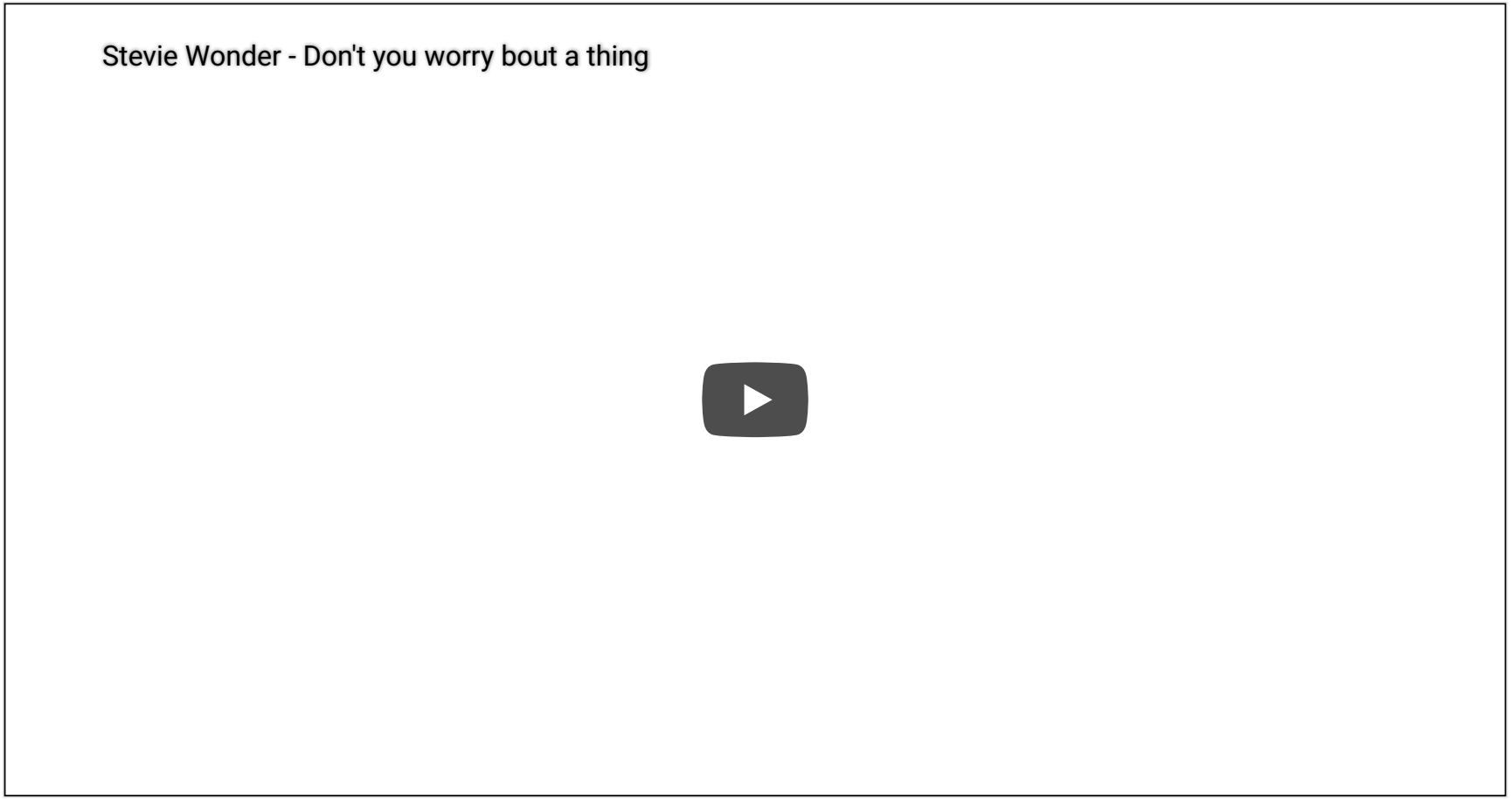
511-2018-11-02-fear-stress-reward

Rick Gilmore

2018-11-02 11:17:31

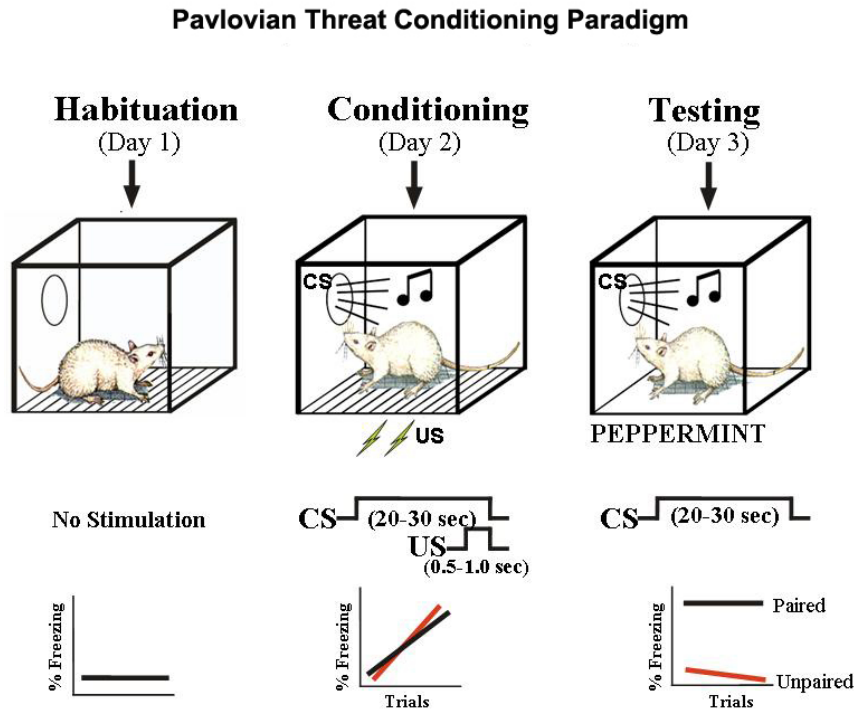
Don't You Worry 'Bout a Thing



Today's topics

- Fear
- Stress
- Reward

Animal model of learned 'fear'



http://www.cns.nyu.edu/labs/ledouxlab/images/image_research/fear_conditioning.jpg

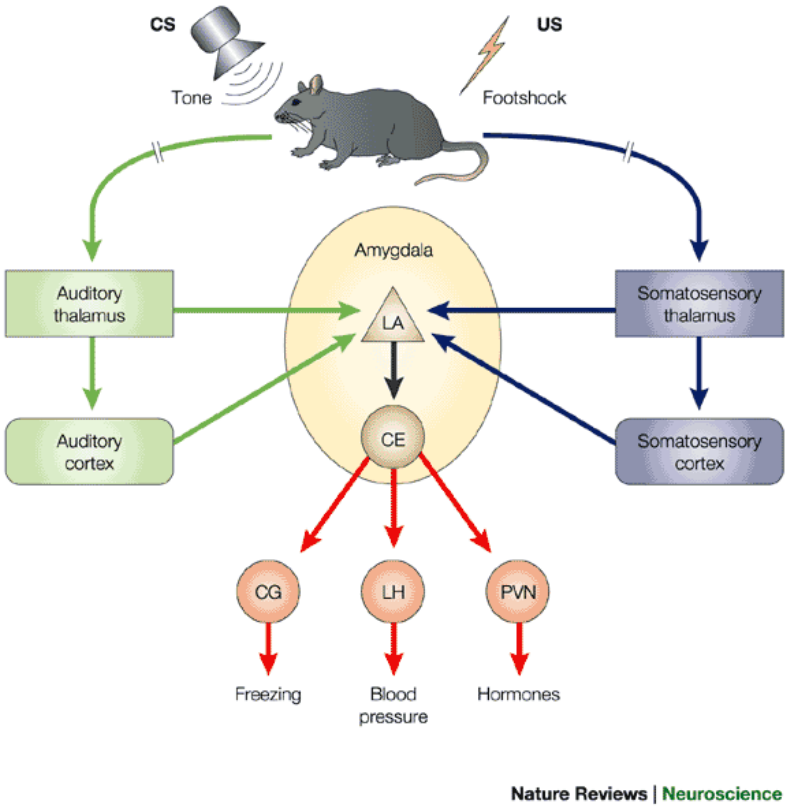
Conditioned suppression of a rat's lever pressing

Rat vs. Human

Measures in Animal Model	DSM-III: Generalized Anxiety
Heart rate increase	Heart pounding
Salivation decrease	Dry mouth
Stomach ulcers	Upset stomach
Respiration change	Respiration increase
Scanning & vigilance	Scanning & vigilance
Startle response increase	Jumpiness, easy startle
Urination	Frequent urination
Defecation	Diarrhea
Grooming	Fidgeting
Freezing	Apprehensive expectation

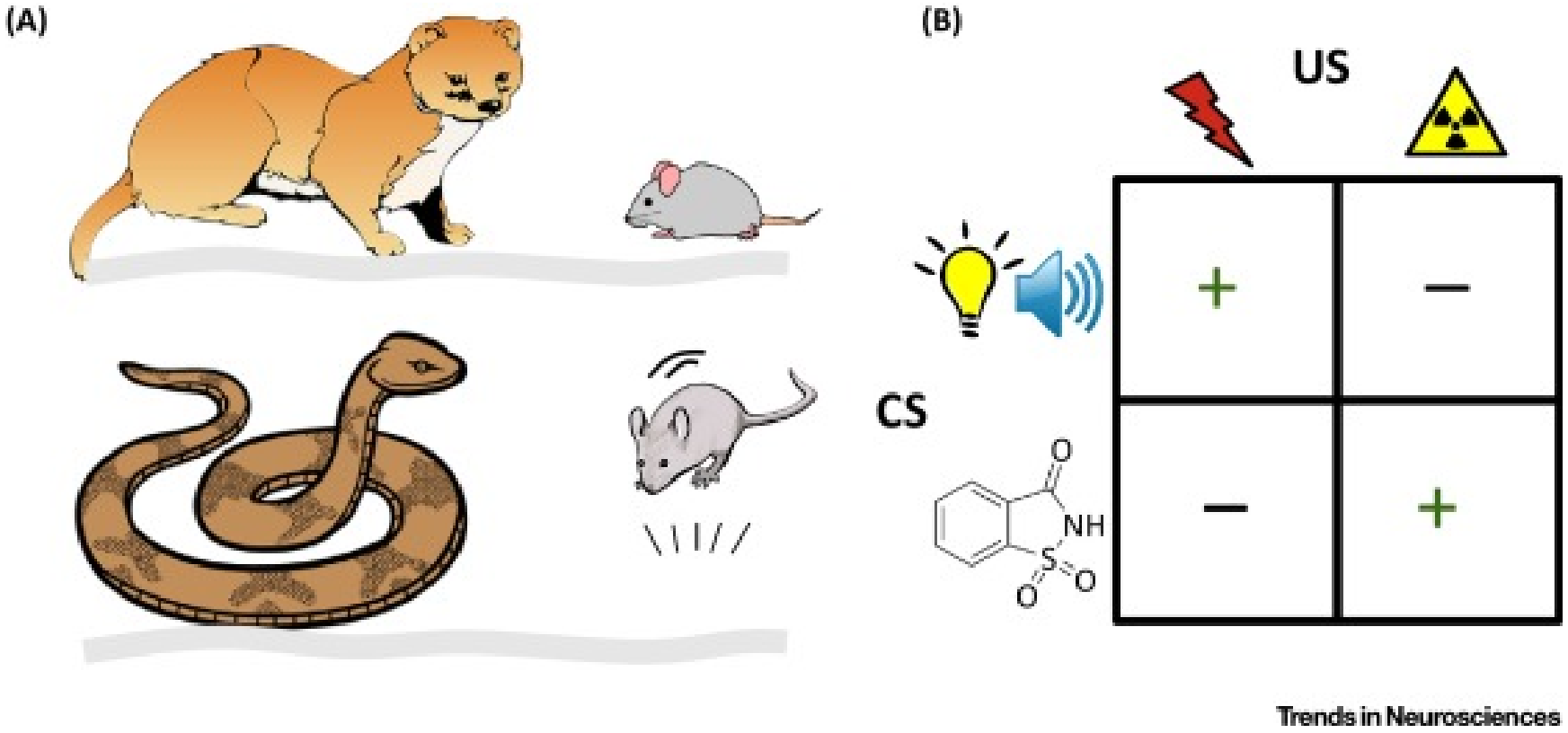
Adapted from (Davis, 1992)

Amygdala circuits



(Medina, Repa, Mauk, & LeDoux, 2002)

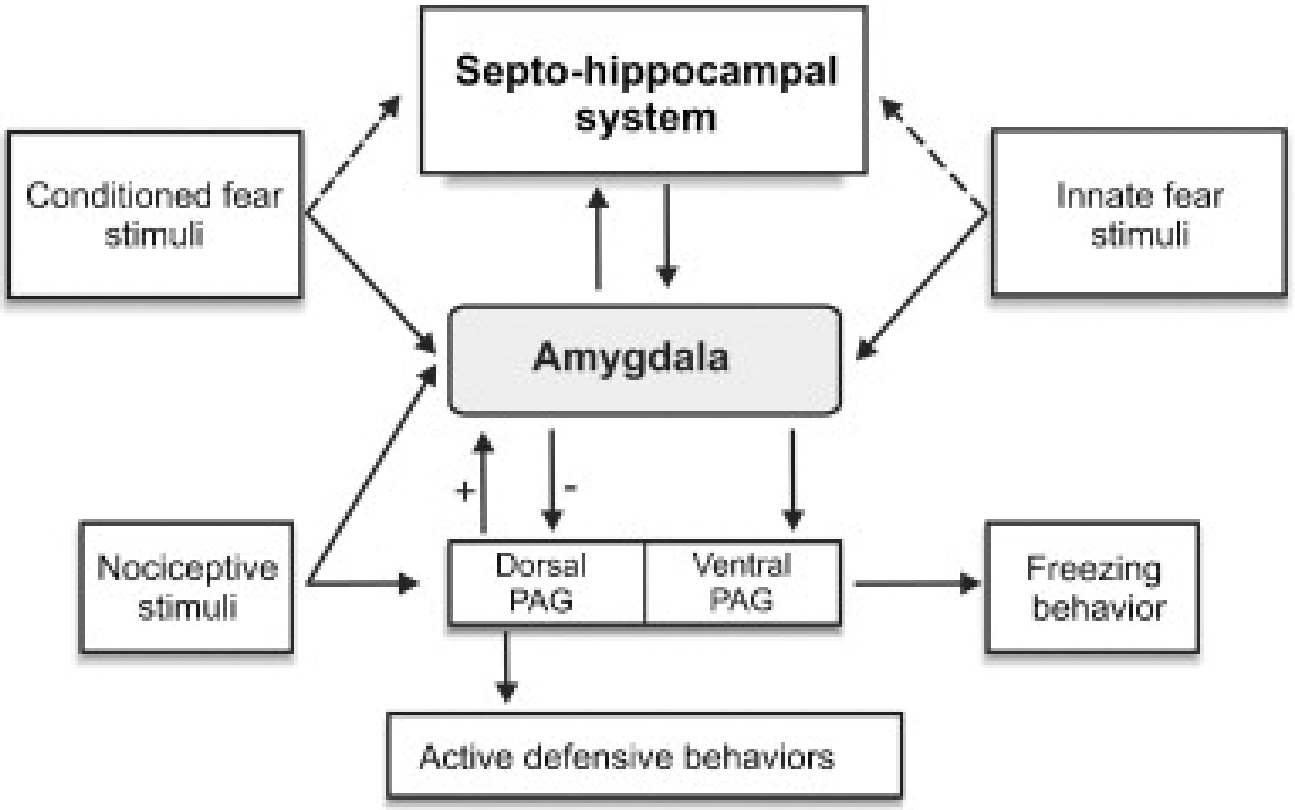
Specificity of learning



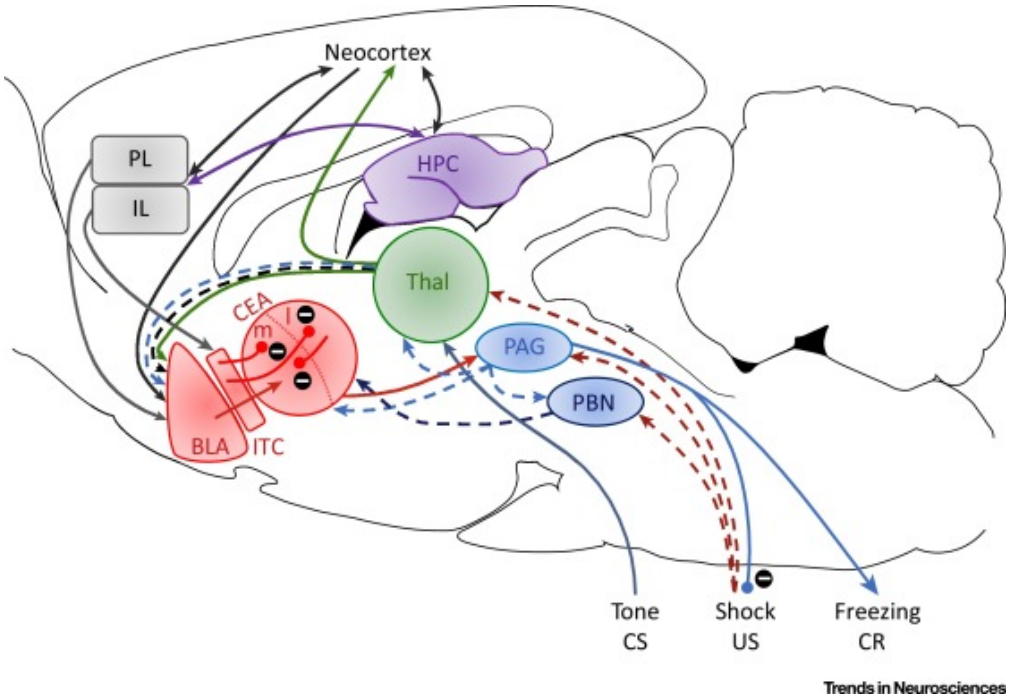
Trends in Neurosciences

- Light/sound + footshock OR X-ray + saccharin vs
- Light/sound + X-ray or footshock + saccharin

Circuitry



(Brandão, Zanoveli, Ruiz-Martinez, Oliveira, & Landeira-Fernandez, 2008)



(Pellman & Kim, 2016)

- BLA, basolateral complex of the amygdala
- CEA, central nucleus of the amygdala
- ITC, intercalated cells of the amygdala
- PL, prelimbic cortex
- IL, infralimbic cortex
- HPC, hippocampus
- Thal, thalamus
- PAG, periaqueductal gray
- PBN, parabrachial nucleus

Brain under stress

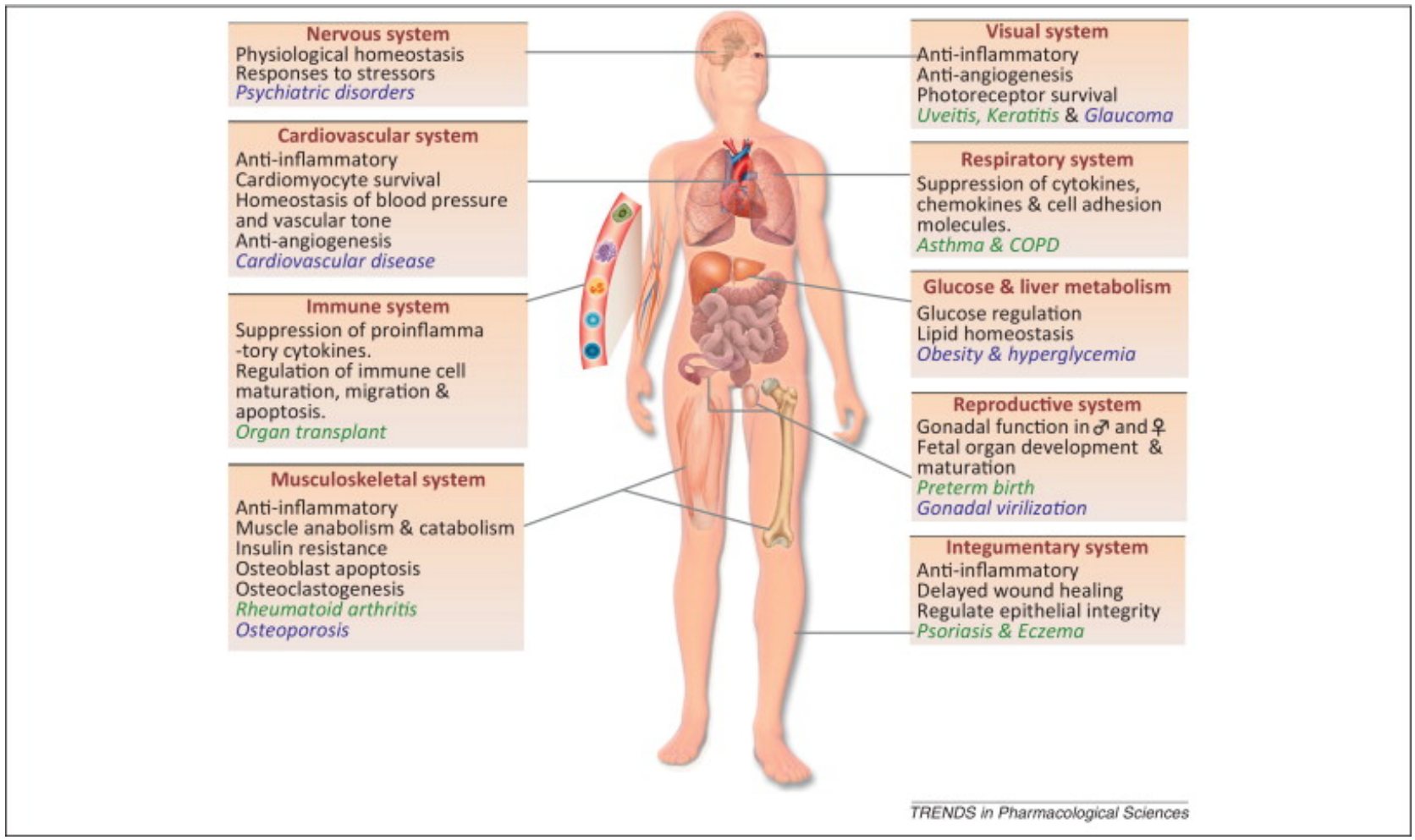
- **Acute** stress
  - Short duration
  - Fast action required
  - HPA (Cortisol), SAM (NE/Epi) axes
- Brain detects threat
- Mobilizes physiological, behavioral responses

Brain under stress

- vs. **Chronic** or stress
    - Long duration, persistent

Glucocorticoids

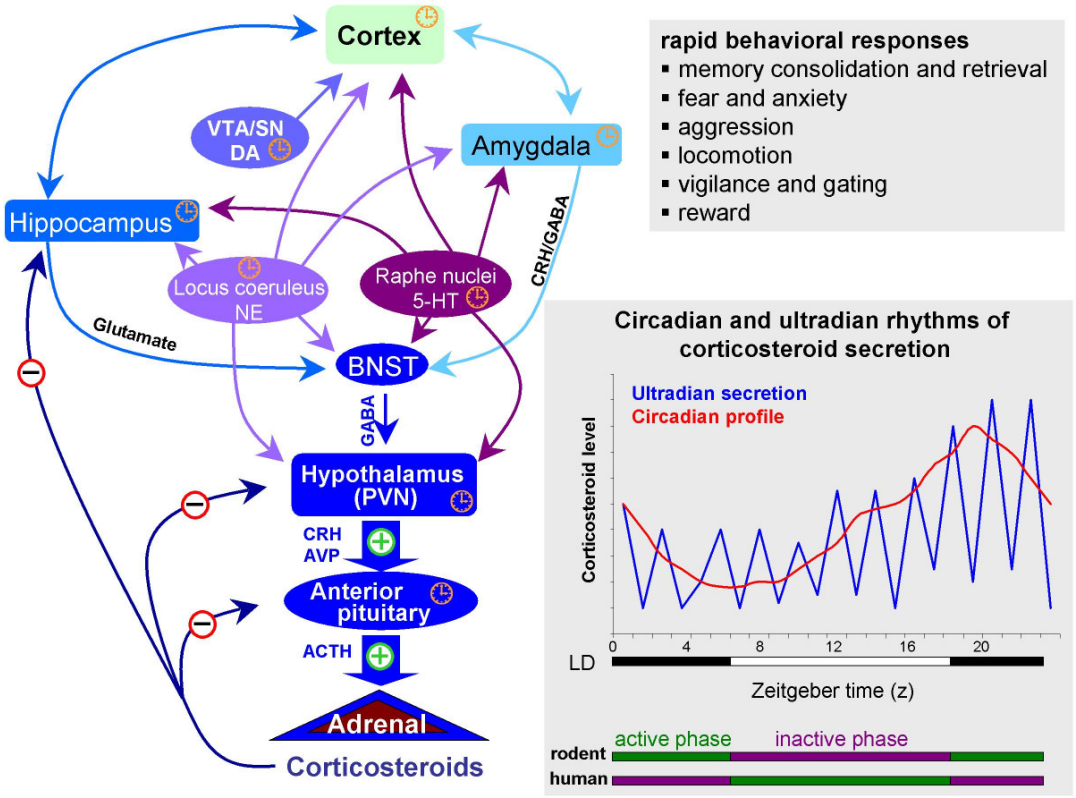
- Adrenal cortex releases hormones
  - Cortisol (hydrocortisone)
    - Increases blood glucose levels
    - Suppresses immune system
    - Reduces inflammation
    - Aids in metabolism
  - Receptors in brain and body



(Kadmiel & Cidlowski, 2013)

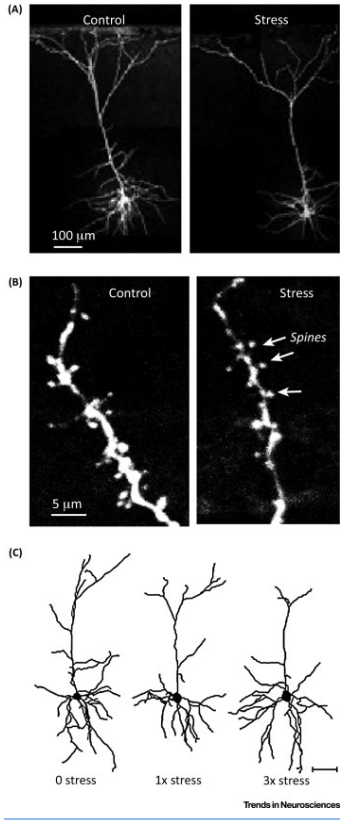
Glucorticoid receptors in body

Cortisol and the brain



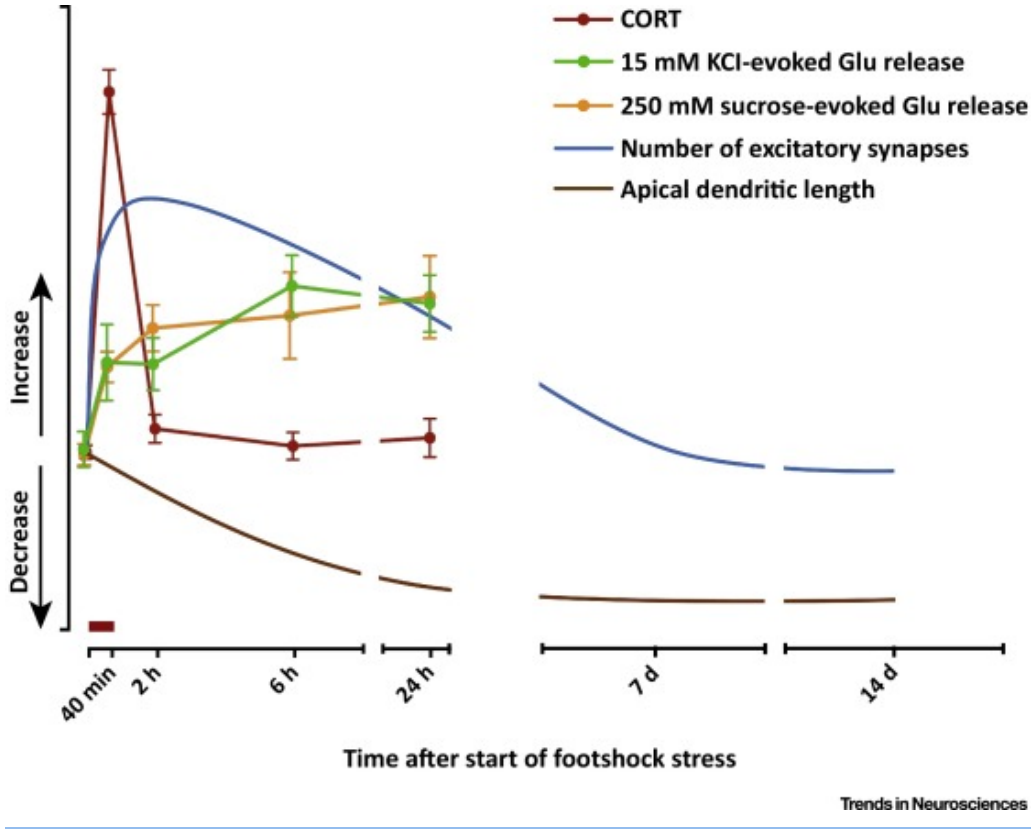
http://www.molecularbrain.com/content/figures/1756-6606-3-2-1-l.jpg

Impacts of acute stress



(Musazzi, Tornese, Sala, & Popoli, 2017)

From cortisol to enhanced glutamate



ROBERT M. SAPOLSKY

Author of *A Primate's Memoir*

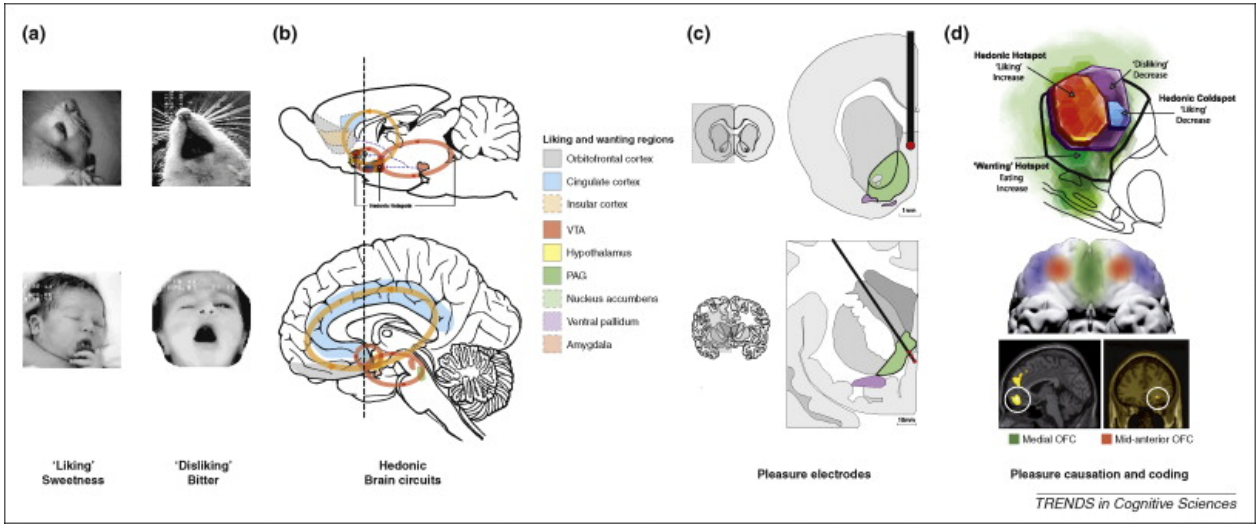
WHY ZEBRAS DON'T GET ULCERS

The Acclaimed Guide to Stress, Stress-Related Diseases, and Coping—Now Revised and Updated

"One of the best science writers of our time."
—Oliver Sacks

Pleasure/reward

Neuroanatomy of 'happiness'



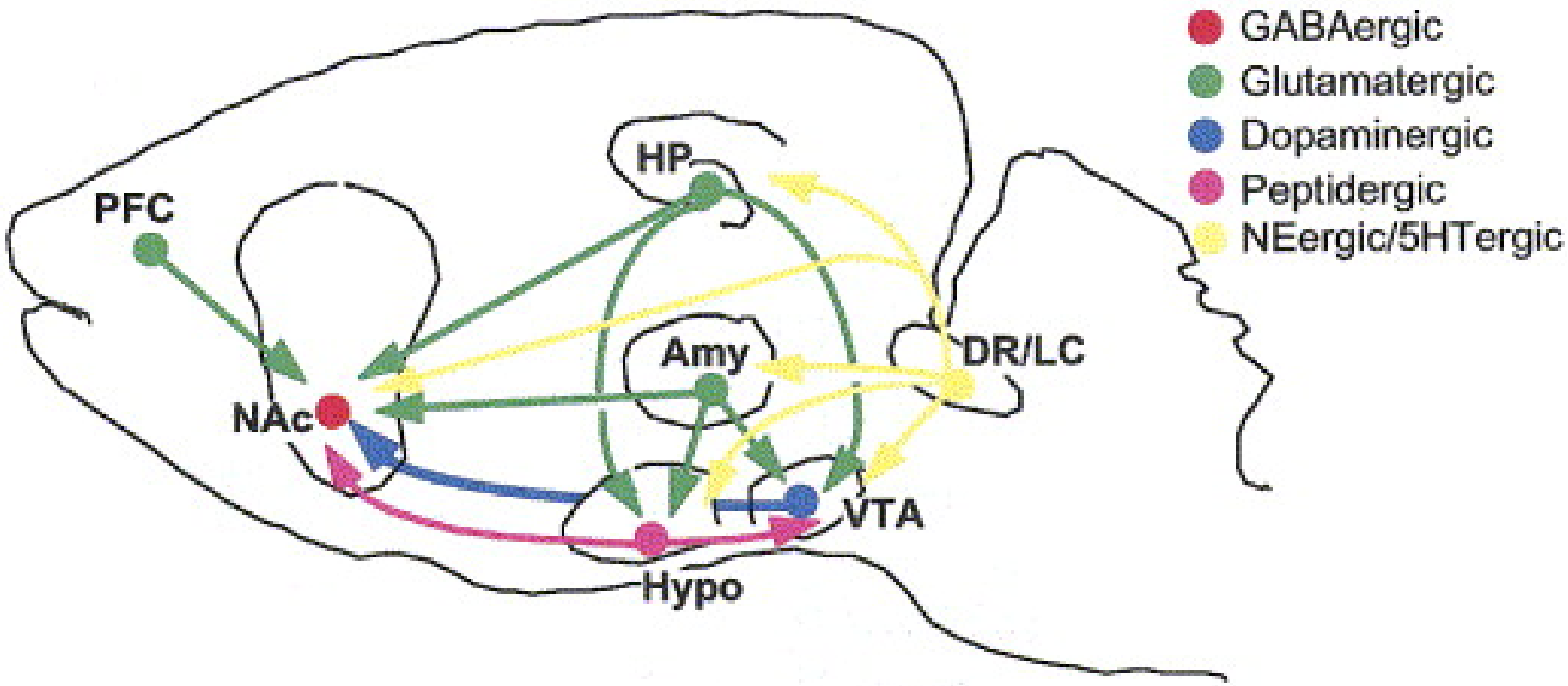
(Kringelbach & Berridge, 2009)

Rewards

- A reinforces (makes more prevalent/probable) some behavior
- Milner and Olds (Milner, 1989) discovered 'rewarding' power of electrical self-stimulation
- (Heath, 1963) studied effects in human patients.

Electrical self-stimulation

"Reward" circuitry in the brain



(Nestler & Carlezon, 2006)

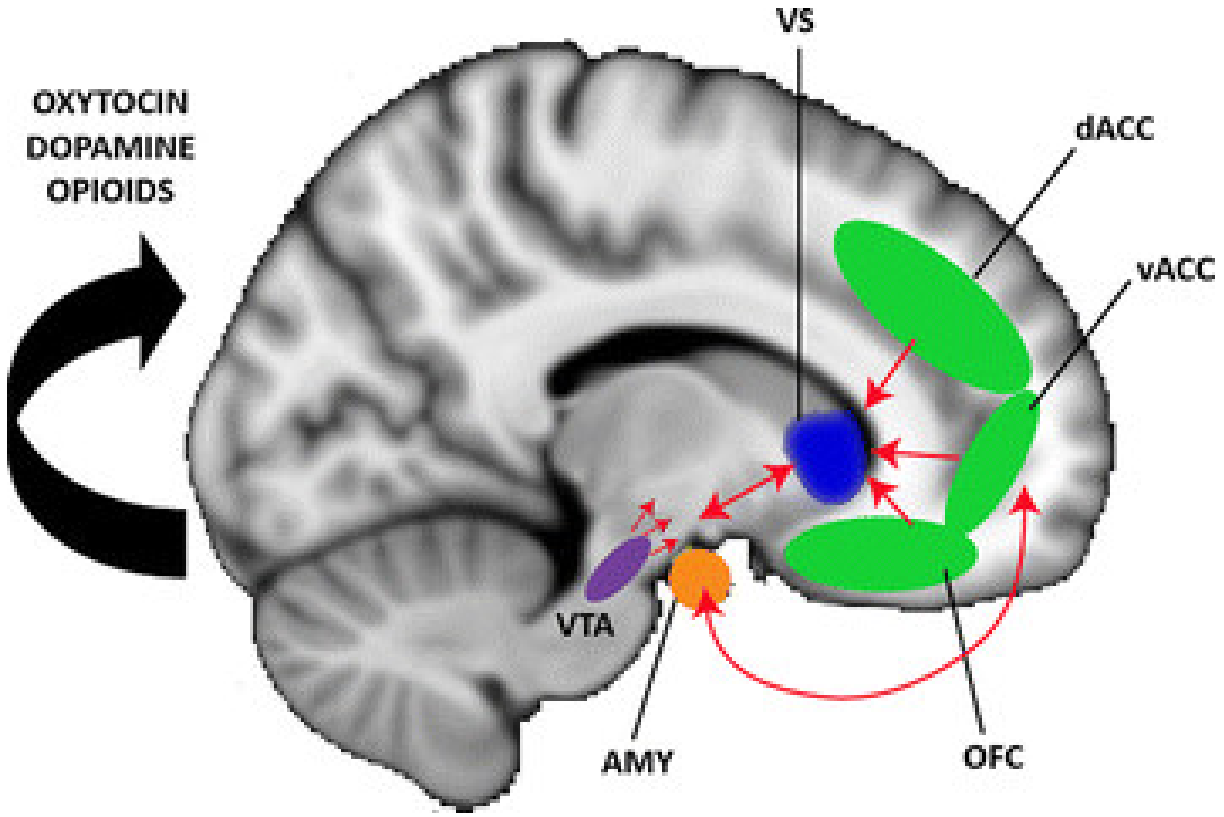
Components of the "reward" circuit

- Lateral Hypothalamus (Hyp)
- Medial forebrain bundle (MFB)
- Ventral tegmental area (VTA) in midbrain
- Nucleus accumbens (nAcc)
- Dorsal Raphe Nucleus/Locus Coeruleus (DR/LC)

Components of the "reward" circuit

- Amygdala (Amy)
- Hippocampus (HP)
- Prefrontal cortex (PFC)

Nucleus accumbens and dorsal striatum

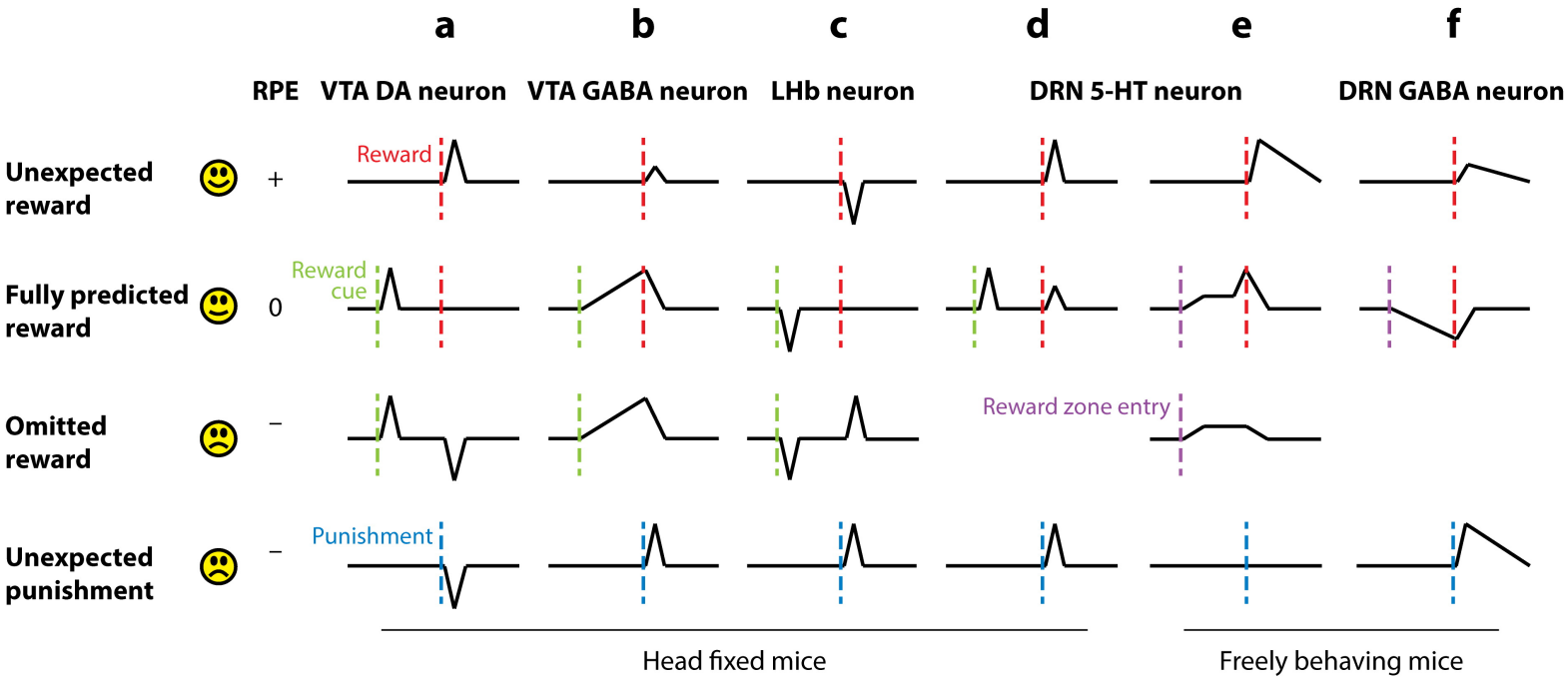


(Kohls, Chevallier, Troiani, & Schultz, 2012)

What does DA signal?

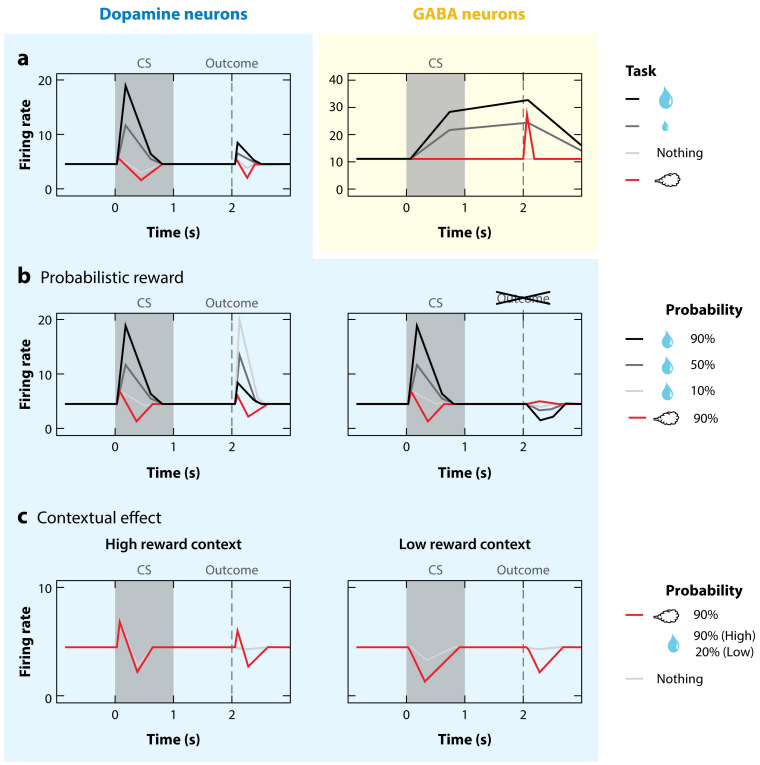
- Hedonia and anhedonia
- Incentive salience
- Reward prediction error (RPE)

RPE



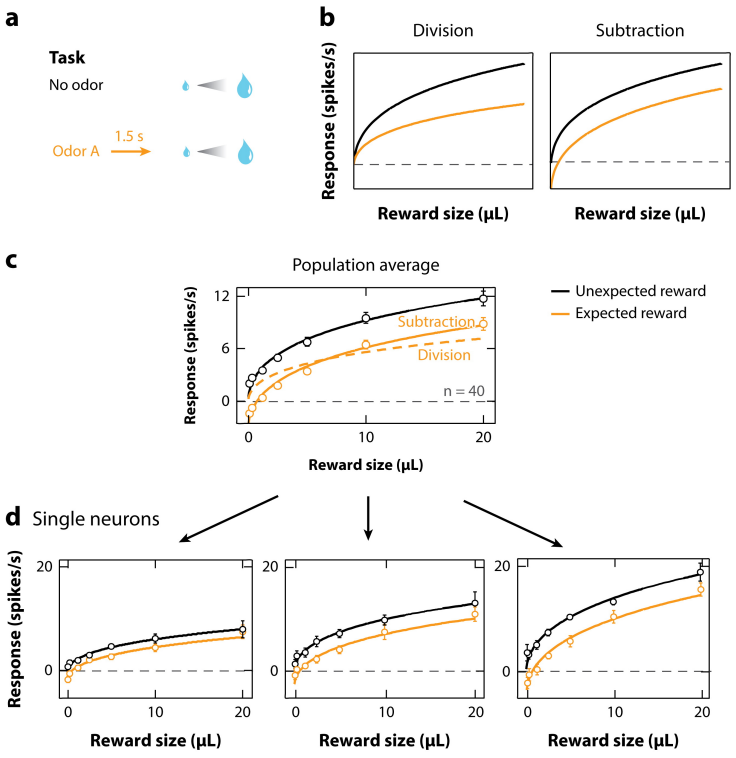
Hu H. 2016.
Annu. Rev. Neurosci. 39:297–324

DA & GABA signaling in RPE



Watabe-Uchida M, et al. 2017.
Annu. Rev. Neurosci. 40:373–94

Expectation modulates DA signaling



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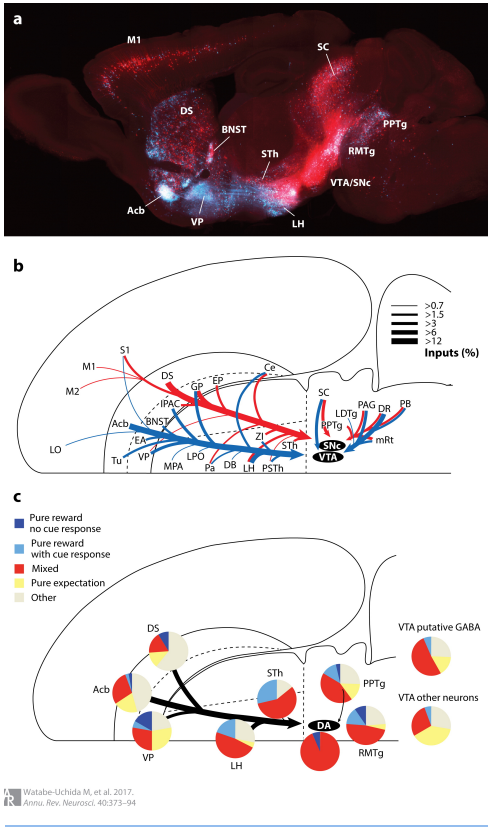
DA network



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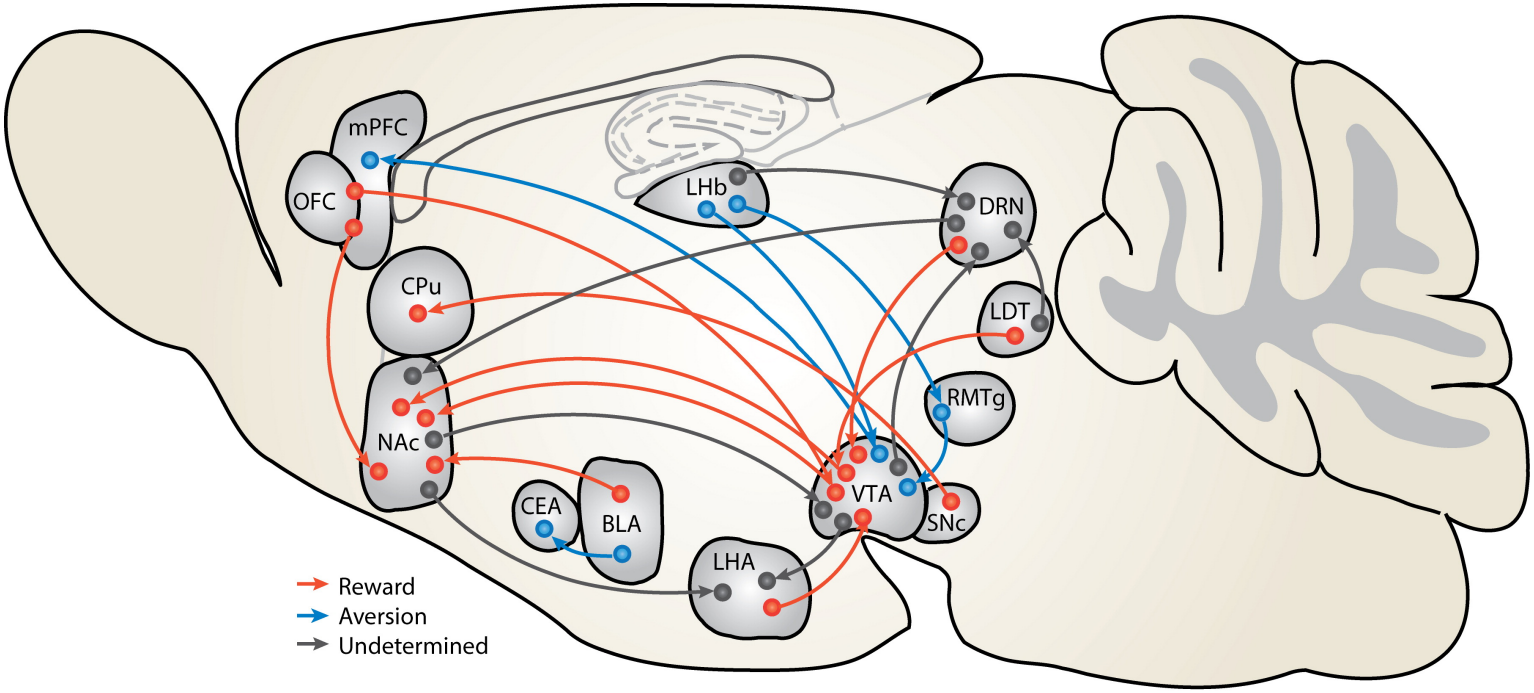
Reward & Aversion Networks



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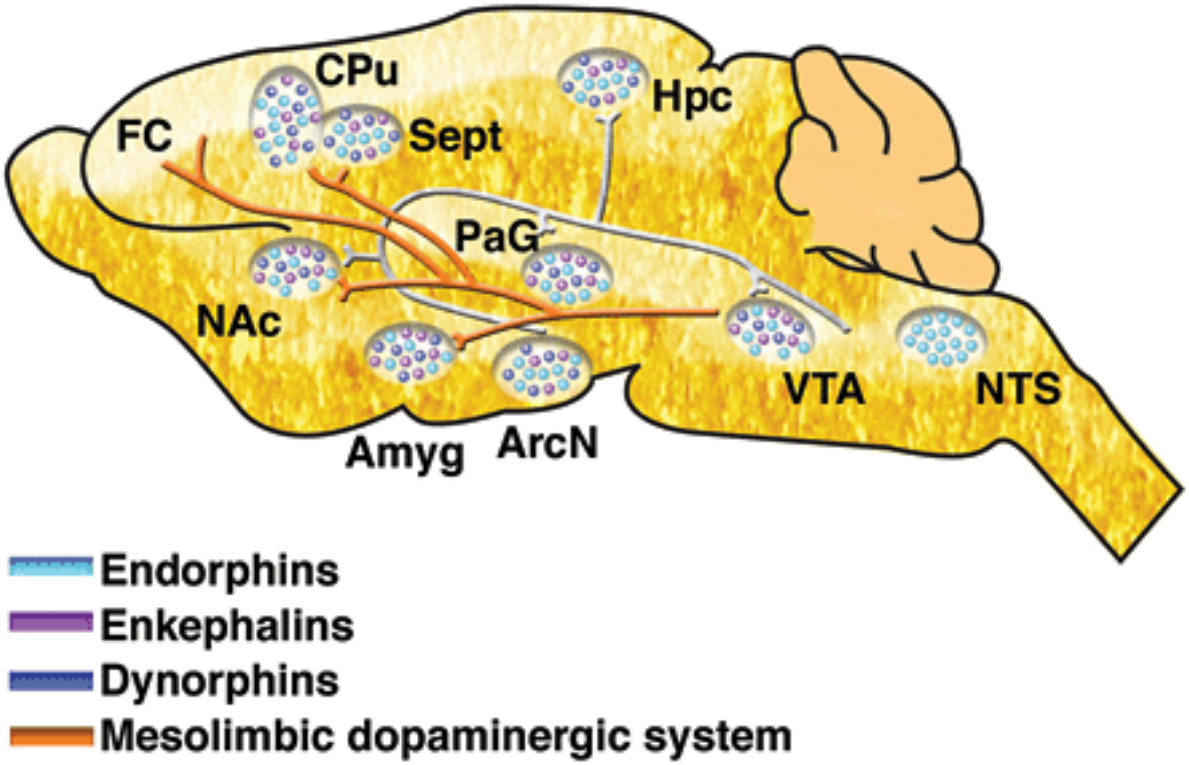
Psychopharmacology of pleasure

- Dopamine
- Opioids
- Cannabinoids
- Serotonin, Norepinephrine
- ACh

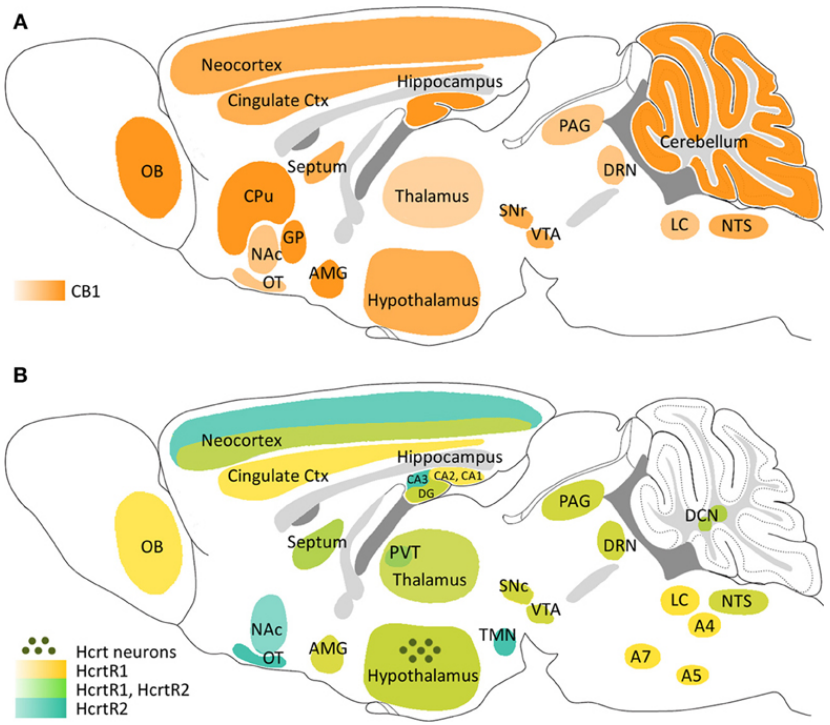
Endogenous morphine-like NTs (endorphins) from hyp, NST



(Clapp, Bhave, & Hoffman, n.d.)

Endogenous cannabinoid system

- Cannabinoids, psychoactive compounds found in cannibis
- Cannabinoid CB1 receptors in CNS; CB2 in body, immune system

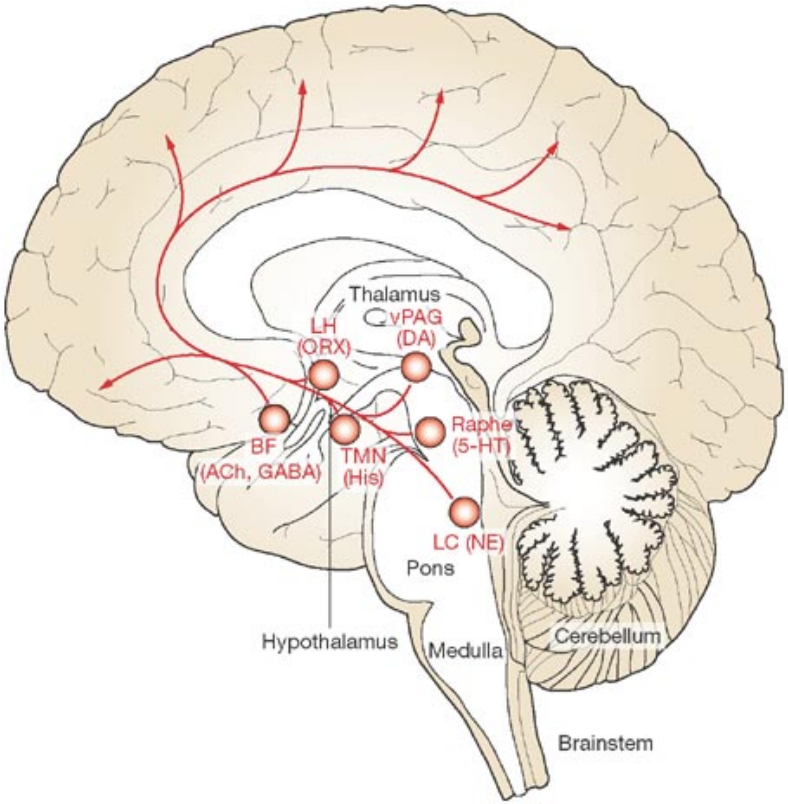


(Flores, Maldonado, & Berrendero, 2013)

Brain contains its own systems for binding drugs associated with 'pleasure'

- Endogenous opioids (endorphins)
- Endogenous cannabinoids

ACh projections in the CNS



(Cock, Vidailhet, & Arnulf, 2008)

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