How the Brain Controls Pain

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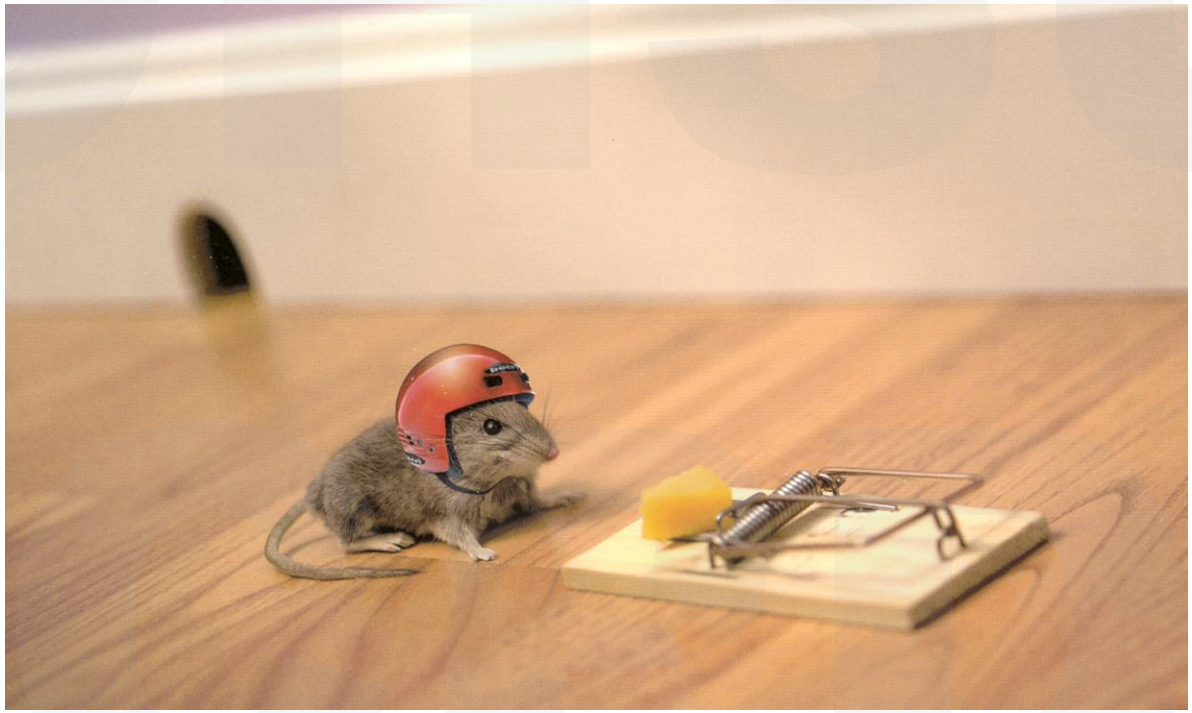
Disclosures:

I have nothing to disclose.

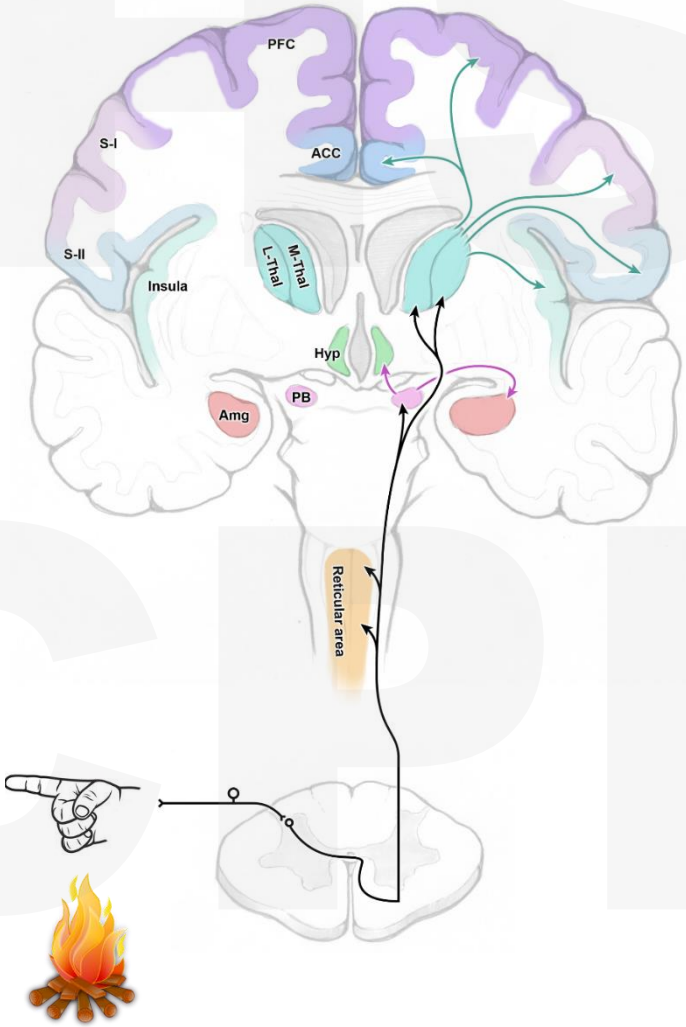
What is pain?

Acute pain is protective



Escape and *avoid* in future

Information about *injury* is relayed to the brain



Pain ≠ Injury

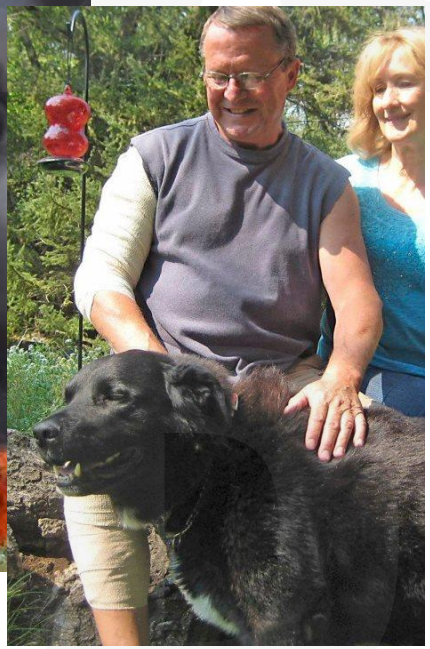
Pain: An unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.

IASP definition, 2020

Pain ≠ Injury

- Stimulus history
- Individual
- Situation

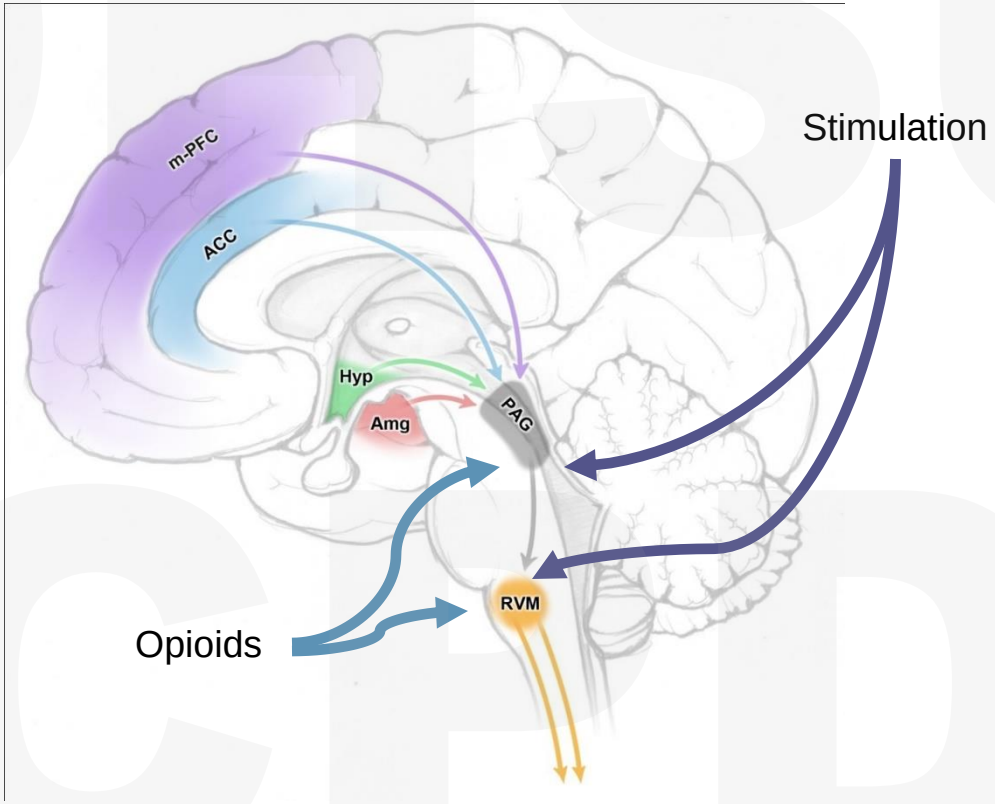
Pain ≠ Injury



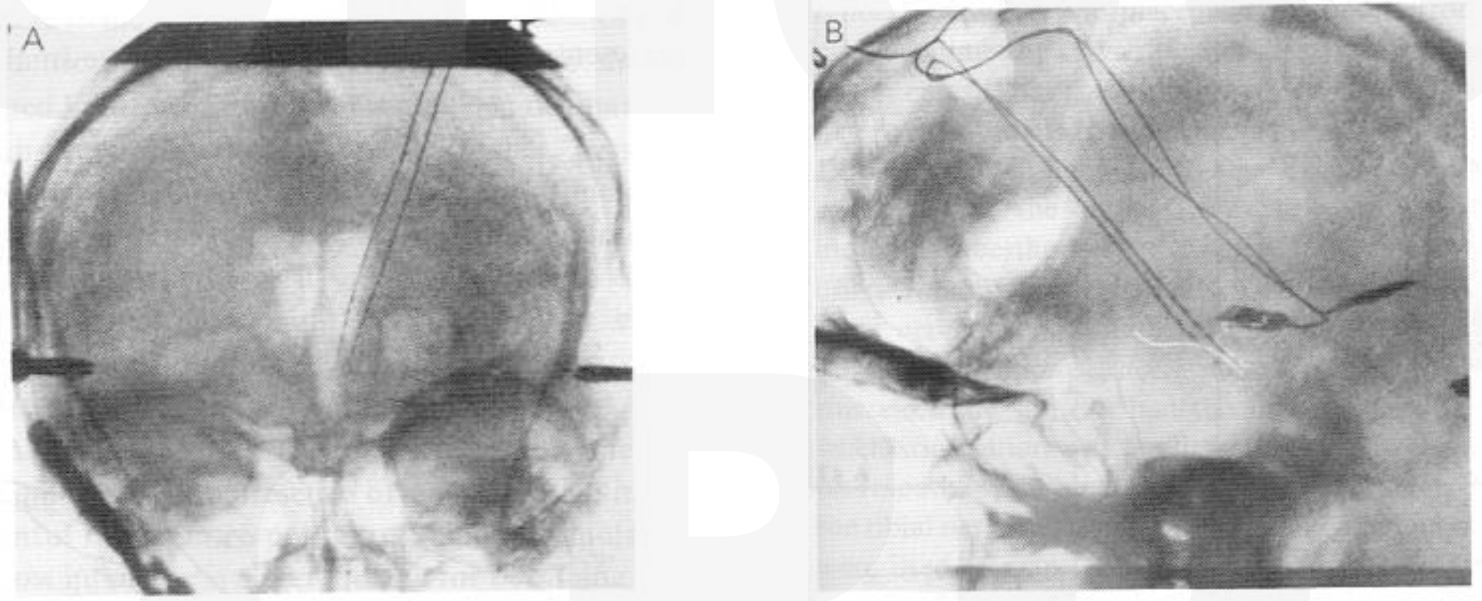
“I was just so busy trying to get our stuff out of the barn, I didn’t know I’d been burned.”

Scott Pittman, Pine Creek Fire, 2012

Intrinsic Pain-Modulating System

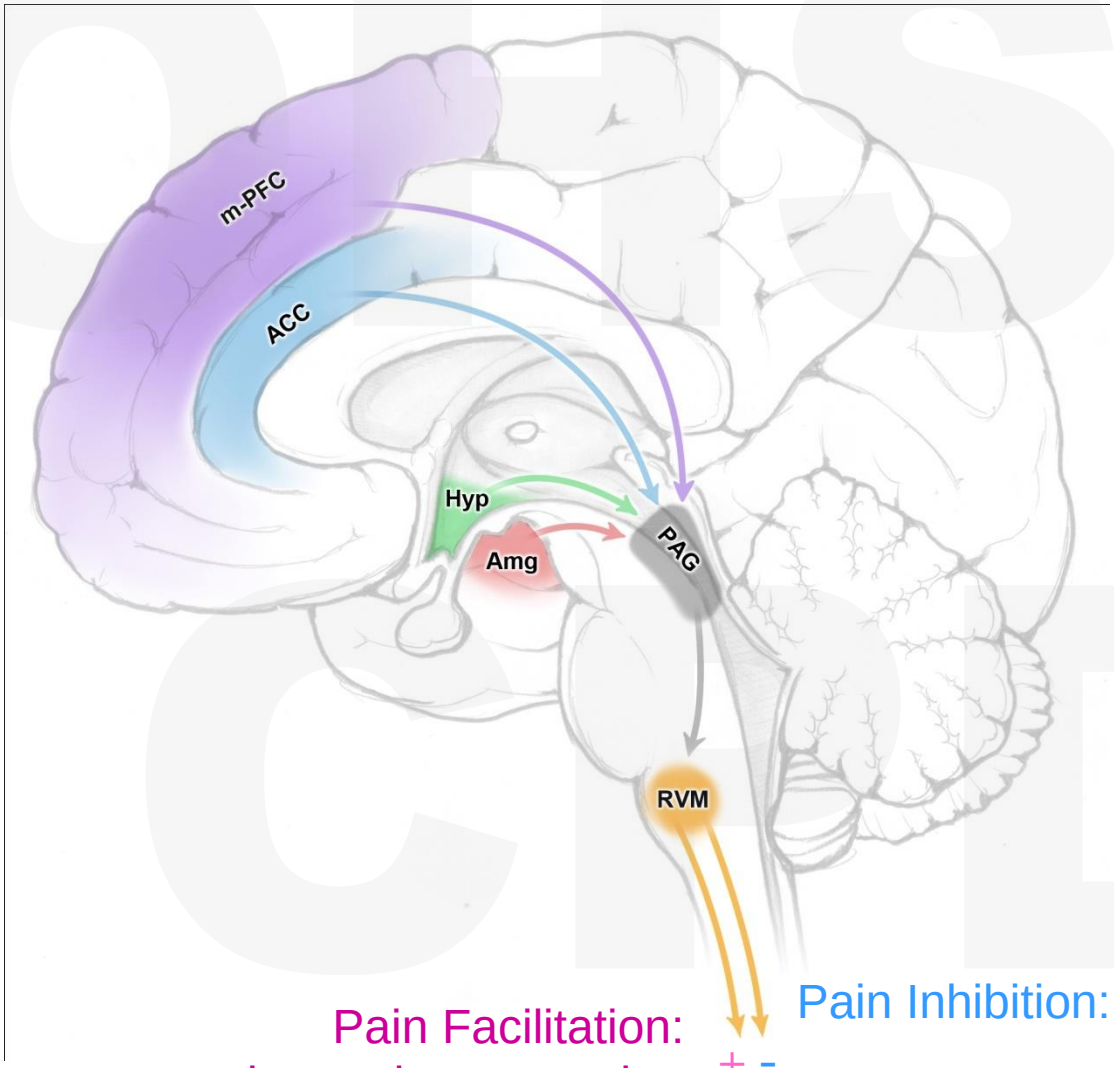


Translates to human



From Meyerson, *Prog Brain Res.*, 1988

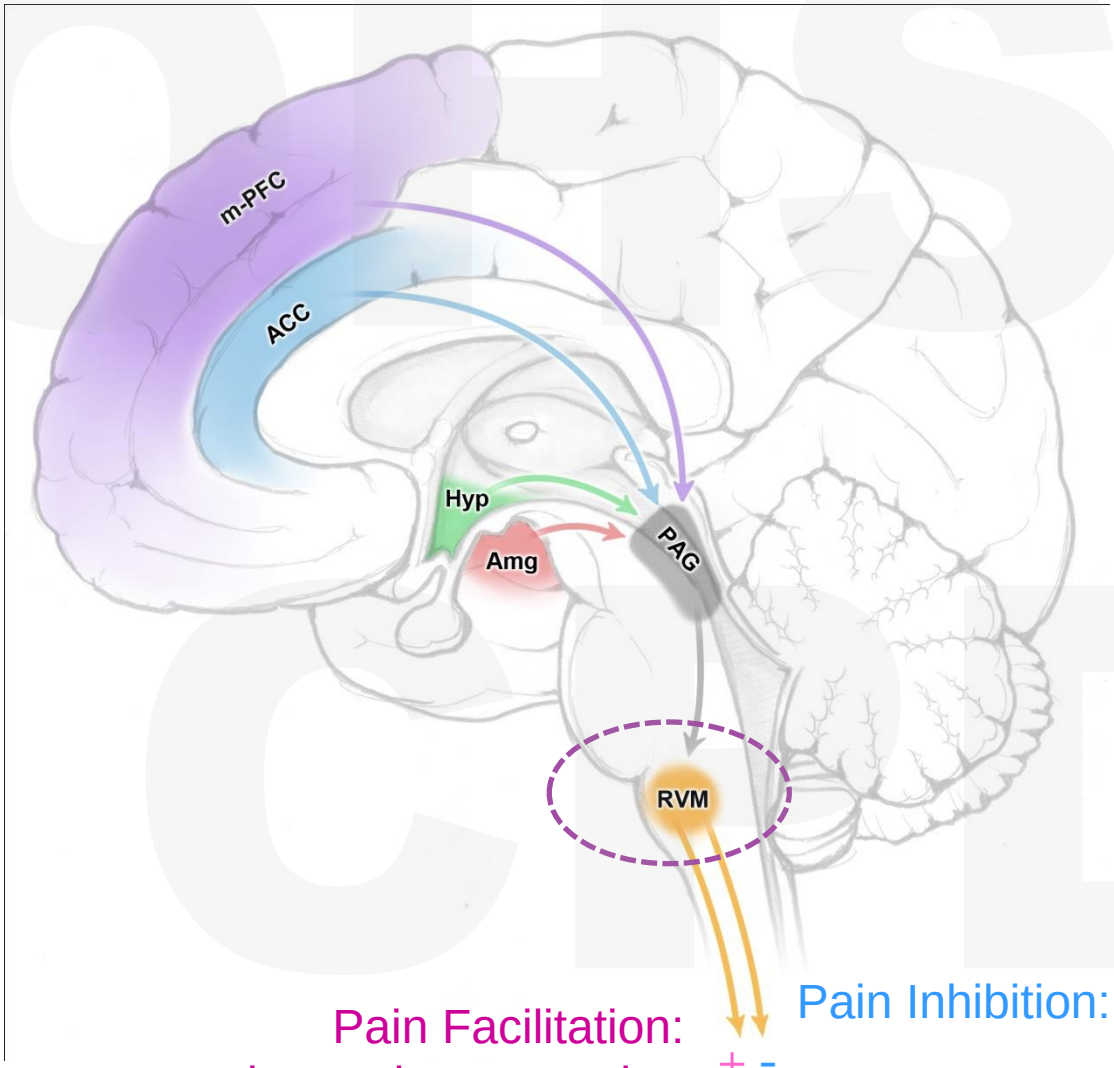
Pain modulating system: "Descending control"



Pain Facilitation:
protection and recuperation

Pain Inhibition: higher priorities

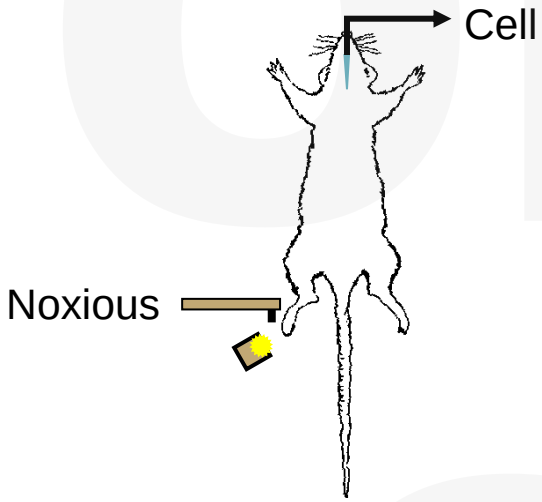
Pain modulating system: "Descending control"

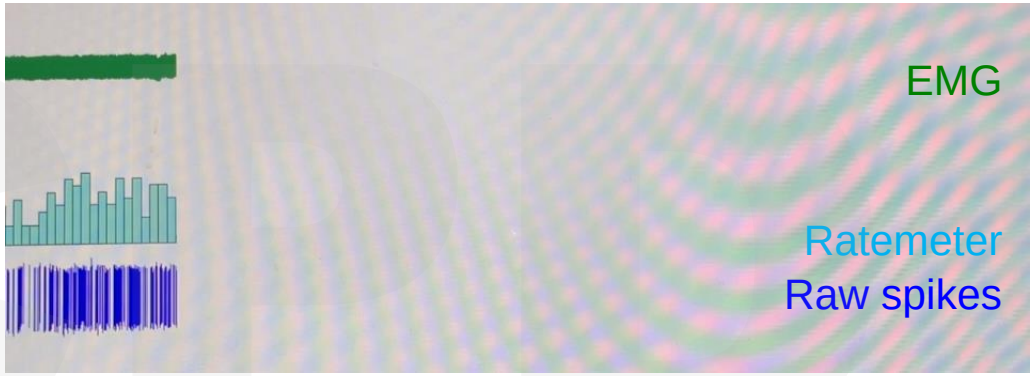


Pain Facilitation:
protection and recuperation

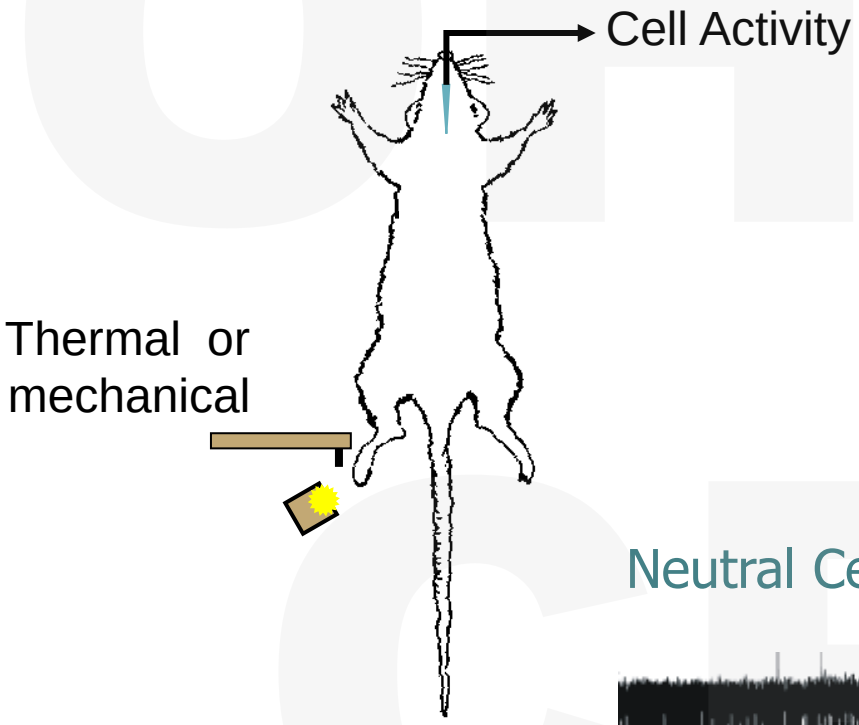
Pain Inhibition: higher priorities

Cell activity – in a behavioral context

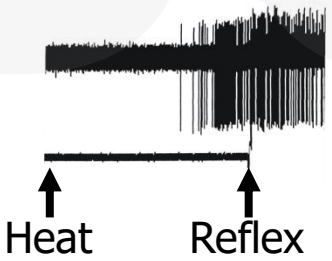




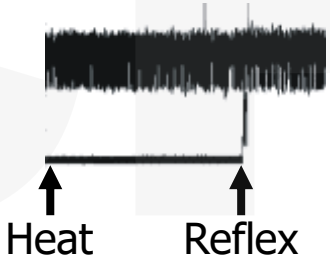
Cell activity – in a behavioral context



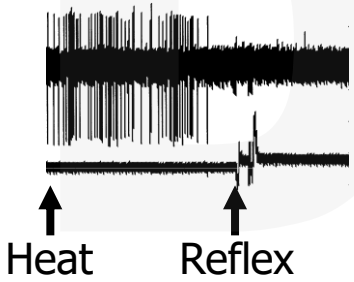
On-Cell



Neutral Cell



Off-Cell



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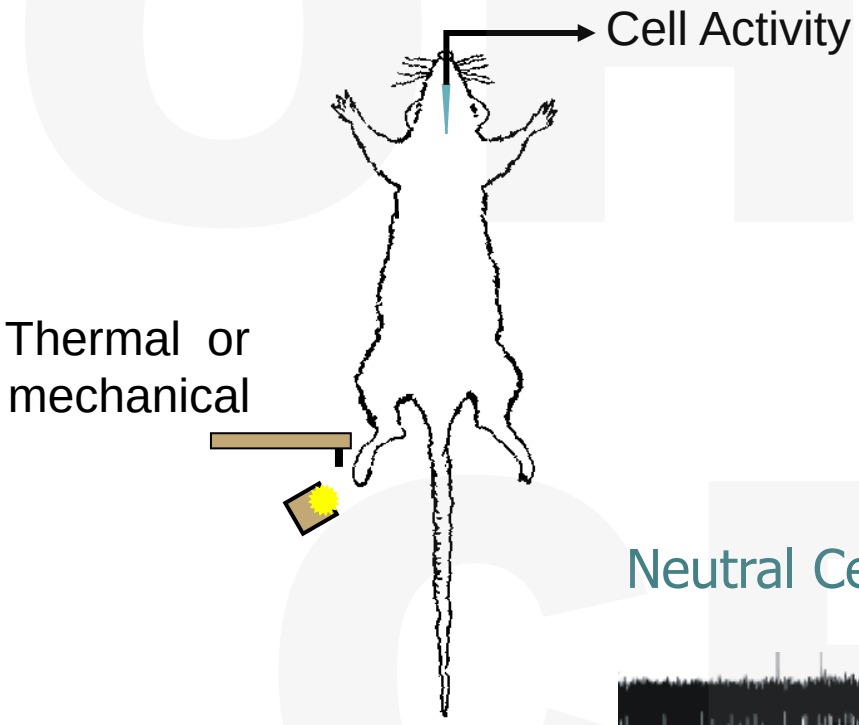

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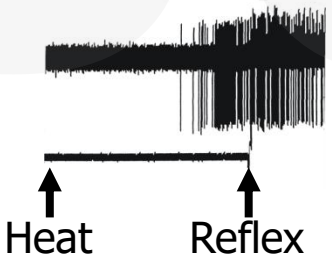

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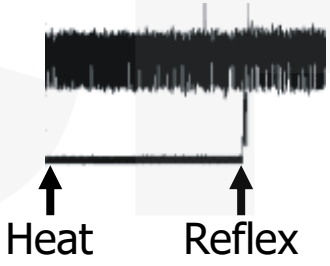
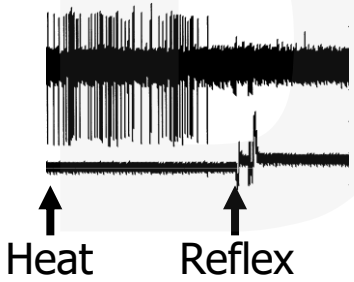
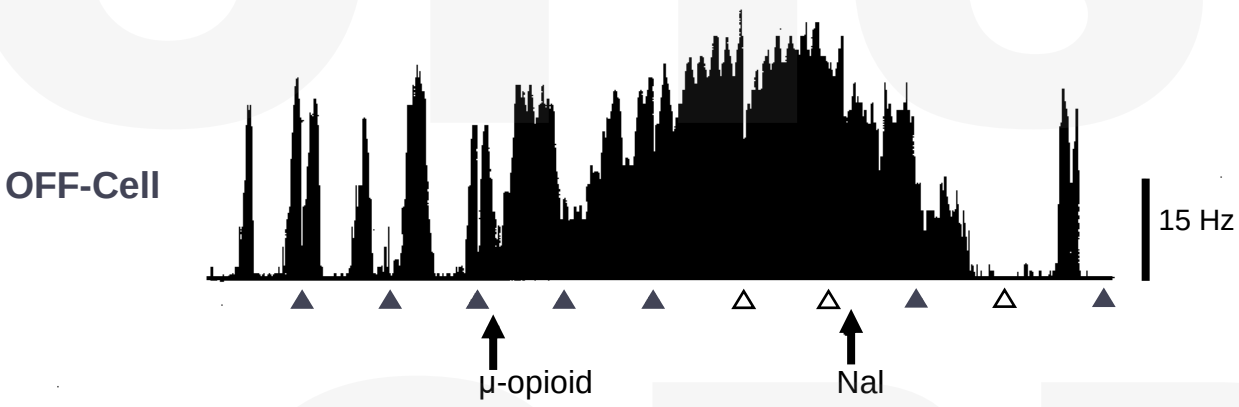
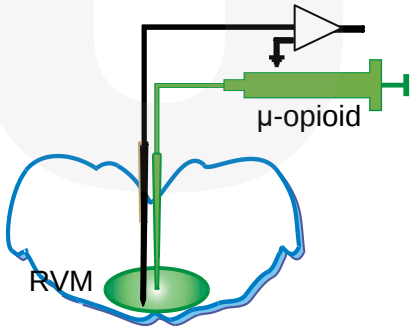


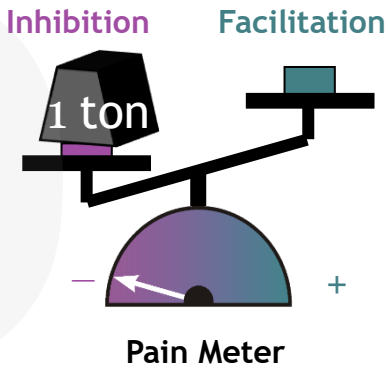
Off-Cell



Opioids activate OFF-cells, suppress ON-cells

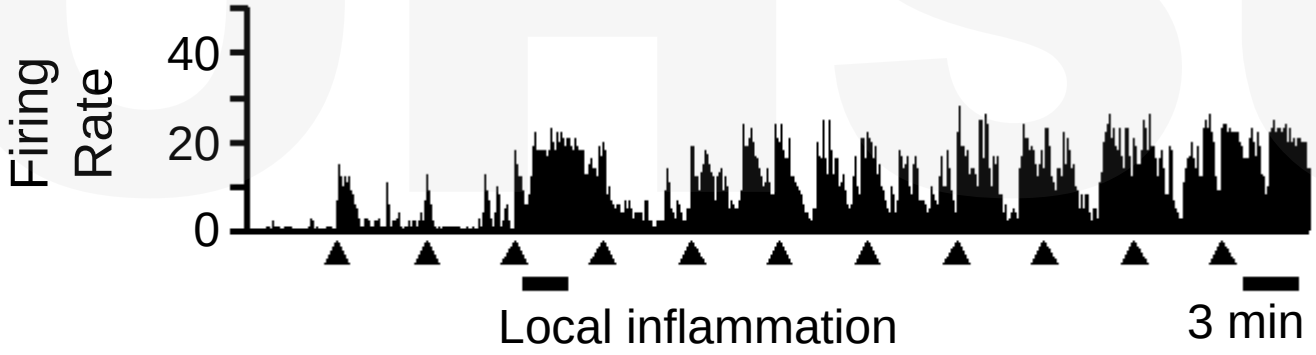


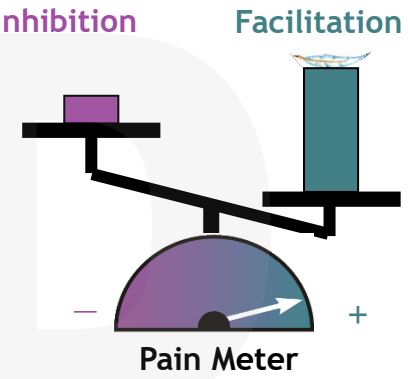




Heinricher et al., Neuroscience, 1994

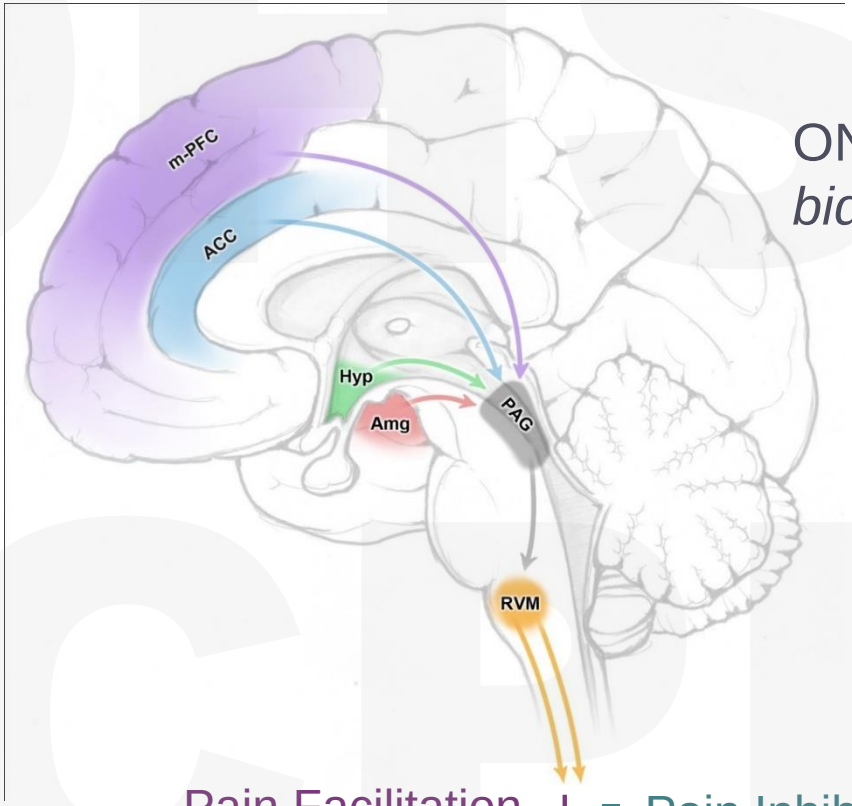
“ON-cells” are activated by injury





Increased pain → protection/recuperation

Intrinsic Pain-Modulating System

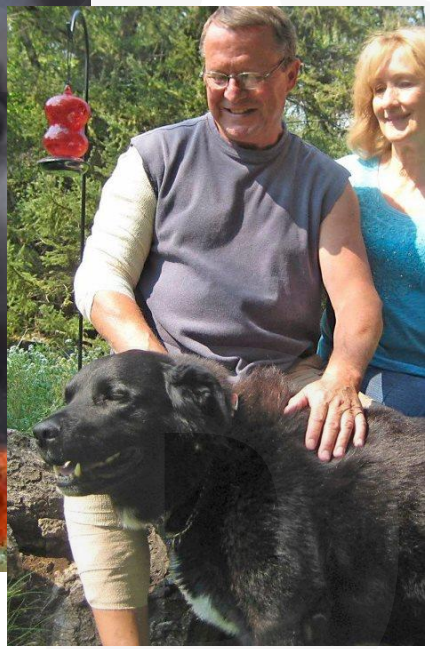


ON/OFF-cells basis for *bidirectional control*.

Pain Facilitation + - Pain Inhibition

When and how are these neurons recruited to enhance or suppress pain?

Injury ≠ Pain



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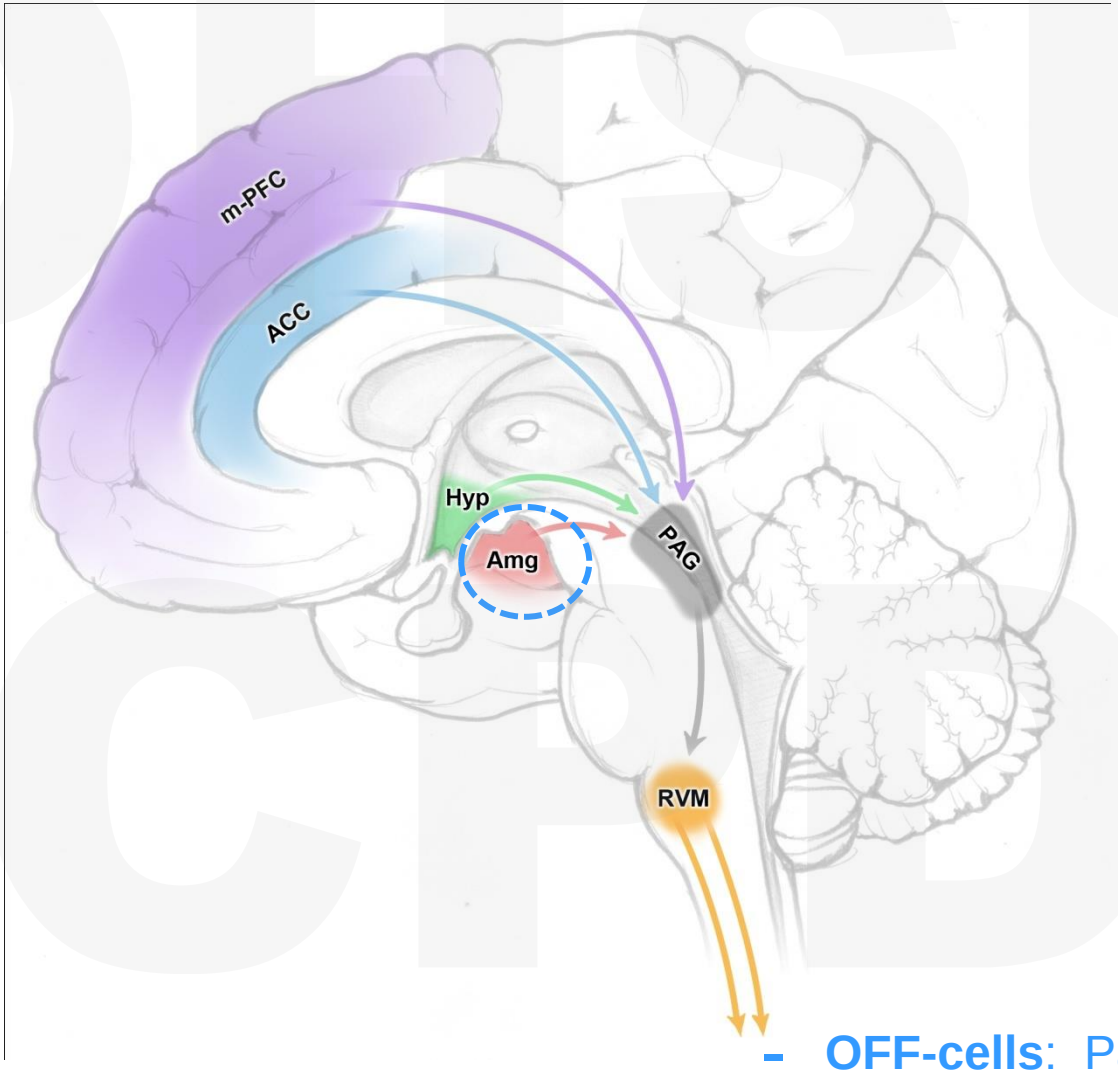
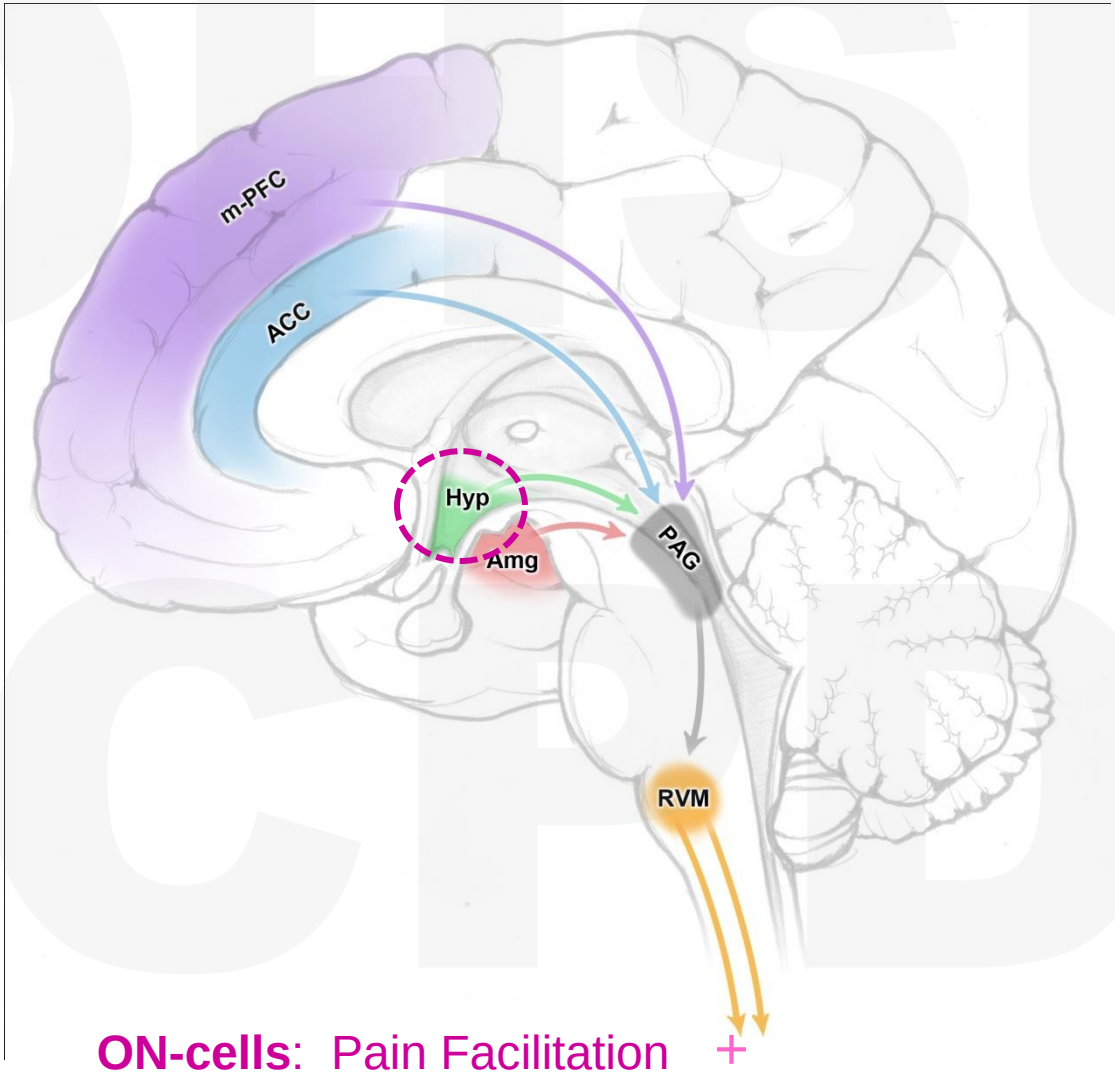
Top-down control: stress-induced analgesia



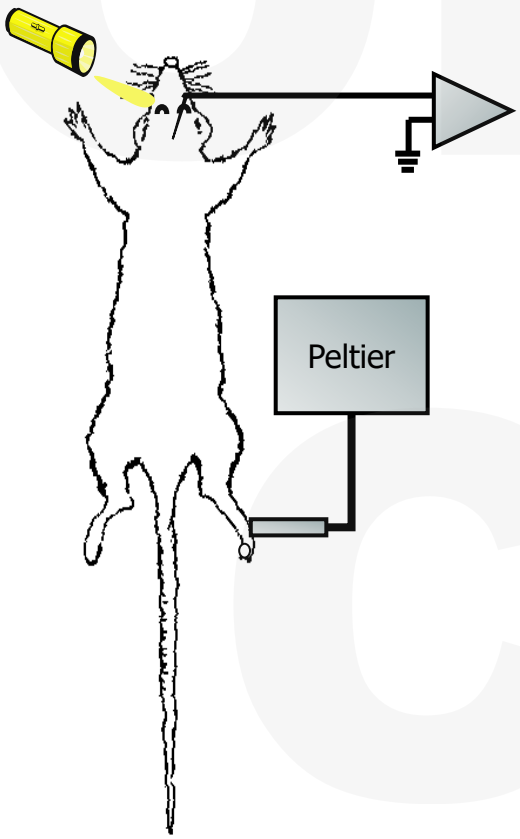
- **OFF-cells**: Pain Inhibition

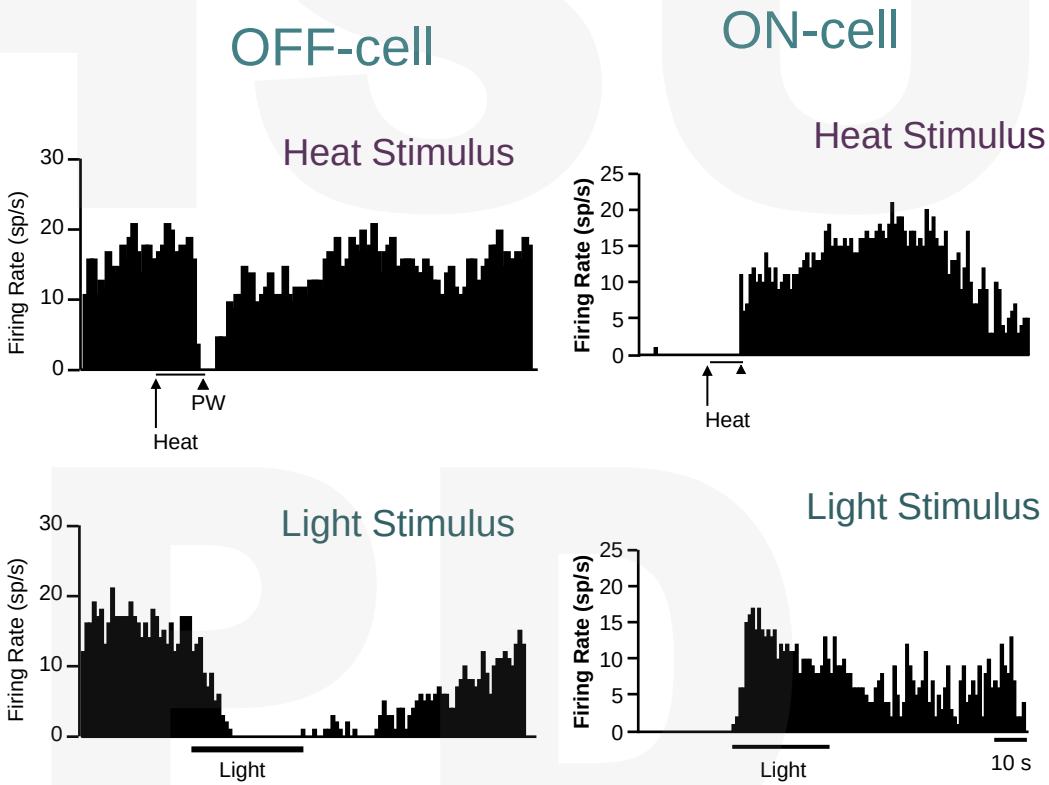
Top-down control: stress-induced hyperalgesia



ON-cells: Pain Facilitation +

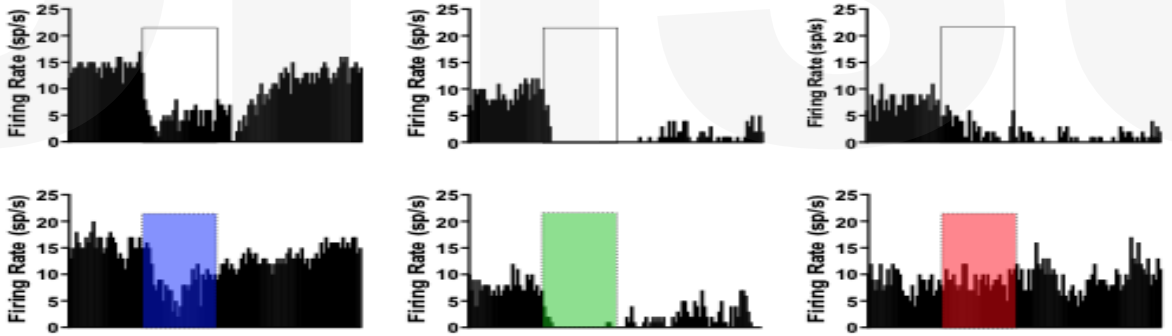
Light: A window into pain in the brain



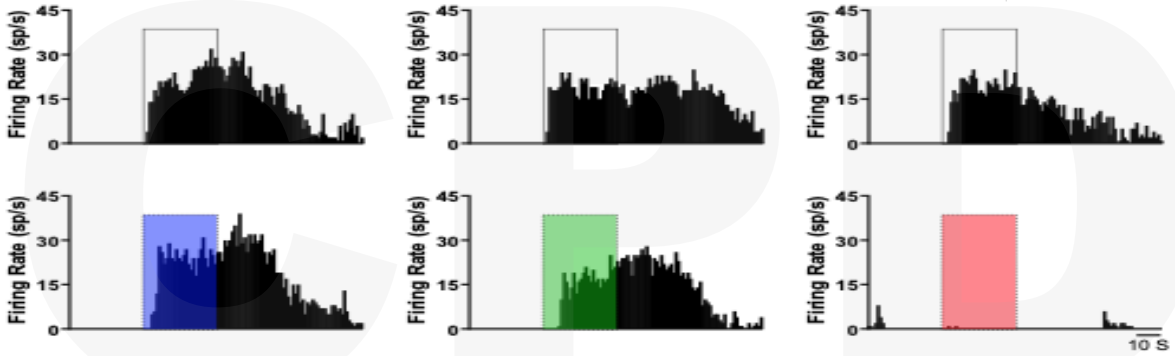


Spectral sensitivity

OFF-cell

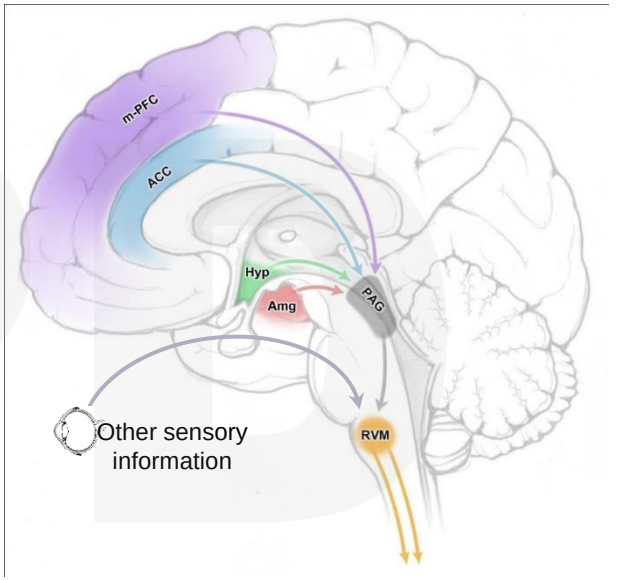


ON-cell



So what?

- RVM effectively transduces light into lowered *somatic* pain threshold.
- *Implications for pain and chronic pain?*
  - Photosensitivity/photoaversion is reported by many chronic pain patients.
  - A defined neural pathway – not “psychogenic”
  - Possible “marker” for central sensitization in patients?



Light as a window into pain in the (human) brain

- Individuals who have sustained a TBI are particularly likely to experience chronic pain (40-60%)
- Also present with abnormal sensitivity to *light*
- Light can engage elements of "central sensitization" in animal models
- Photosensitivity as a potential marker for individuals with chronic pain associated with TBI

Questions:

- Is photosensitivity correlated with clinical chronic pain and functional outcomes?
- Is light processed differently in individuals with chronic pain?

Study design

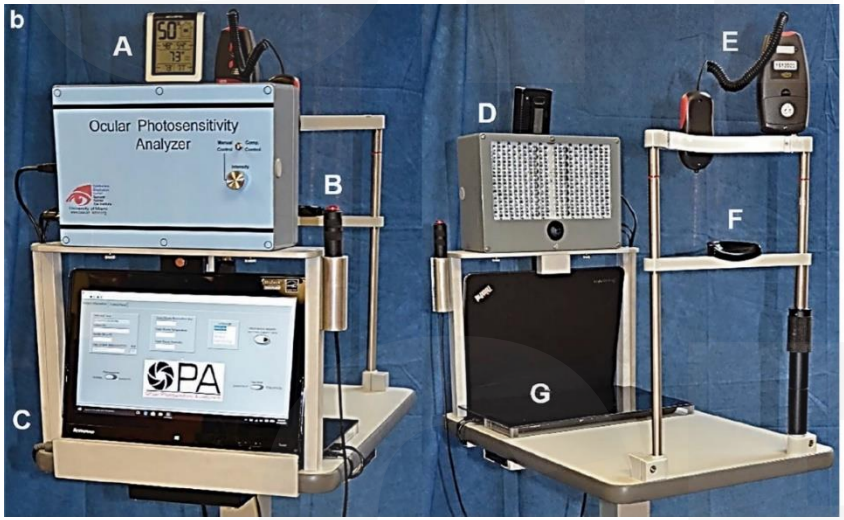
Phase 1: Consent/questionnaires and sensory scaling

- Questionnaires: pain, sleep, TBI symptoms, overall functional outcomes
- Photosensitivity testing
- Pressure-pain testing
- N = 433

Phase 2: Functional imaging

- Light, one-half discomfort threshold
- Pressure eliciting 4/10 rating
- Proposed N = 21

Outcome measures: sensory testing



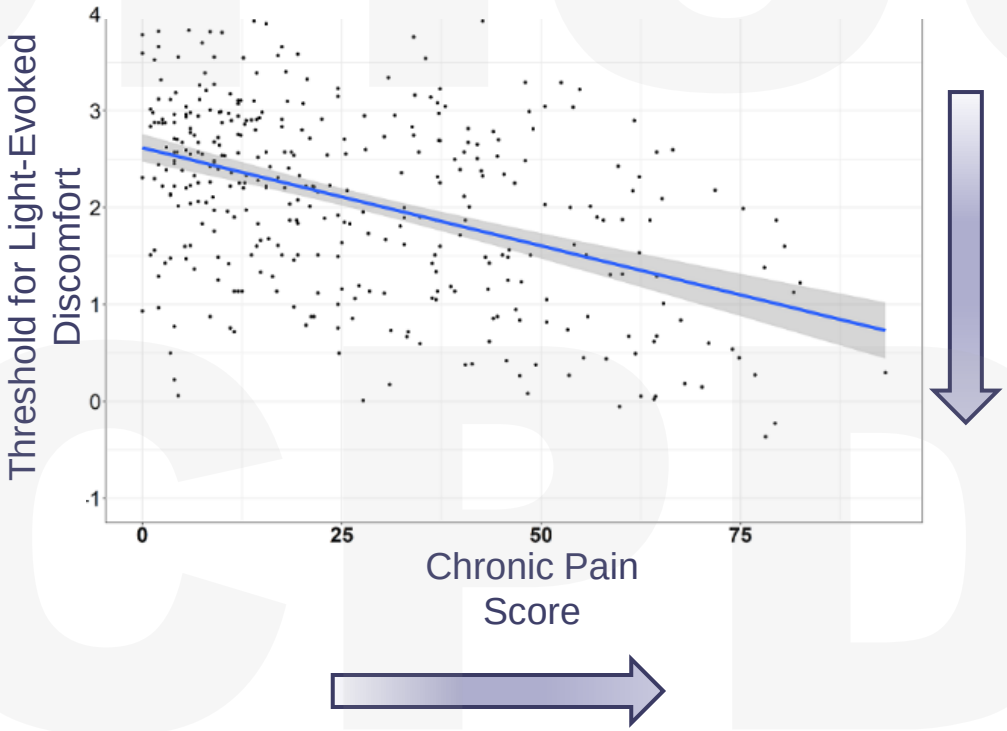
"Visual photosensitivity analyzer"

Pressure-pain threshold

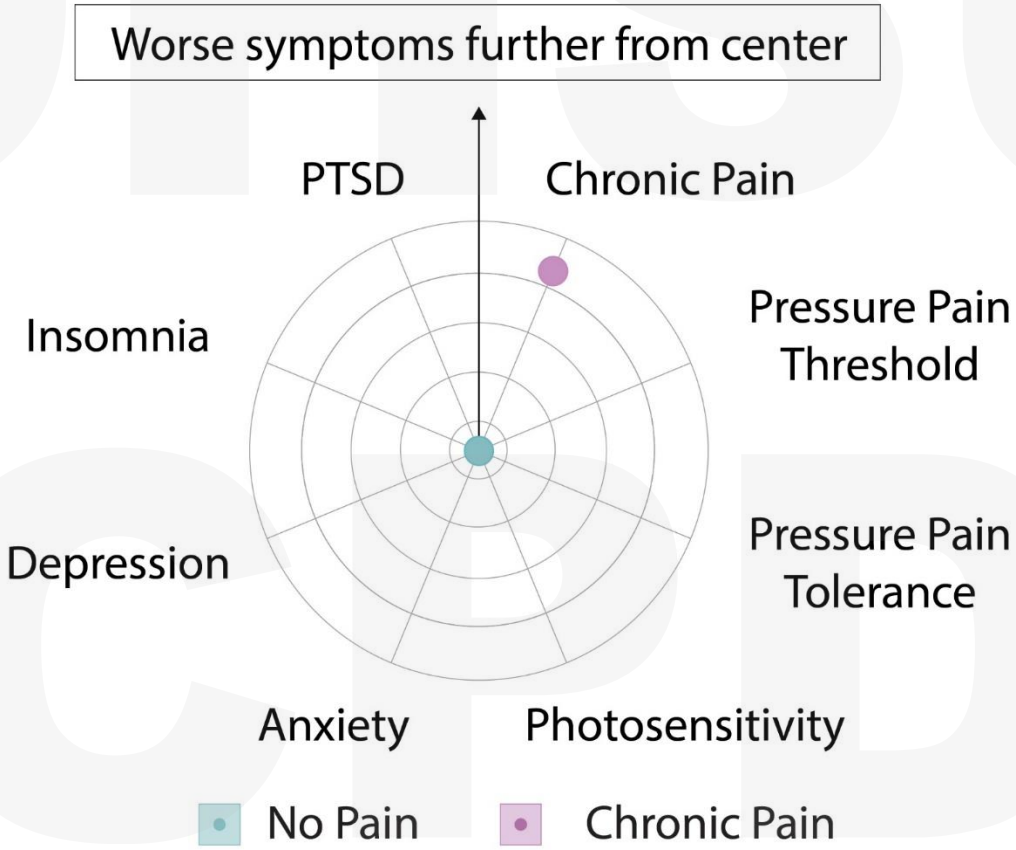
Outcome measures: self-report surveys

- *Chronic pain:* Symptom Inventory Questionnaire, Revised (SIQR)
- *TBI symptom severity:* Neurobehavioral Symptom Inventory (NSI)
- *Sleep quality:* Insomnia Severity Index (ISI)
- *PTSD symptoms:* PCL-5
- *Depression*: PHQ-9
- *Disability:* World Health Organization Disability Assessment Schedule (WHODAS)

Photosensitivity correlates with chronic pain



Photosensitivity correlates with pain-related *disability*



"High-impact chronic pain"

Study design

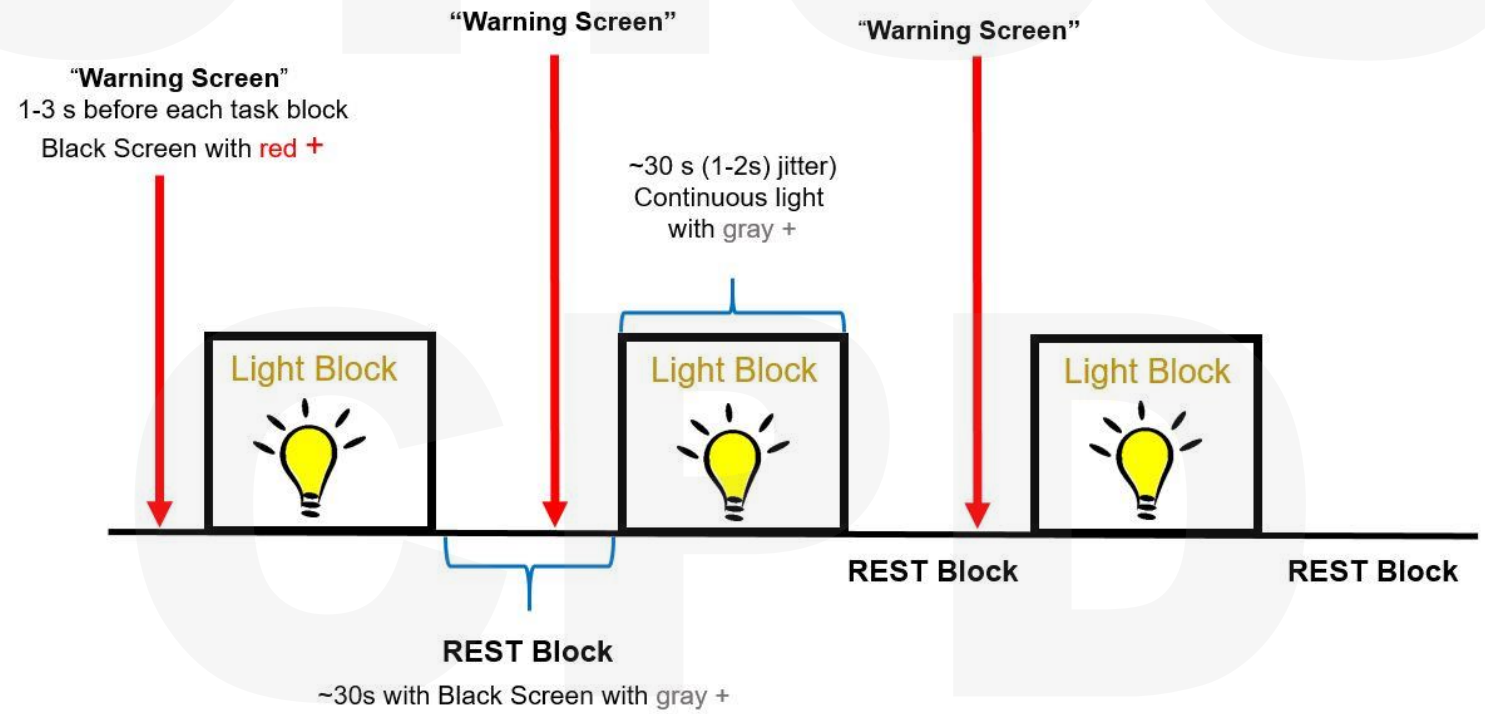
Phase 1: Consent/questionnaires and sensory scaling

- Questionnaires: pain, sleep, TBI symptoms, overall functional outcomes
- Photosensitivity testing
- Pressure-pain testing
- N = 433

Phase 2: Functional imaging

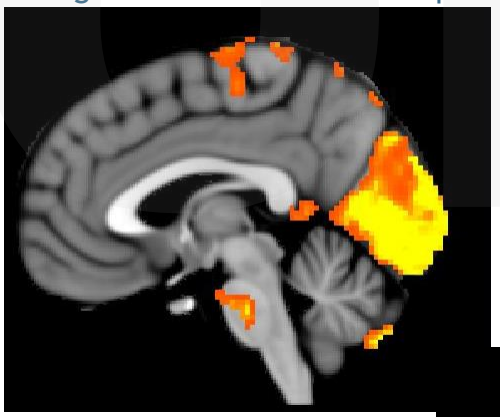
- Light, one-half discomfort threshold
- Pressure eliciting 4/10 rating
- Proposed N = 58 (21 to date)

Photosensitivity correlated with chronic pain

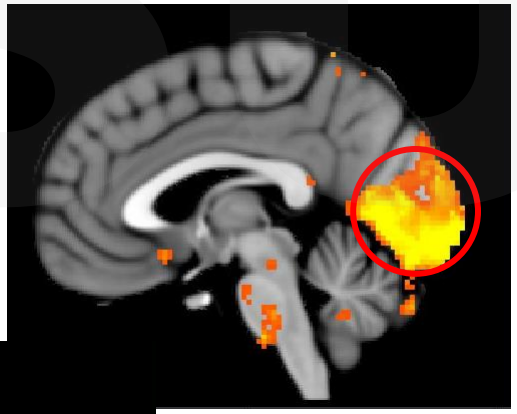


Not increased activation in primary visual pathways

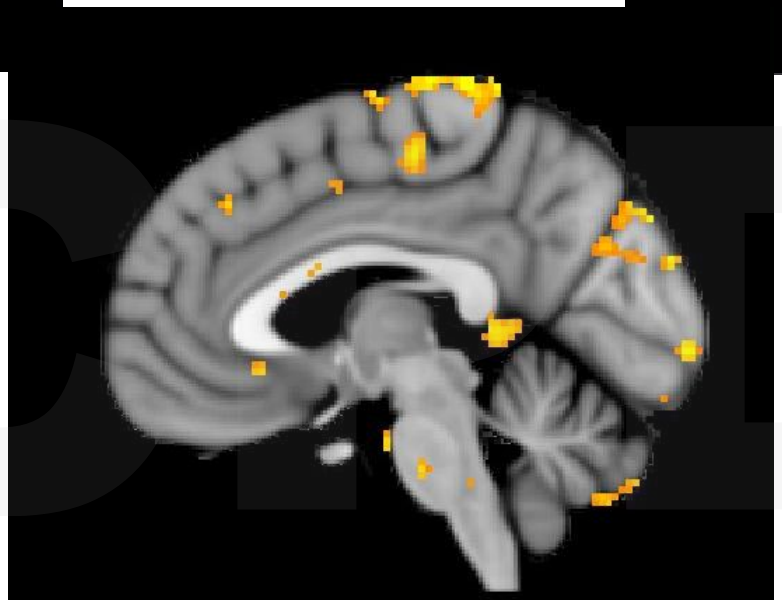
Average activation in “chronic pain”



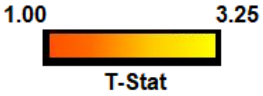
Average activation in “No chronic pain”



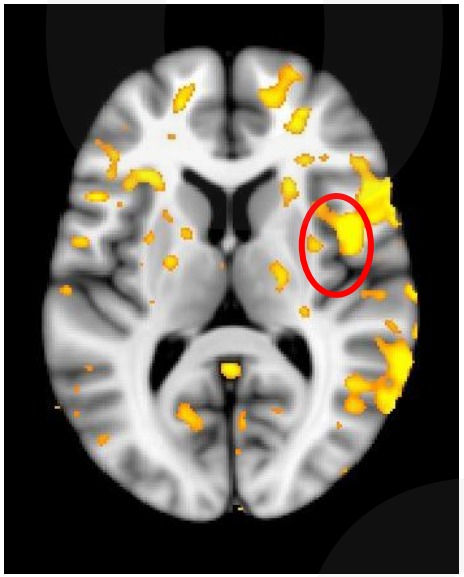
MNI: 6,-90,9
Primary Visual Cortex



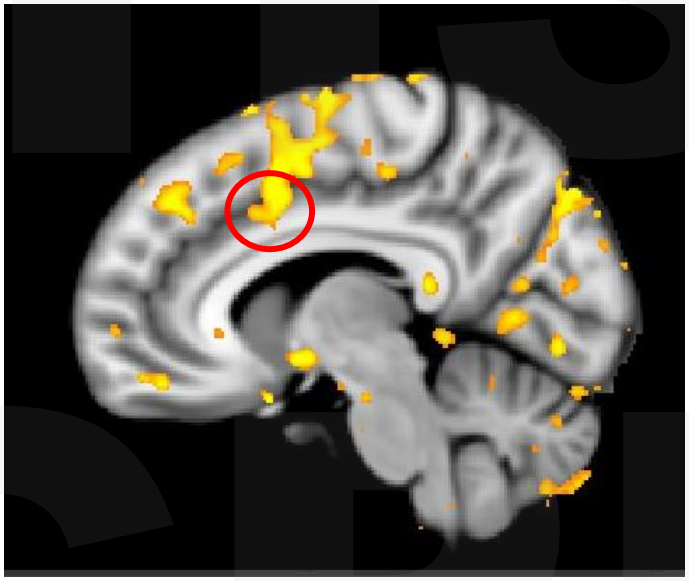
Subtraction map (Chronic pain > no chronic pain)



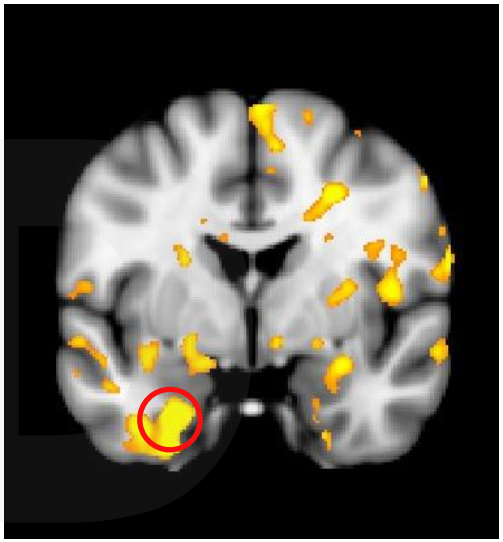
Light-evoked activation: chronic pain vs no chronic pain



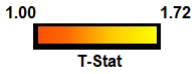
MNI: 44,6,3
Right Anterior
Insula



MNI: 8, 11, 38
Dorsal Anterior
Cingulate Cortex



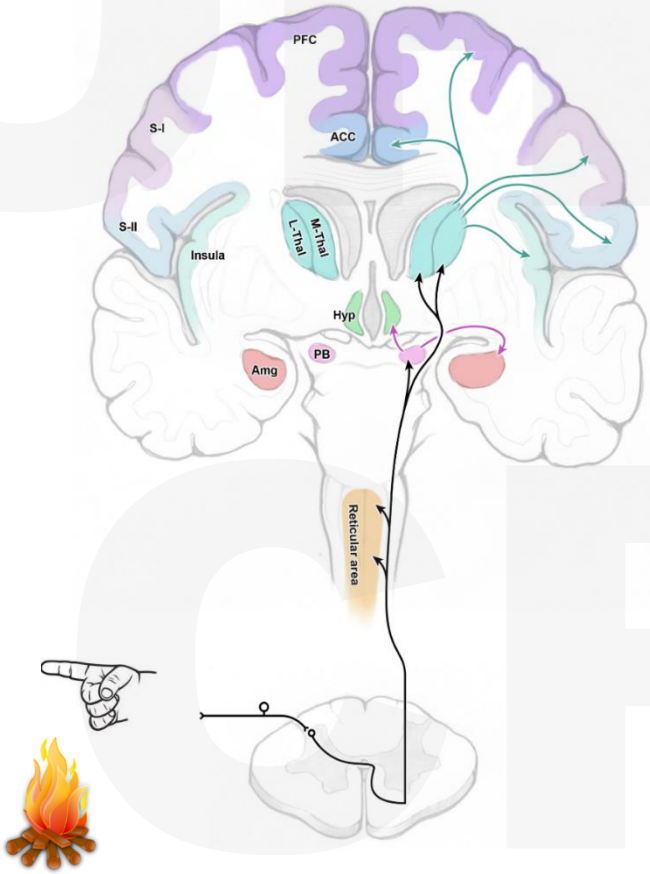
MNI: -22,-2,-34
Left Amygdala

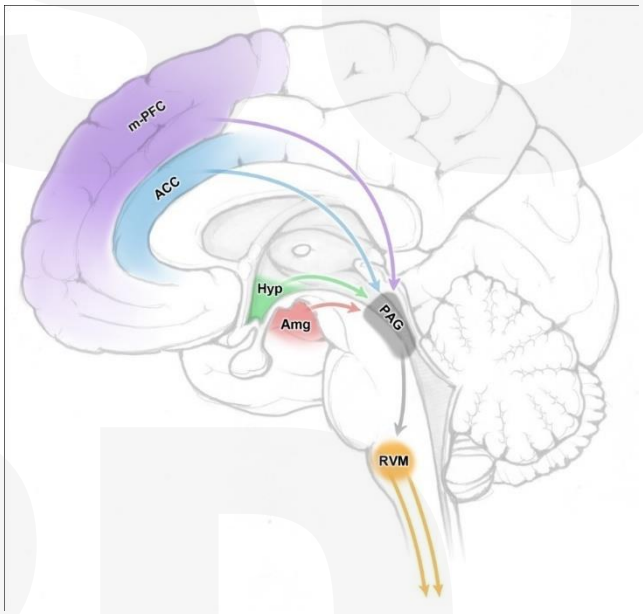


Conclusions and Opportunities

- "*High-impact*" chronic pain is associated with photosensitivity.
- Light is likely processed differently by individuals who endorse chronic pain-related disability
- *Opportunities:*
  - Association with PTSD
  - Longitudinal studies (e.g., post-trauma)
  - Photosensitivity as a predictor of treatment effects
  - Light effects on experimental and clinical pain, including modification of light environment
- Pain is always in your head!

Pain: Distributed, recurrent system





Transmission

Modulation

- My laboratory:
  - Melissa Martenson
  - Gwen Hryciw
  - Zhigang Shi
  - Stephanie Radu
  - Caitlynn De Preter
  - Nadir Balba
- Miranda Lim
- Matt Butler
- Scott Mist
- Kim Jones (Emory)

- Supported by NINDS, NIDA, NIAAA, DoD