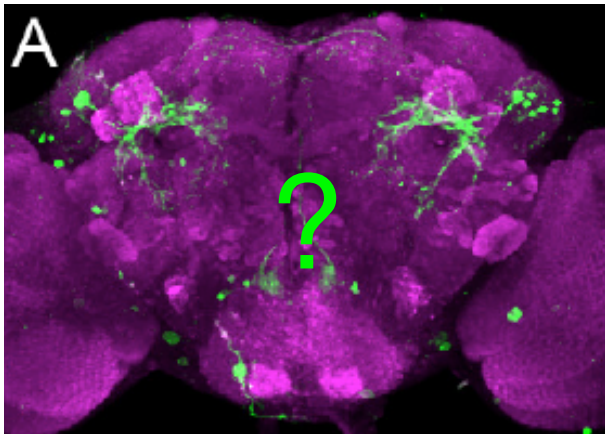
mating (oxytocin/vasopressin), feeding (NPY), pain (SP)

Bargmann, Waddell, Nitabach, Taghert

ACTIVATION SCREEN FOR NEUROPEPTIDE NEURONS INVOLVED IN AGGRESSION

Kenta Asahina





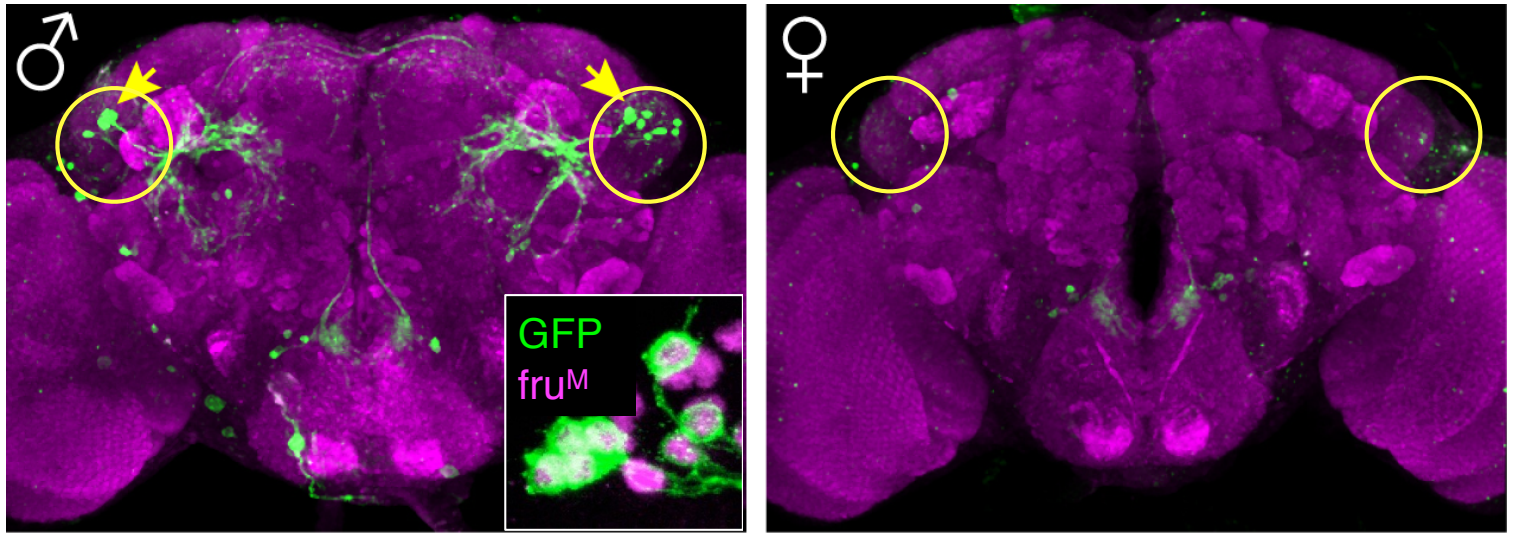
Kenta Asahina

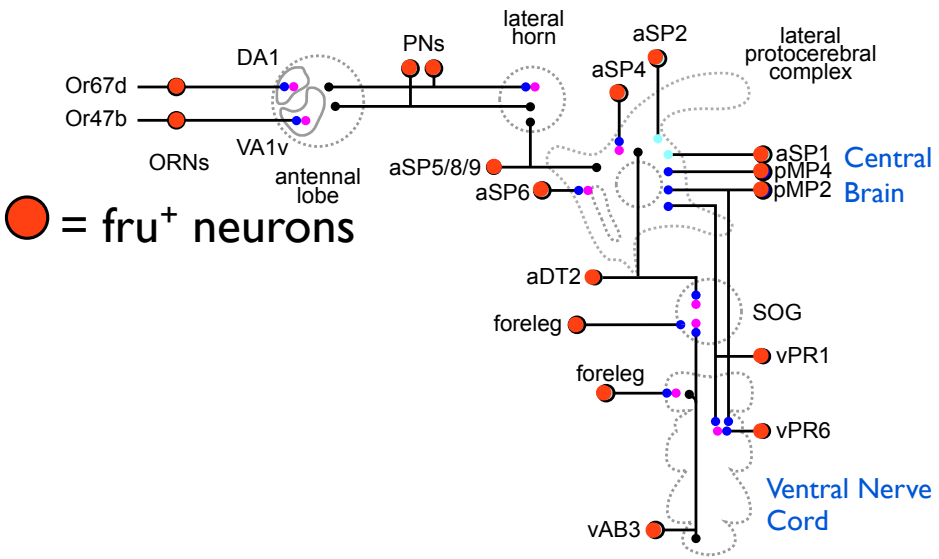
Tim Tayler

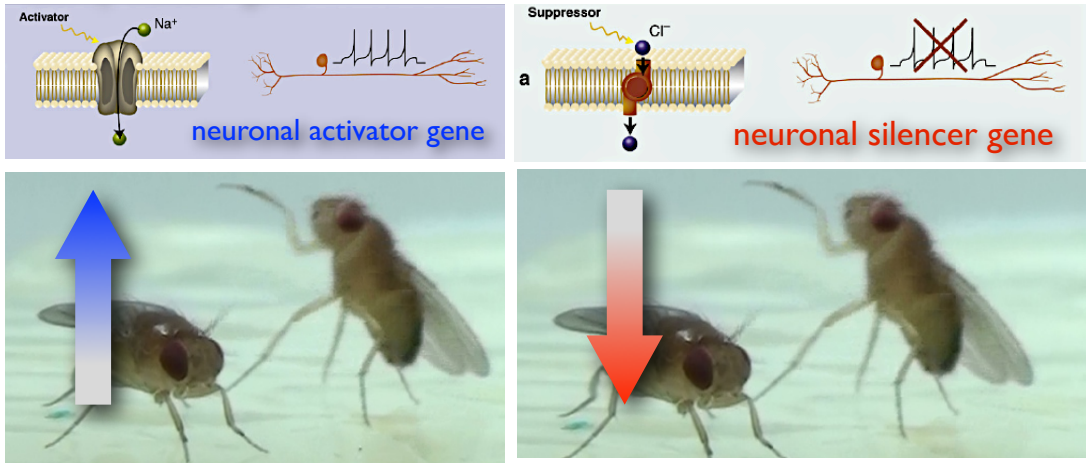
MALES OF MOST SPECIES ARE MORE AGGRESSIVE THAN FEMALES

Dickson, Kravitz

MALE-SPECIFIC NEURONS THAT CONTROL AGGRESSION IN *Drosophila*



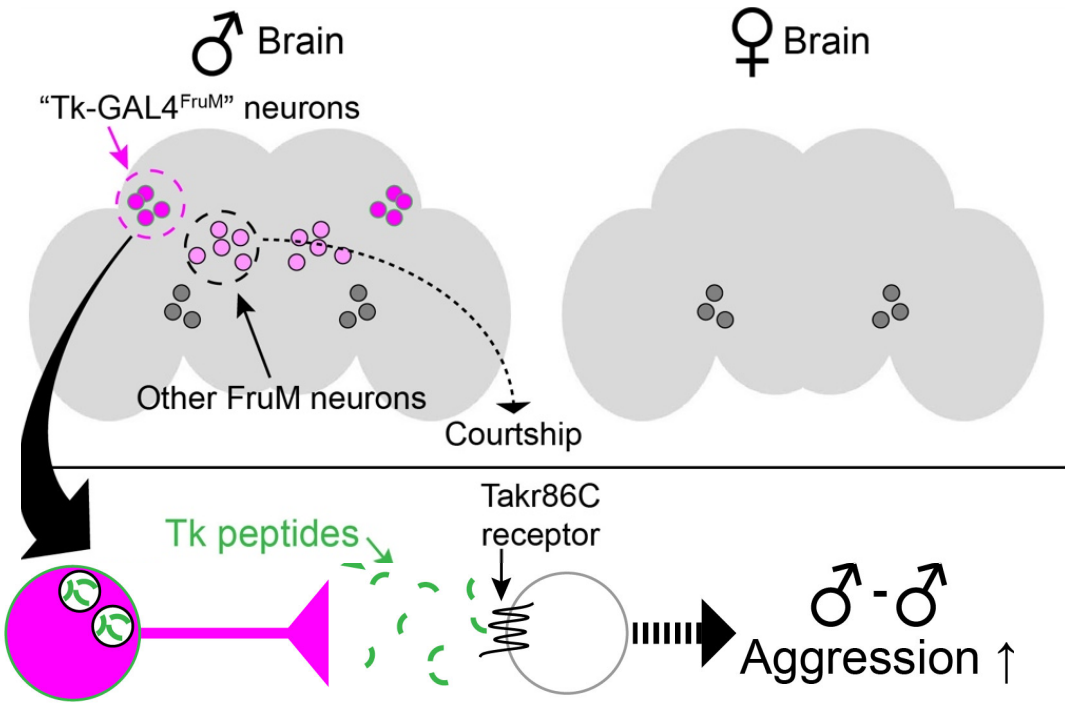


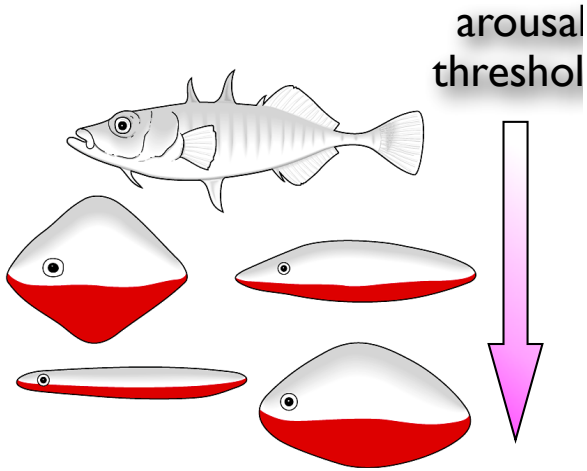


- No effect on courtship!

Asahina et al., Cell (2014)

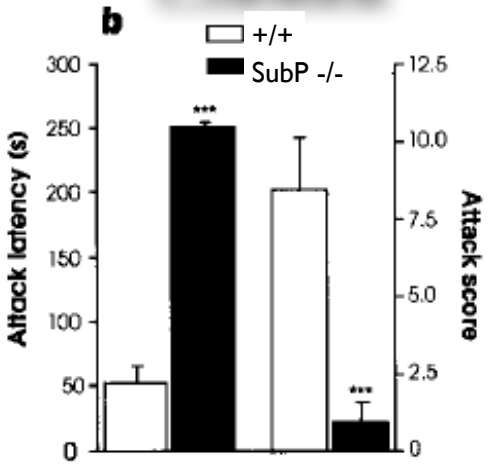
A NEUROPEPTIDE AND A MALE-SPECIFIC NEURON THAT CONTROL AGGRESSIVE AROUSAL IN *Drosophila*





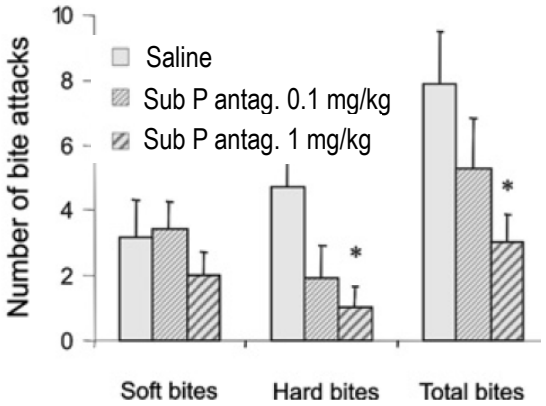
A CONSERVED ROLE FOR TACHYKINININS IN THE CONTROL OF AGGRESSION?

Mouse

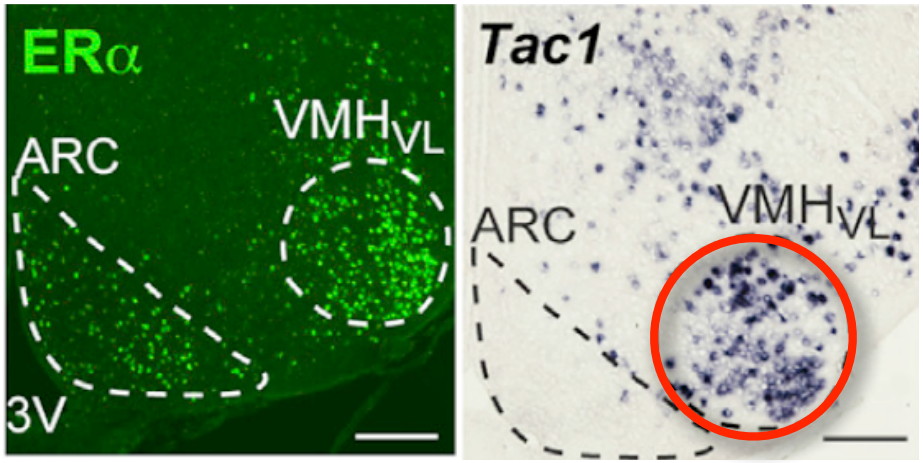


DeFelipe et al. (1998)

Rat



Halasz et al. (2007)



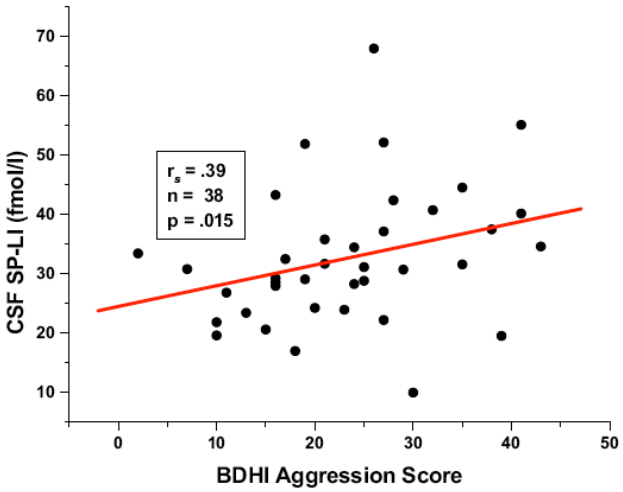
Correa et al. (2015)

Human

Cerebrospinal Fluid Substance P-Like Immunoreactivity Correlates with Aggression in Personality Disordered Subjects

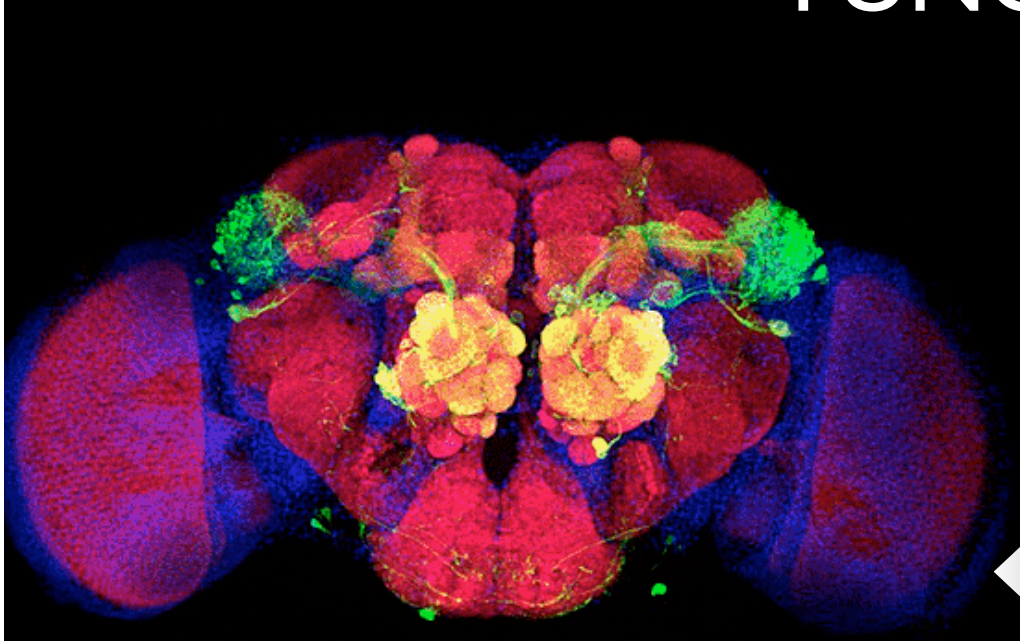
Emil F. Coccaro, Royce Lee, Michael J. Owens, Becky Kinkead, and Charles B. Nemeroff

Biol Psychiatry (2012)72: 238-243



Bargmann, Heberlein, Nitabach, Taghert

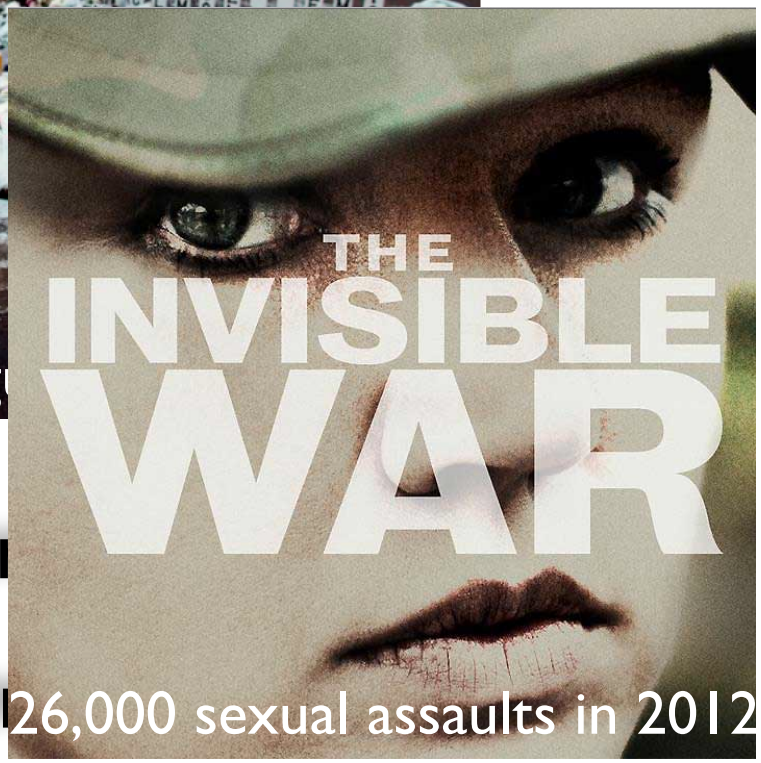
IMPORTANCE OF COMPARATIVE STUDIES IN HIGHLIGHTING PRINCIPLES OF BRAIN FUNCTION



Axel, Bargmann

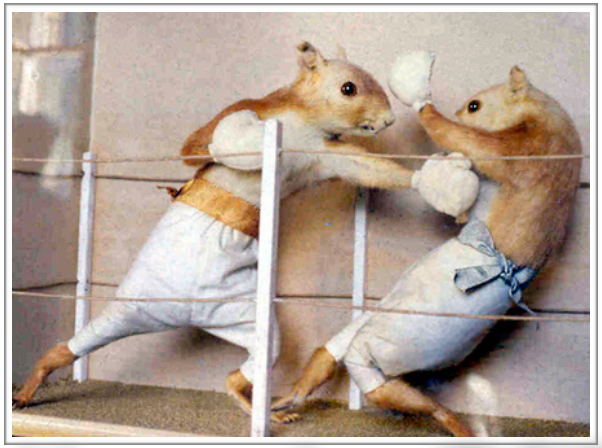
VIOLENCE AS A SYMPTOM DOMAIN OF PSYCHIATRIC DISORDERS

- Autism
- Schizophrenia
- PTSD
- Depression
- Intermittent Explosive Disorder
- Borderline Personality Disorder



80,000 prisoners in solitary confinement in US @ $75K/yr x prisoner = $6B/yr

CREDITS



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THANK YOU!