The self in pain:
From basic circuits to psychological intervention

Tor D. Wager

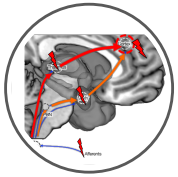
Department of Psychological and Brain Sciences
Dartmouth College



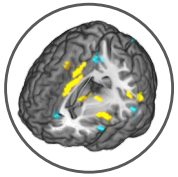
sites.dartmouth.edu/canlab

@torwager

Roadmap



Nociceptive pain and
beyond



Self in context:
Brain systems for conceptual thought



A psycho-behavioral intervention



In December 2005, I woke up from hysterectomy surgery, and **my world changed**.

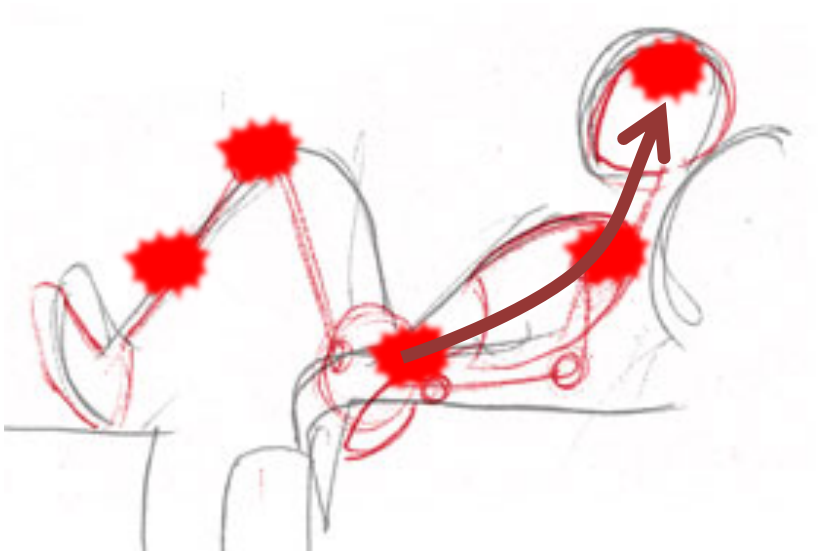
I had **electrifying, shocking pain going through my body**, and my left leg was numb. … my doctors told me it was just the effects from anesthesia.

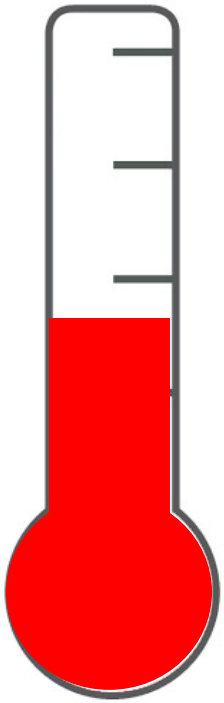
… When I went home, I was **hurting everywhere**. I curled up on the couch, and I stayed on that couch **for 16 months**.

I had heart irregularities, metabolic syndrome…and three kinds of **migraine headaches**.

I had so much pain that **nobody could touch me**.

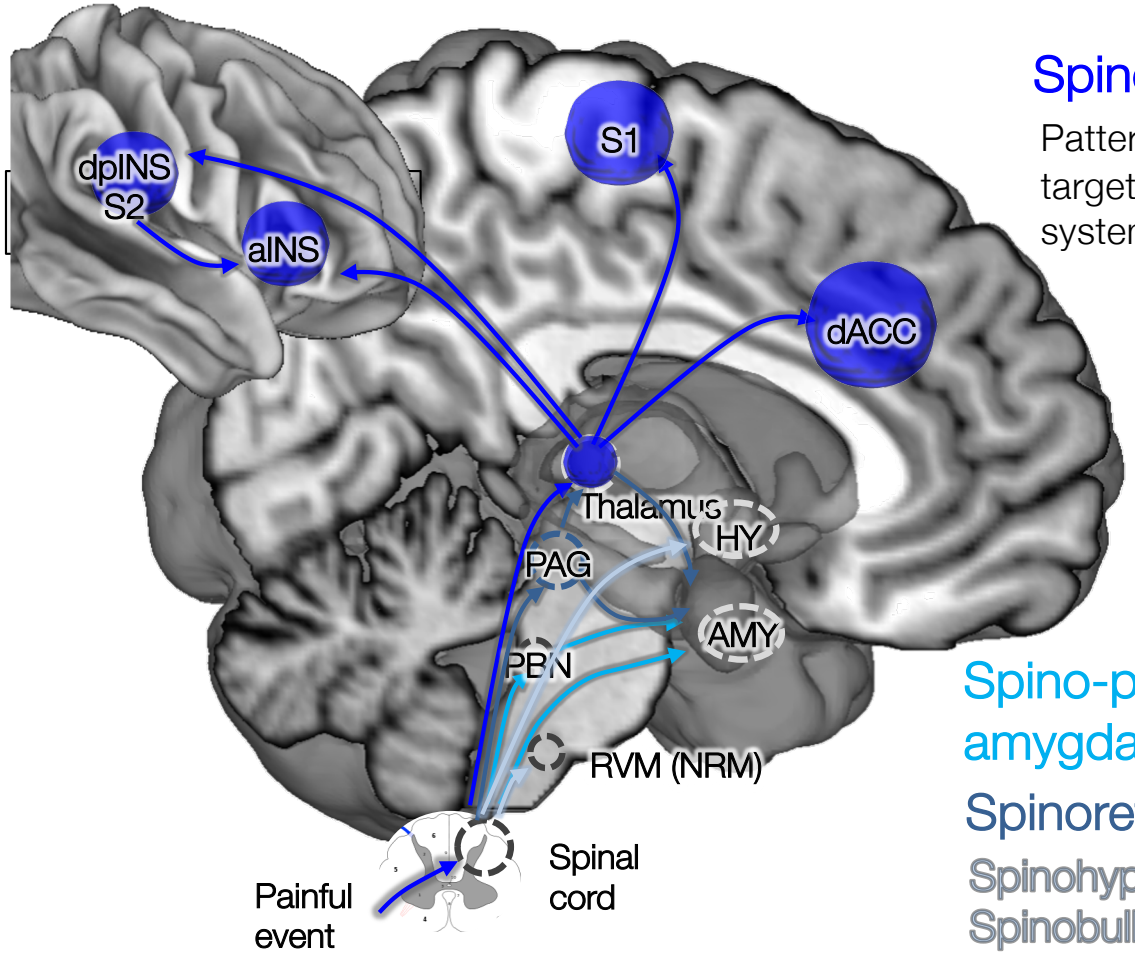
What's wrong?





Nociception

Ascending nociceptive pathways



Spinothalamic

Patterns within classical targets of nociceptive systems

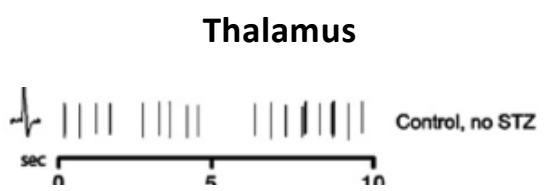
Spino-parabrachial-amygdalar

Spinoreticular

Spinohypothalamic

Spinobulbar

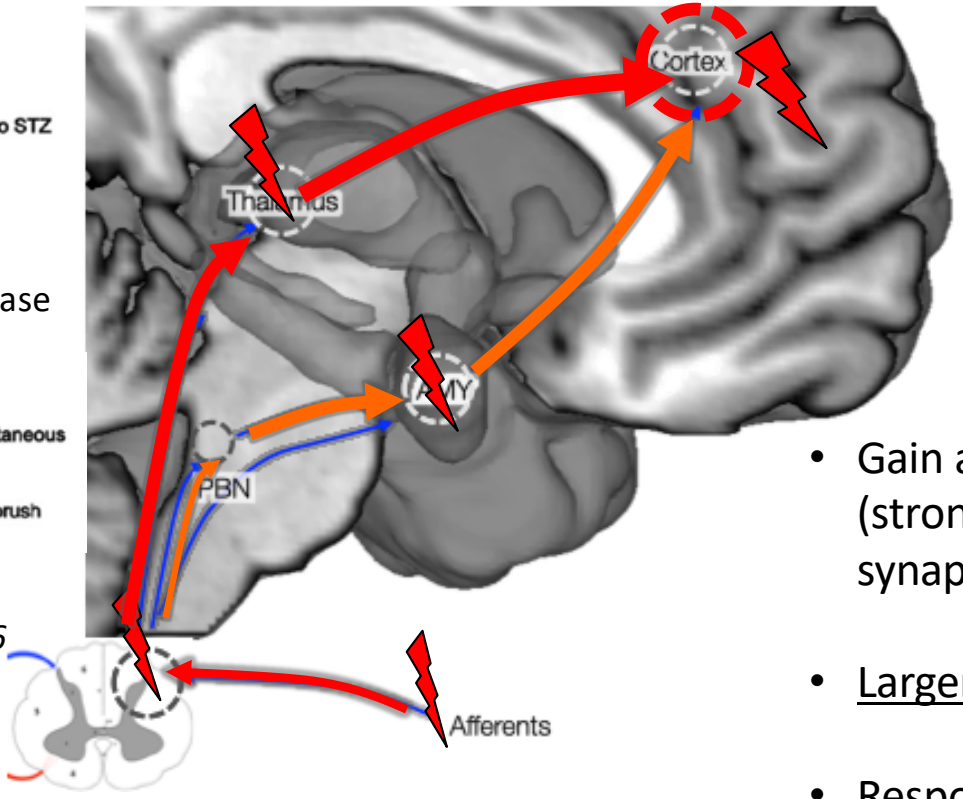
Sensitization in nociceptive pathways



Diabetic pain model
Spontaneous activity: 9x increase



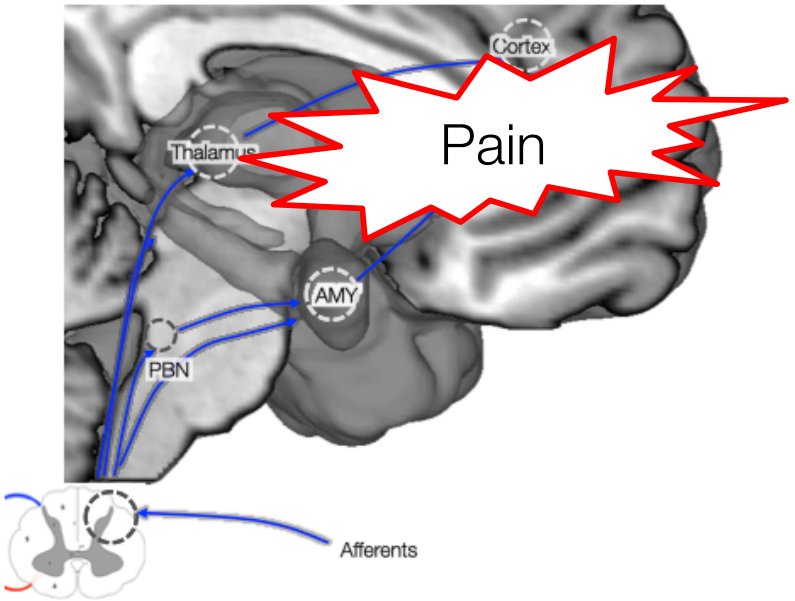
Fischer, Tan, & Waxman 2006



- Gain amplification: Sensitization (stronger responses) in brain synapses
- <u>Larger</u> receptive fields
- Responses to neurons that are normally non-nociceptive

Waxman; Kuner; Flor; Devor; Ji; de Konick; Wang; Gereau; Carrasquillo; Neugebauer; Kato; many others

There is more to the story

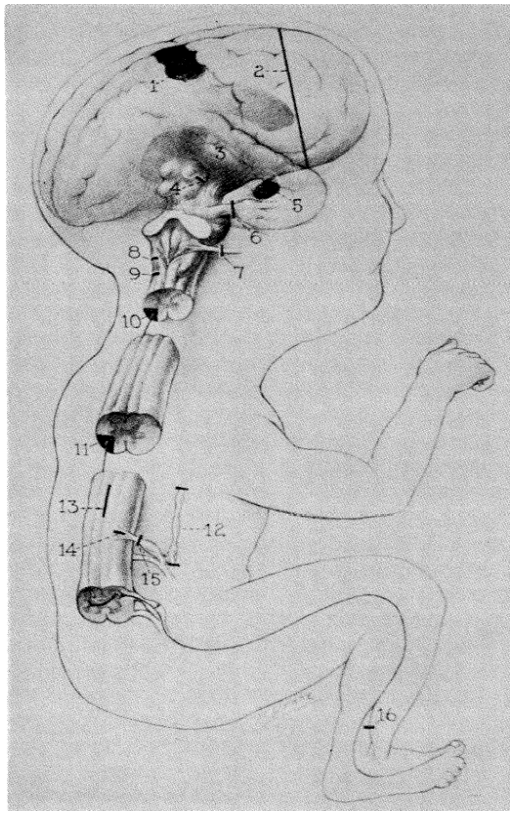


Where is the pain?
The suffering?
The resilience?
The hope?

Do thoughts and emotions matter?

There is more to the story

Surgical interventions for pain



1 gyrectomy (cingulotomy)
2 Frontal lobotomy
3 Thalamotomy
4 Mesencephalic tractotomy
5 Hypophysectomy (pituitary)
6 C.N. V
7 C.N. IX
8 Medullary tract
9 Trigeminal tract
10, 11 Spinal cord
12 Sympathetic ganglia
13 Crossing STT fibers
14 Zone of Lissauer
15, 16 Peripheral nerves or roots

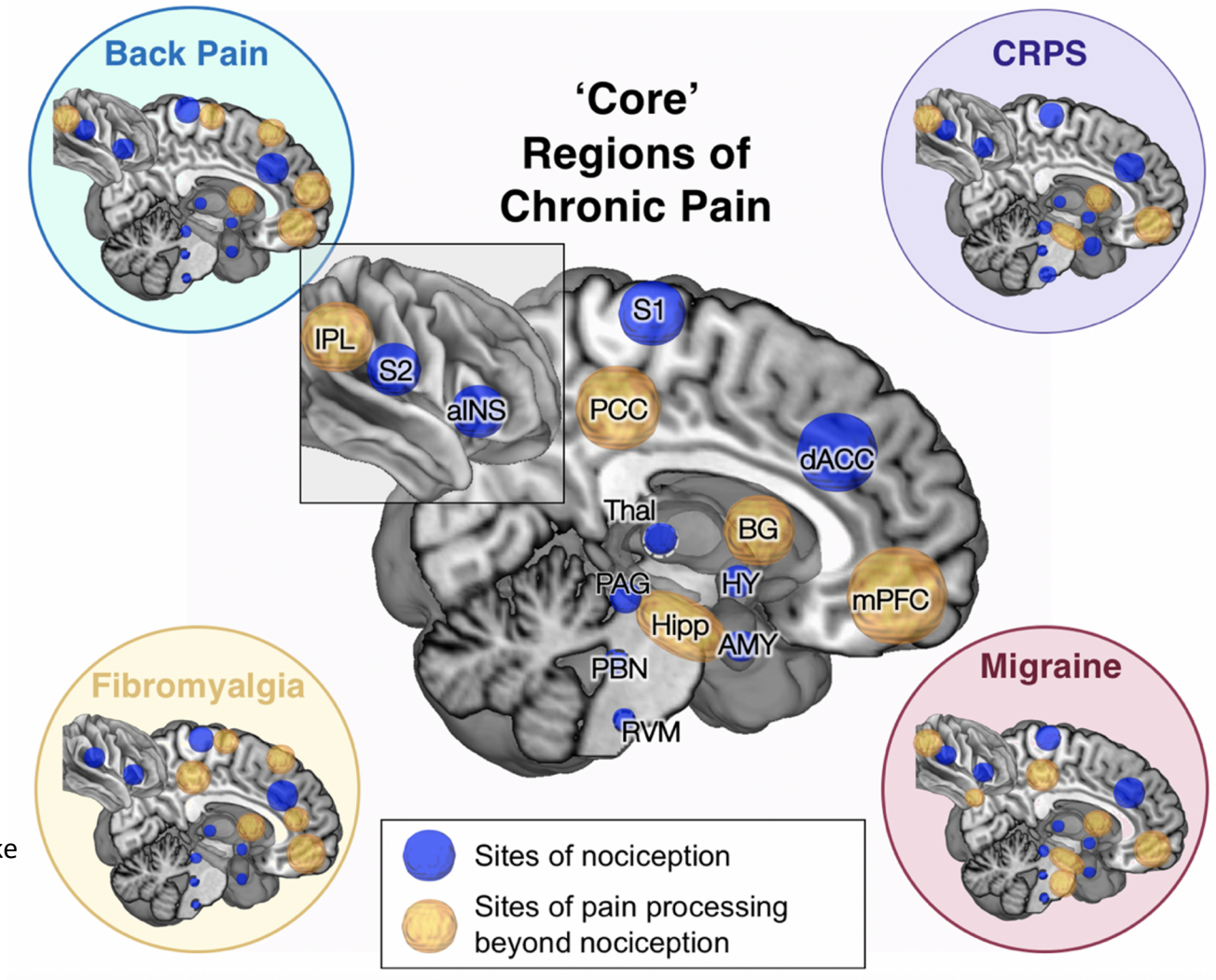
Peripheral blocks often effective for immediate pain

Don't work consistently for chronic pain

No interventions are consistently effective

Melzack and Wall, Science, 1965

(Baliki et al., 2006, 2008, 2011, 2014; Callan et al., 2014; Loggia et al., 2015)



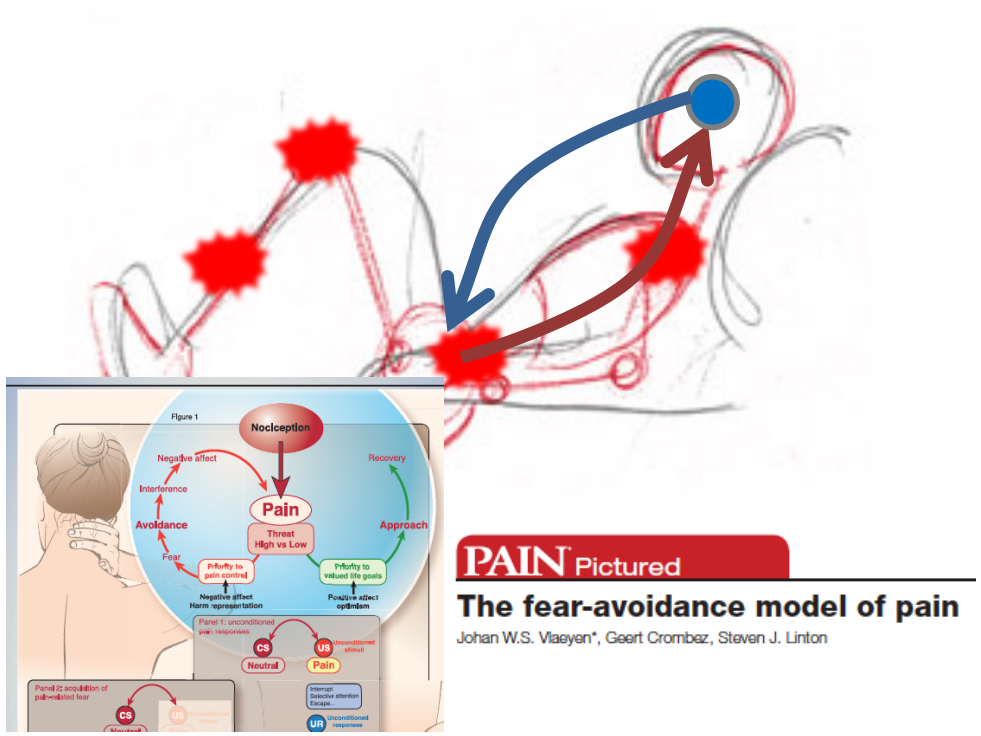
(Azqueta-Gavaldon et al., 2016; Schwartzman et al., 2006; Baliki et al., 2012; GEha et al., 2008)

(Napadow et al., 2012; Harris et al., 2009; Schmidt-Wilcke et al., 2007)

(Maleki et al., 2011; 2012; Russo et al, 2012; Grazzi et al., 2010; Welch et al., 2001; Caso et al., 2002; Schwedt & Dodick, 2009)

Reddan & Wager 2018; van der Miesen, Lindquist, & Wager 2019

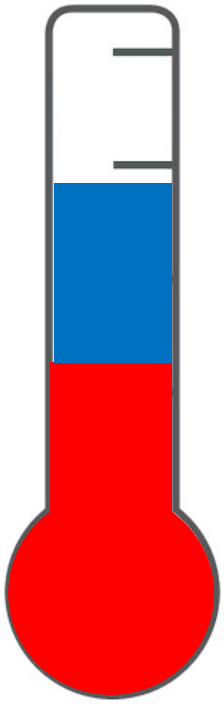
What's wrong?



PAIN Pictured

The fear-avoidance model of pain

Johan W.S. Vlaeyen*, Geert Crombez, Steven J. Linton

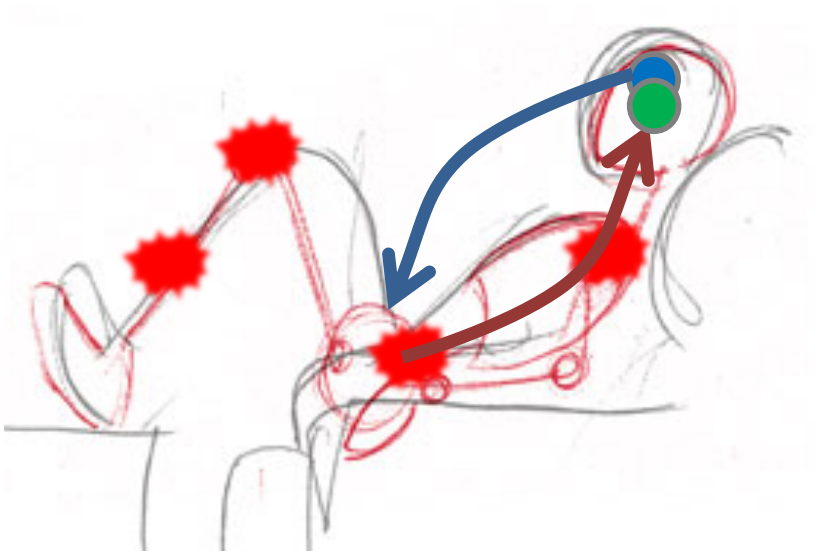


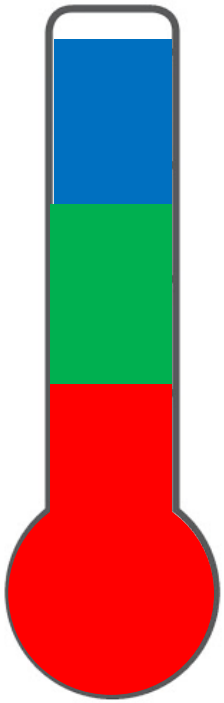
Fear & Avoidance

Nociception

Lethem 1983; Vlaeyen 2000; Leeuw 2007; Sullivan 2001; Wideman 2009

What's wrong?





Fear & Avoidance

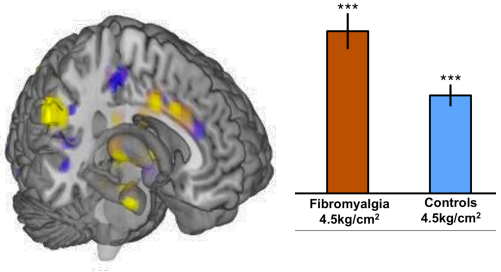
Pain conceptualization

Nociception

Fibromyalgia:
Alterations in other pathways beyond pain transmission

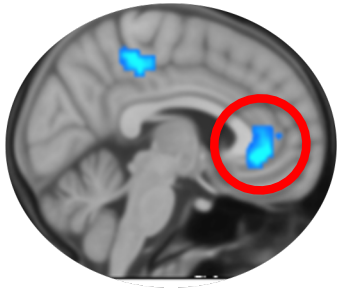


Evoked hypersensitivity



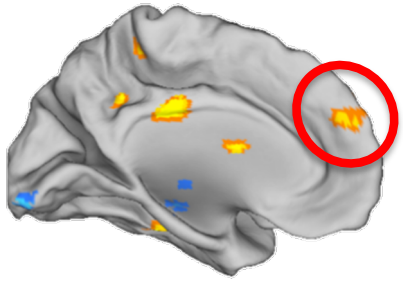
Immediate pain systems hyper-responsive

Alterations in pain-regulatory systems



Medial frontal cortex becomes **pro**-pain

Multisensory responses



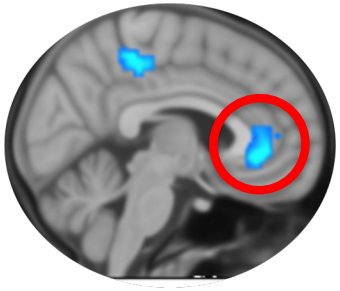
Altered responses to audiovisual stimuli

93% accuracy for fibromyalgia vs. controls

Lopez-Sola et al. 2017

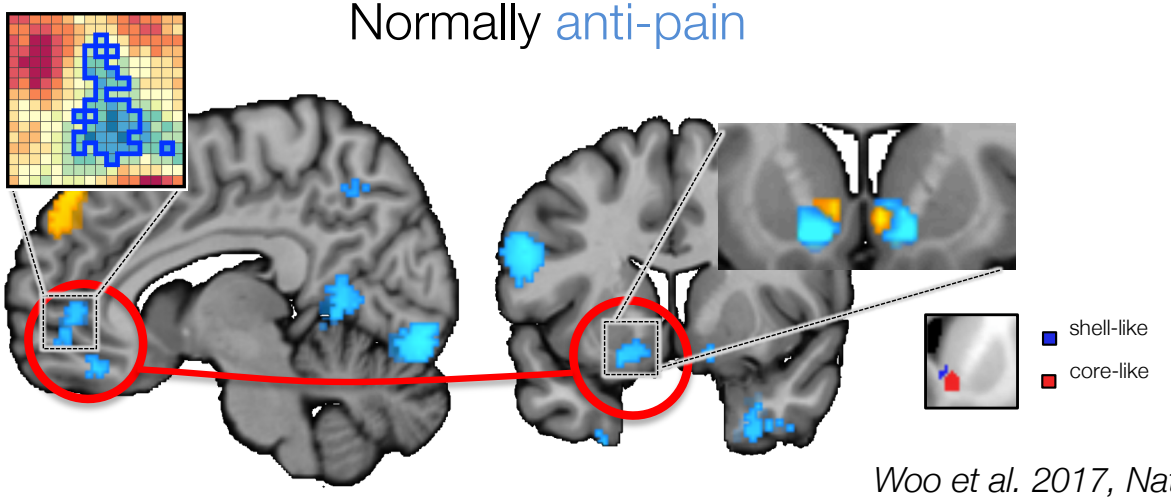
Fibromyalgia:
Alterations in other pathways beyond pain transmission

Alterations in pain-regulatory systems



Medial frontal cortex becomes **pro**-pain

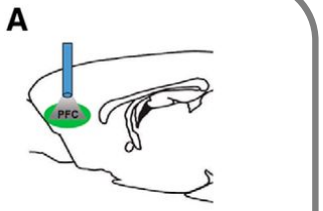
Normally anti-pain



Woo et al. 2017, Nature Comms

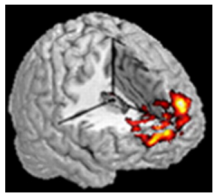
Medial prefrontal cortex and ‘default mode network’ in chronic pain

Pro-pain associations across multiple types of pain



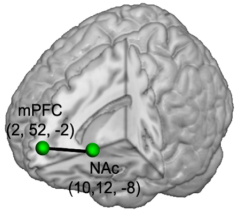
Pain behavior in animals
Lee 2015, Martina 2010; Dale 2018; Schwartz & Fields 2018; Wang 2019

Positive correlations with spontaneous back pain



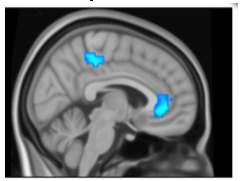
Baliki et al. 2006

Predicts transition to chronic back pain



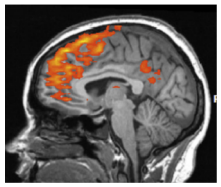
Baliki et al. 2012

Shift to more positive correlations with evoked fibromyalgia pain



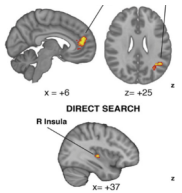
Lopez-Sola et al. 2017

Increased connectivity with insula, cingulate in failed back surgery



Kornelsen et al. 2013

Increased connectivity with posterior insula, back pain

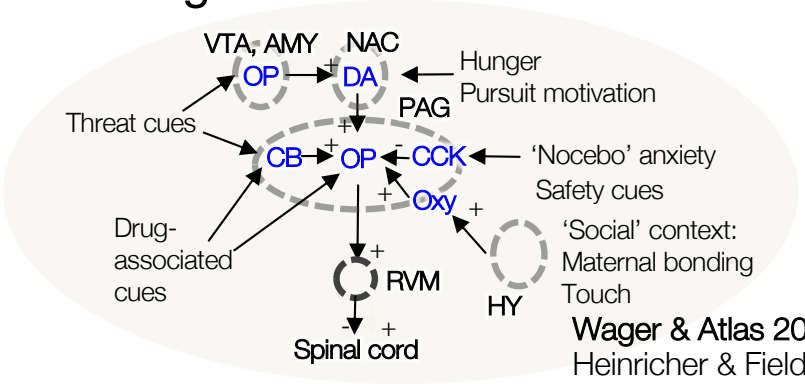


Loggia et al. 2013

See also: Napadow, Harris, Clauw, Jenssen, Apkarian, others

Pain genesis and modulation: Changing views

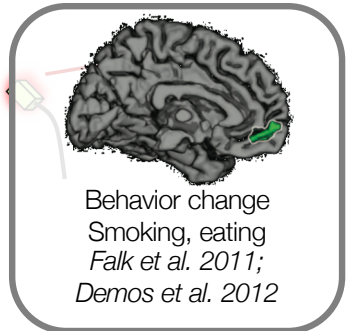
Descending inhibition and facilitation



Wager & Atlas 2015
Heinricher & Fields 2013

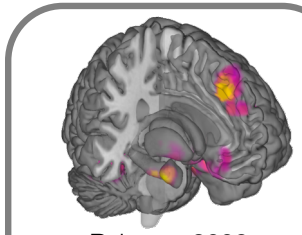
From inhibition to contextualization

Decision-making
Behavior change
Psychopathology

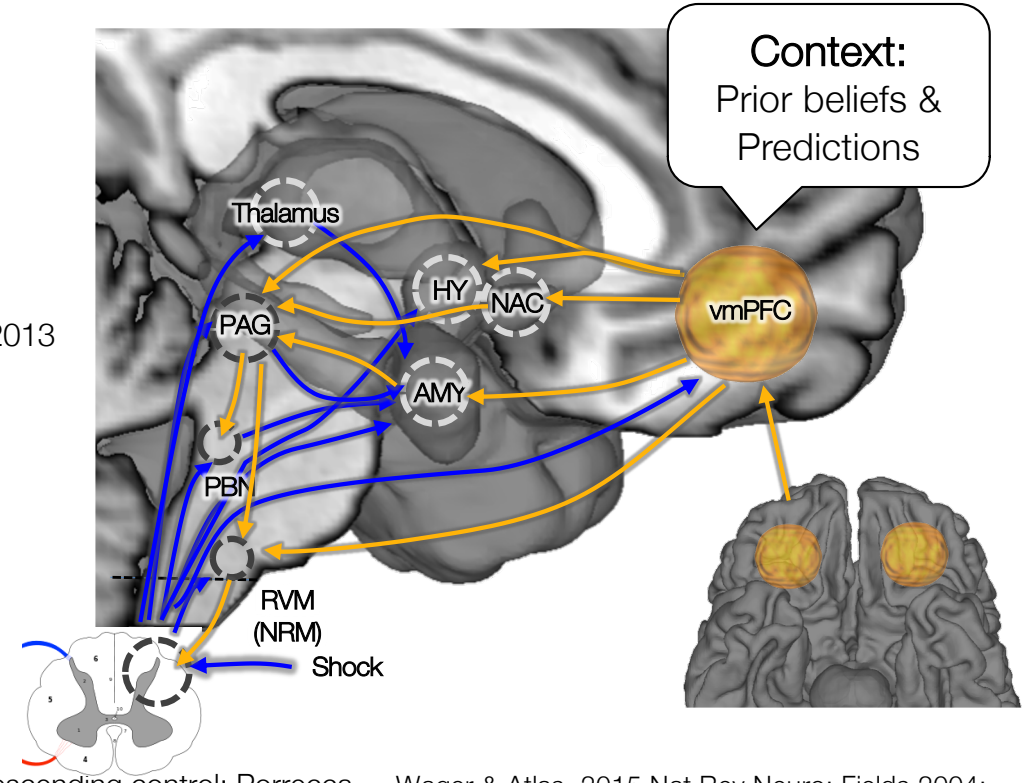


Behavior change
Smoking, eating
Falk et al. 2011; Demos et al. 2012

Autonomic regulation
Immune interactions



Beissner 2008; Gianaros 2015; Geuter 2017; Kraynak 2018; Roberts lab 2020

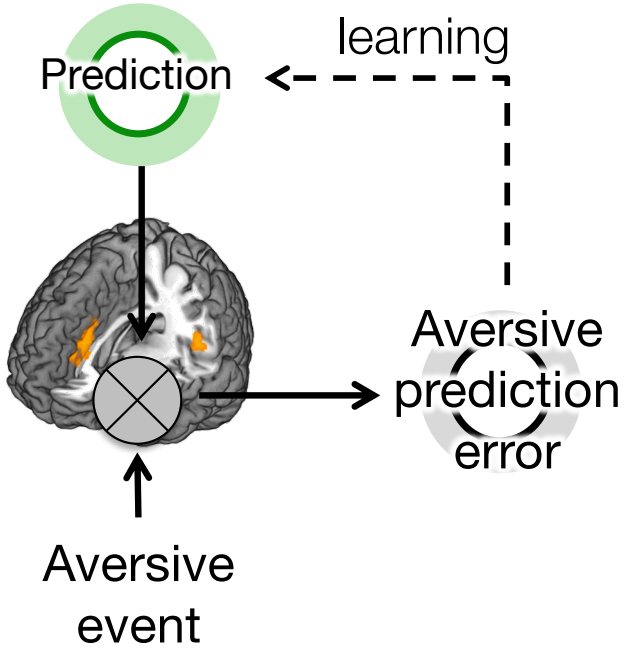


Descending control: Porrecca, Vanderah, Navratilova, others

Wager & Atlas, 2015 Nat Rev Neuro; Fields 2004; Heinricher & Fields 2013; Altier & Stewart 1999; Willis & Westlund 1997; Seth 2015; Feldman Barrett

What to approach, what to avoid?
A circuit for avoidance learning





Roy et al. 2014, Nature Neurosci

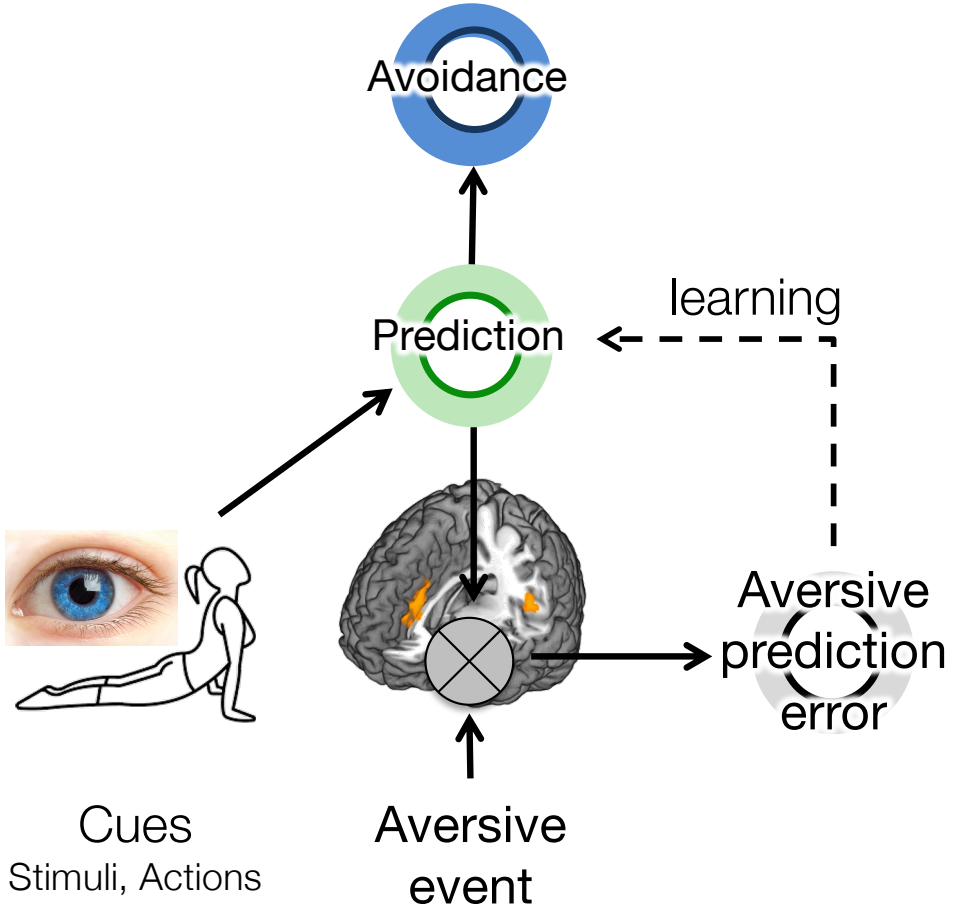
What to approach, what to avoid?
A circuit for avoidance learning

'Fear' learning:
An **adaptive short circuit**…

…but…

increases pain **salience**, **attention**, **expectancy**

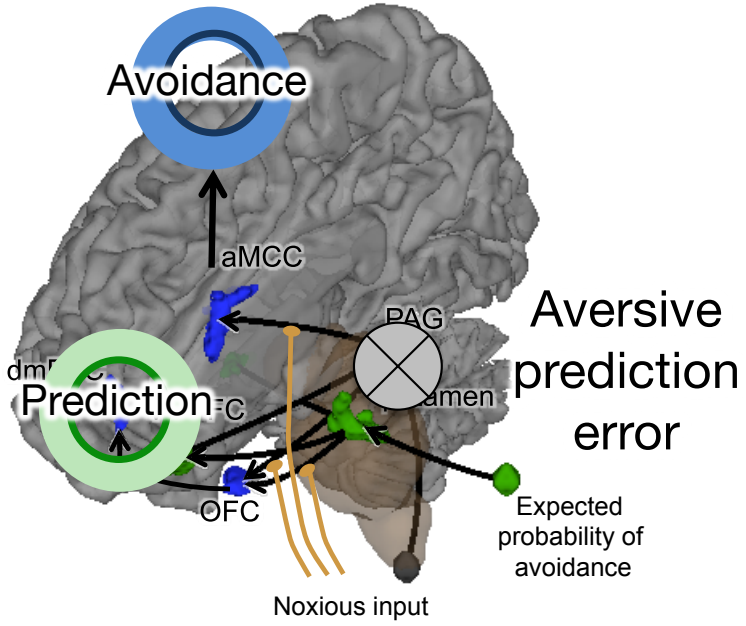
In chronic pain:
Overgeneralized avoidance
Lack of corrective experience



e.g, Meulders, Vlaeyen, Crombez

Roy et al. 2014, Nature Neurosci

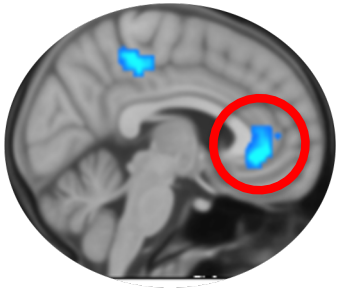
Medial prefrontal cortex and avoidance learning



Roy et al. 2014, Nature Neurosci

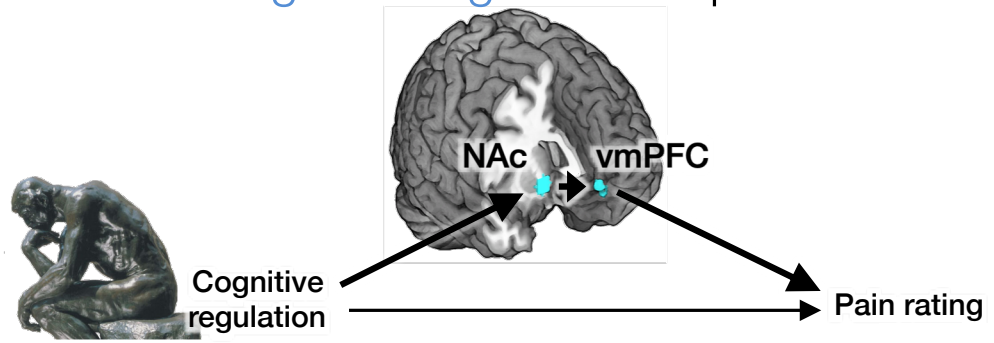
It matters what you think

Alterations in pain-regulatory systems



Medial frontal cortex becomes **pro**-pain

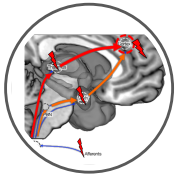
Involved in cognitive regulation of pain and emotion



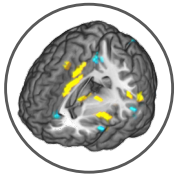
Woo et al. 2015 PLoS Biol

Anticipatory anxiety: Wager 2011; Catastrophizing: Seminowicz /Davis 2010, Lee / Napadow 2018

Roadmap

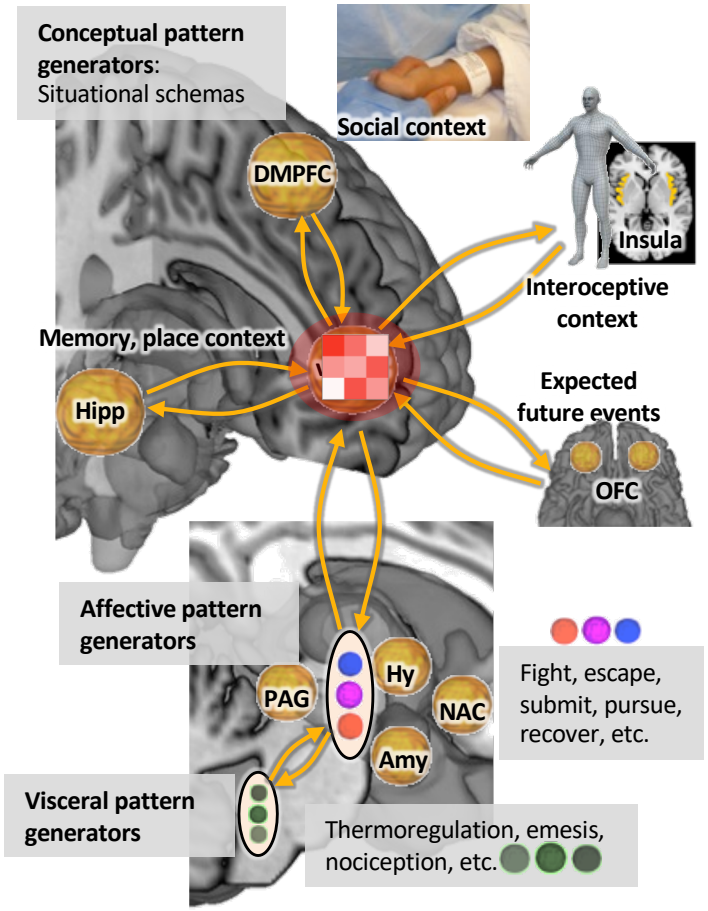


Nociceptive pain and
beyond

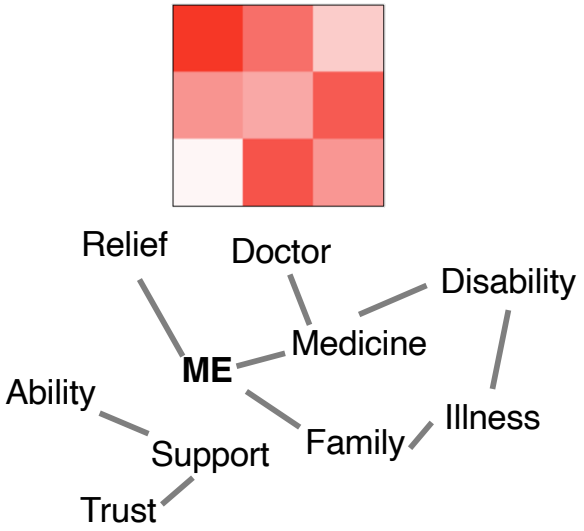


Self in context:
Brain systems for conceptual thought

vmPFC and the ‘meaning response’

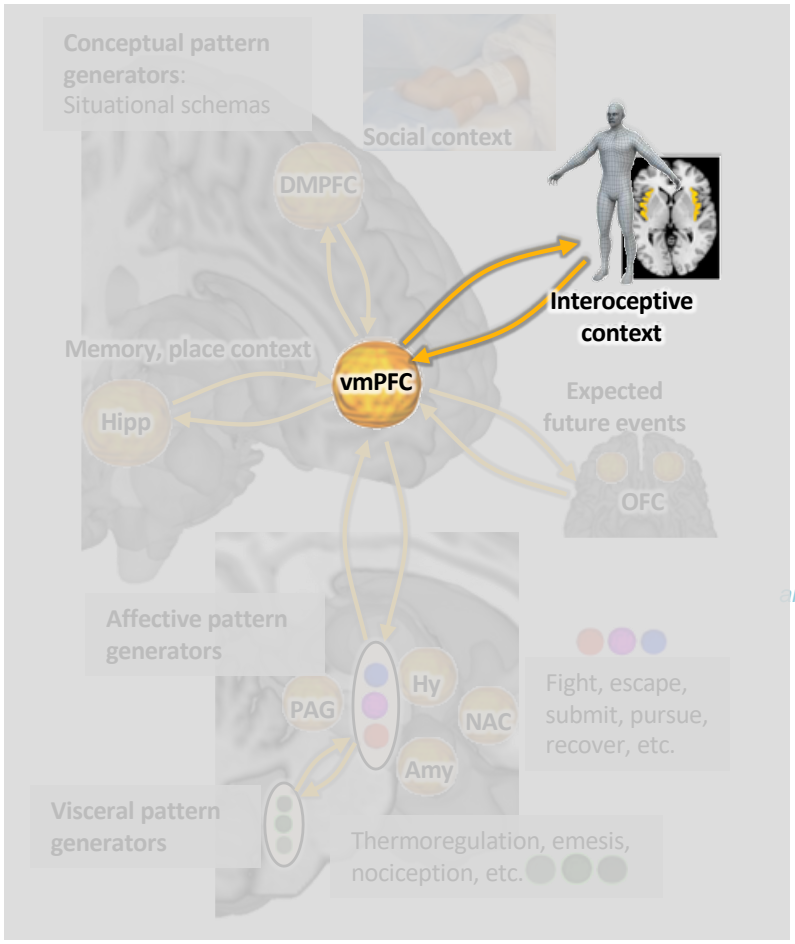


A web of meaning
Influencing pain construction
At multiple levels of body-brain axis



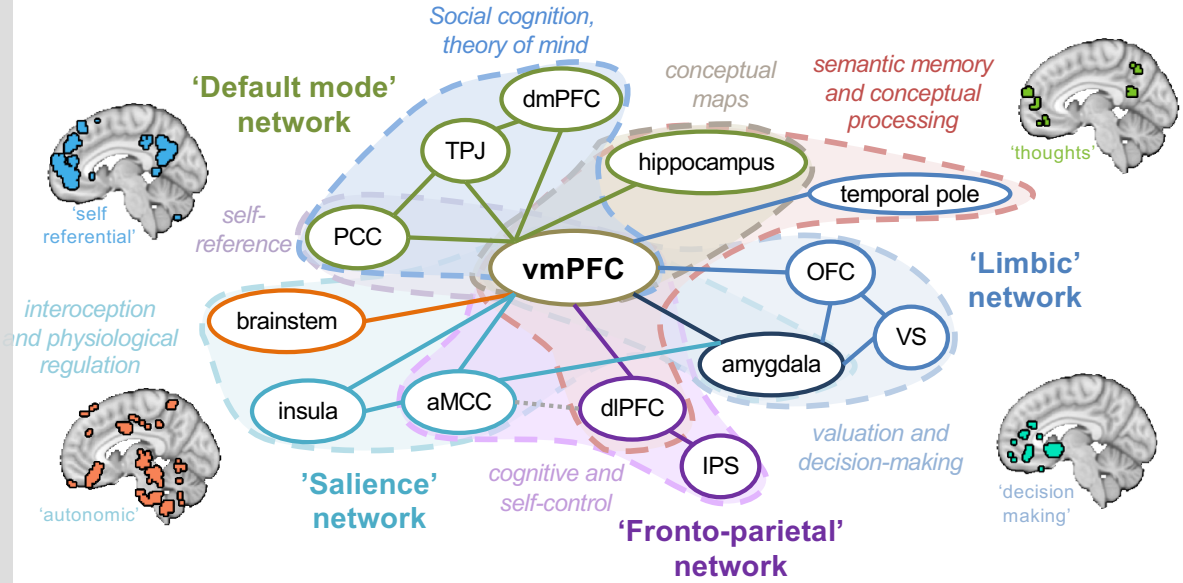
Roy et al. 2012, TICS; Geuter et al. 2017, Ann Rev Neurosci; Koban et al. 2017, 2021 (in press); Craig; Bandler; Saper; Moerman; Feldman Barrett

vmPFC and the ‘meaning response’



Self-in-context:
How we conceptualize ourselves in our current situation

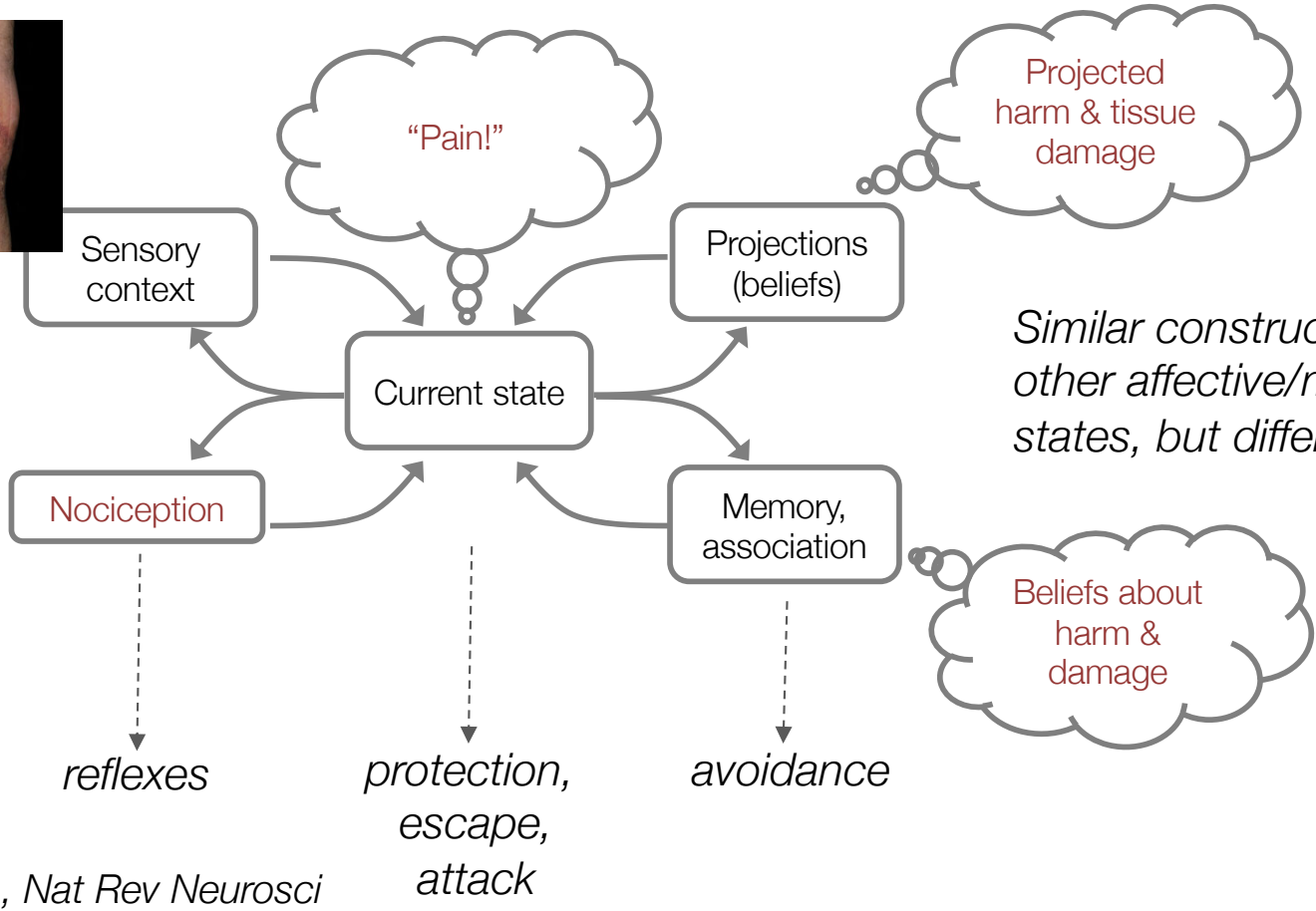
Interactions across multiple networks



Koban et al. 2021 (in press)

Pain as a multimodal construction

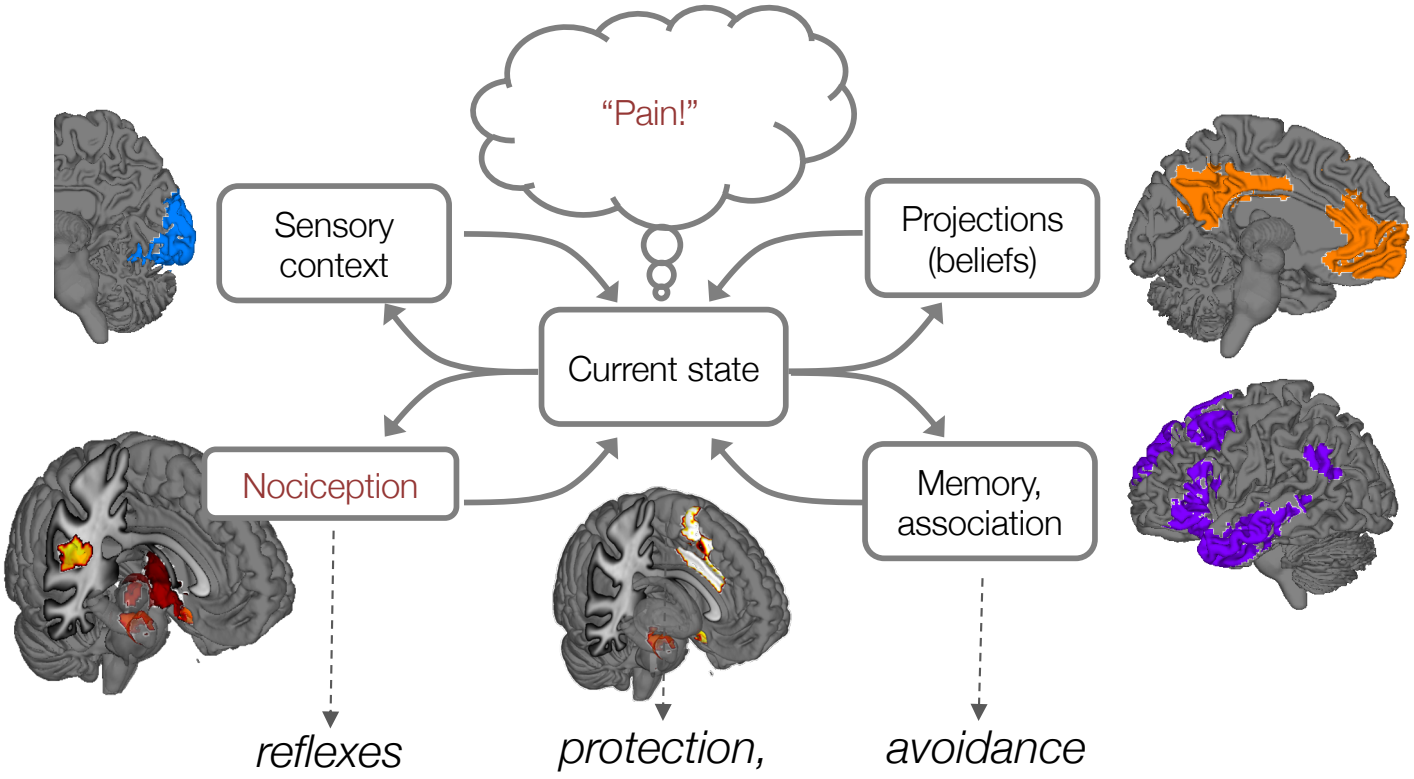




Similar construction process as other affective/motivational states, but different contents

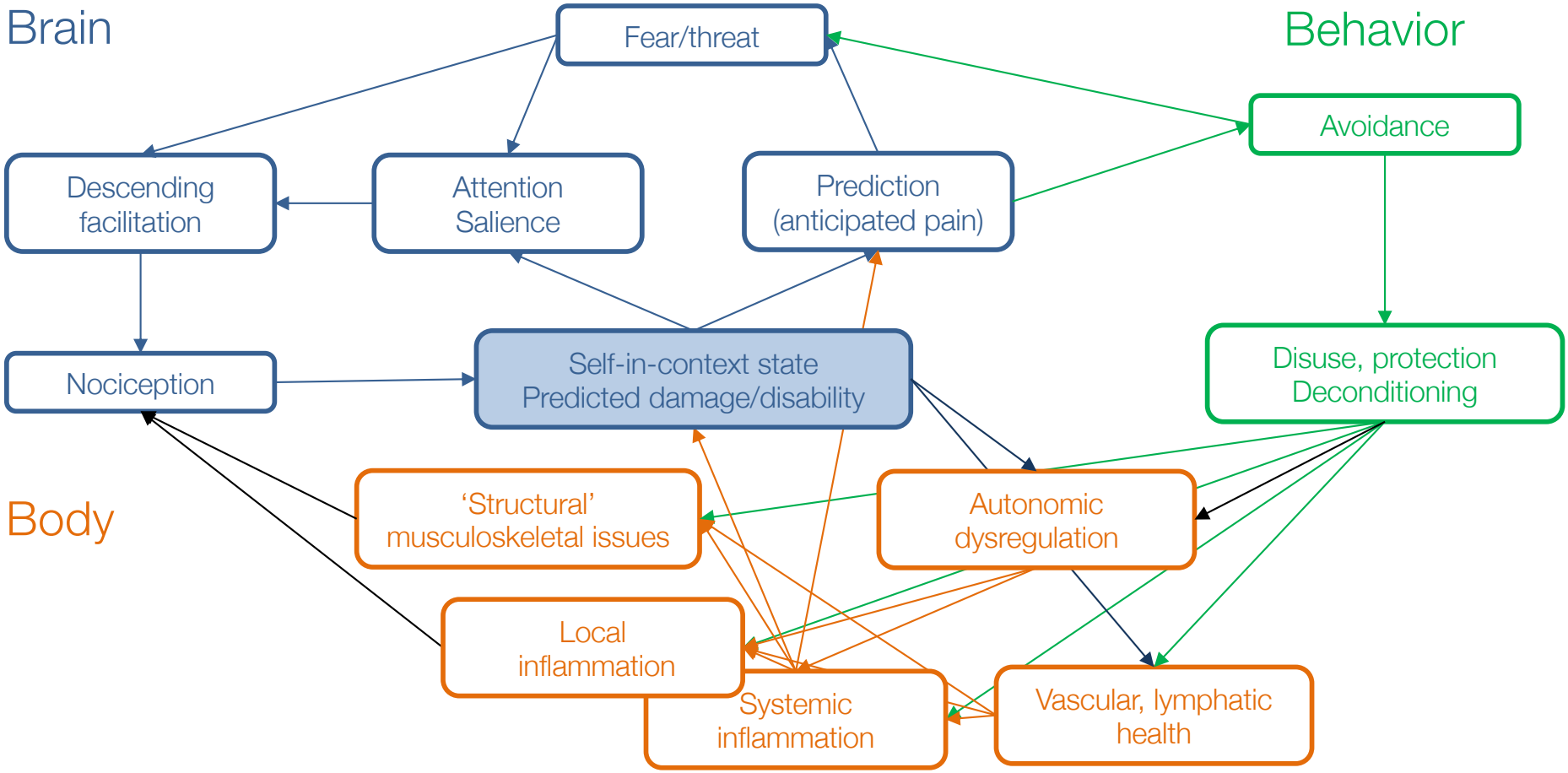
Koban et al. 2021, Nat Rev Neurosci

Pain as a multimodal construction

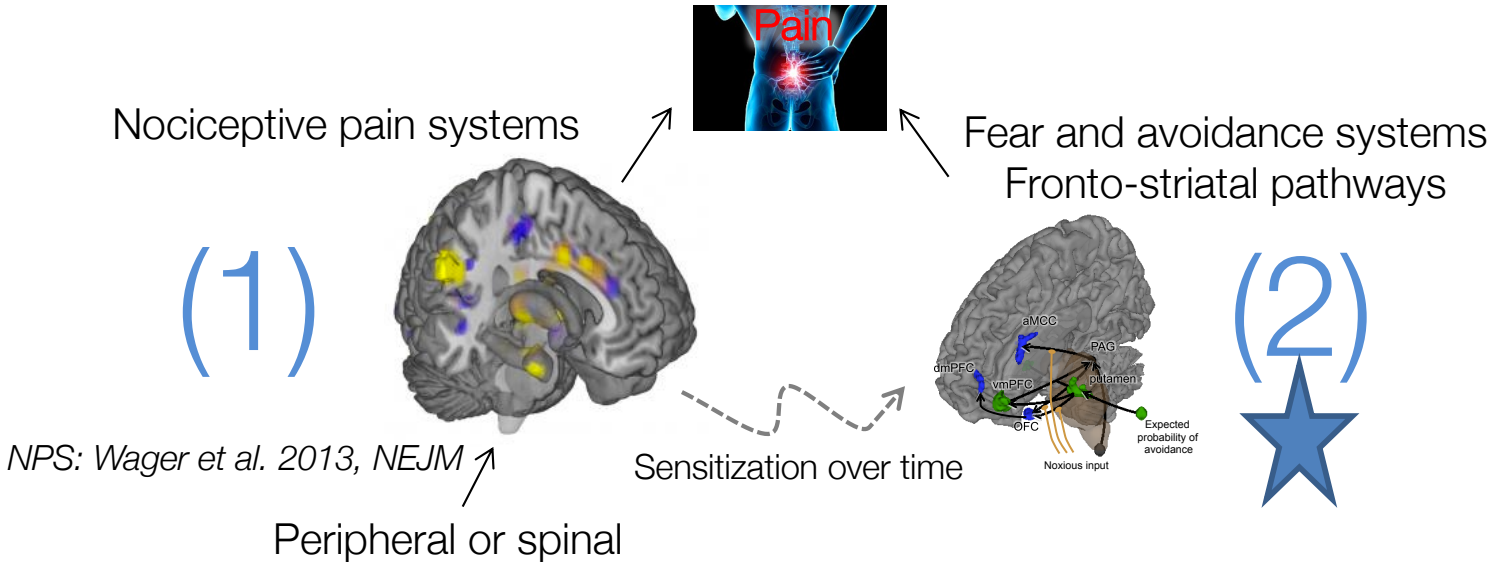


Koban et al. 2021, Nat Rev Neurosci

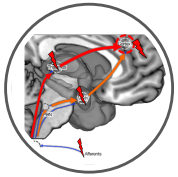
Pain conceptualization and brain-body interactions



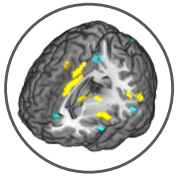
Chronic pain: A shift in meaning



Roadmap



Nociceptive pain and
beyond

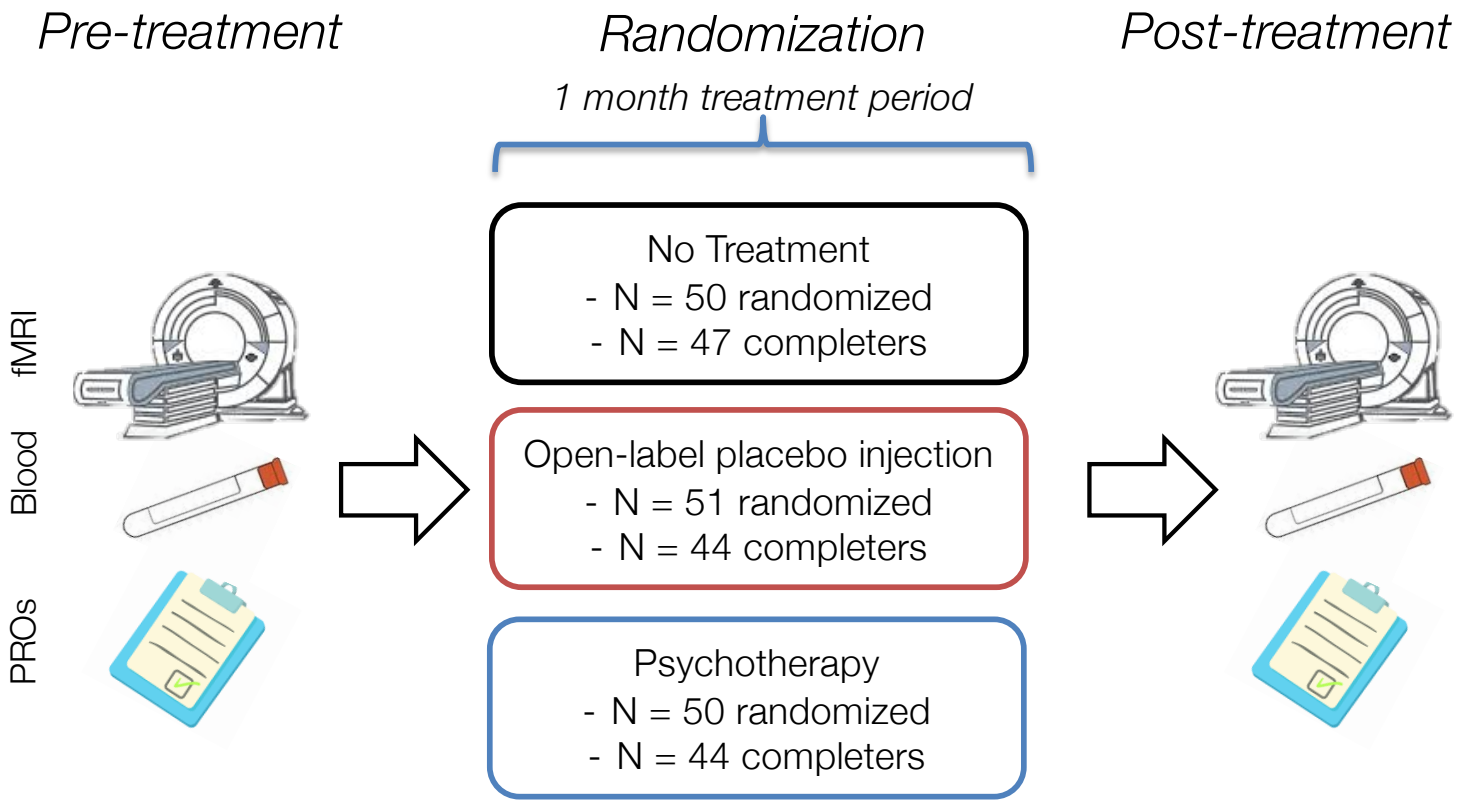


Self in context:
Brain systems for conceptual thought



A psycho-behavioral intervention

CU Boulder Chronic Back Pain Study



Pain Reprocessing Therapy

- **Explanation (narrative):** Pain is a “false alarm;” central sensitization, not tissue damage
- **Expectation**: You can be ‘cured.’ You can ‘teach the brain’ that sensations it is interpreting as dangerous are actually safe.
- **Exposure**: (1) Somatic and emotional awareness without appraisal of harm; (2) movements that challenge/increase pain
- **Engagement**: Increased physical activity, return to activities



Howard Schubiner, M.D.



Alan Gordon, LCSW Director, Pain Psychology Center, L.A.



Christie Uipi



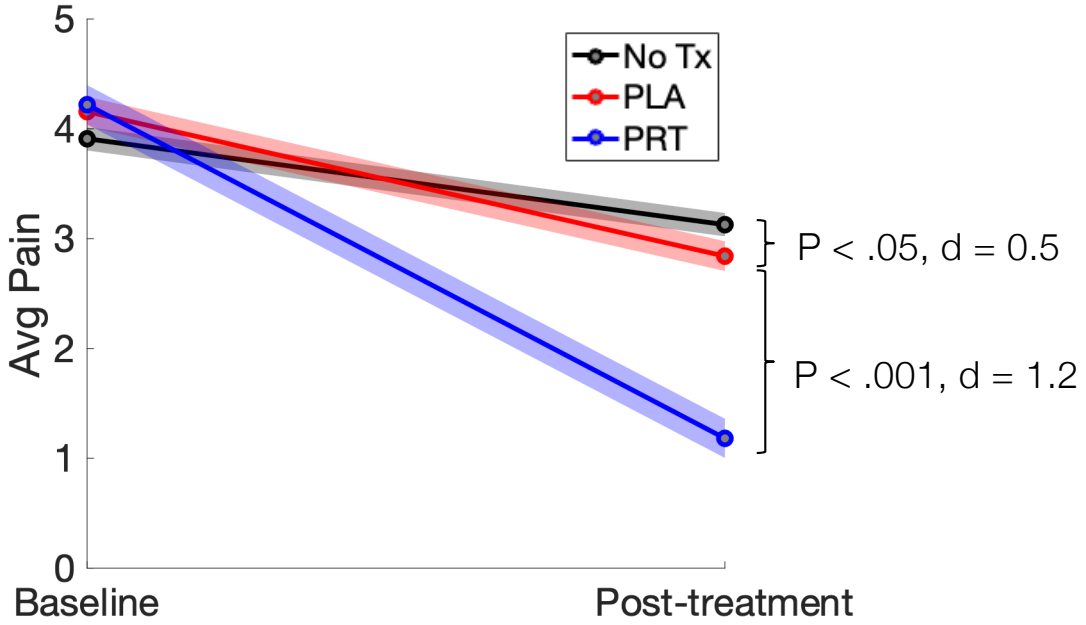
Yoni Ashar, Ph.D.

Lumley and Schubiner, 2018

Average pain over the last week



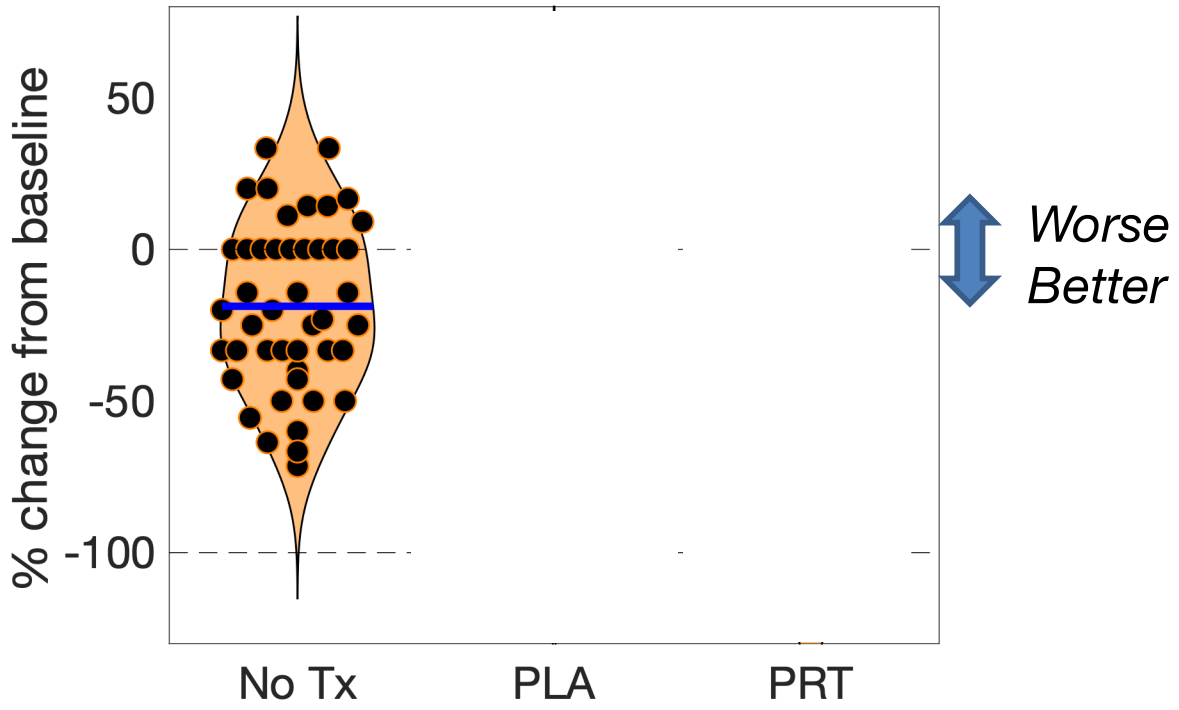
Yoni
Ashar



Ashar et al., under review

Error bars show within-subject standard error

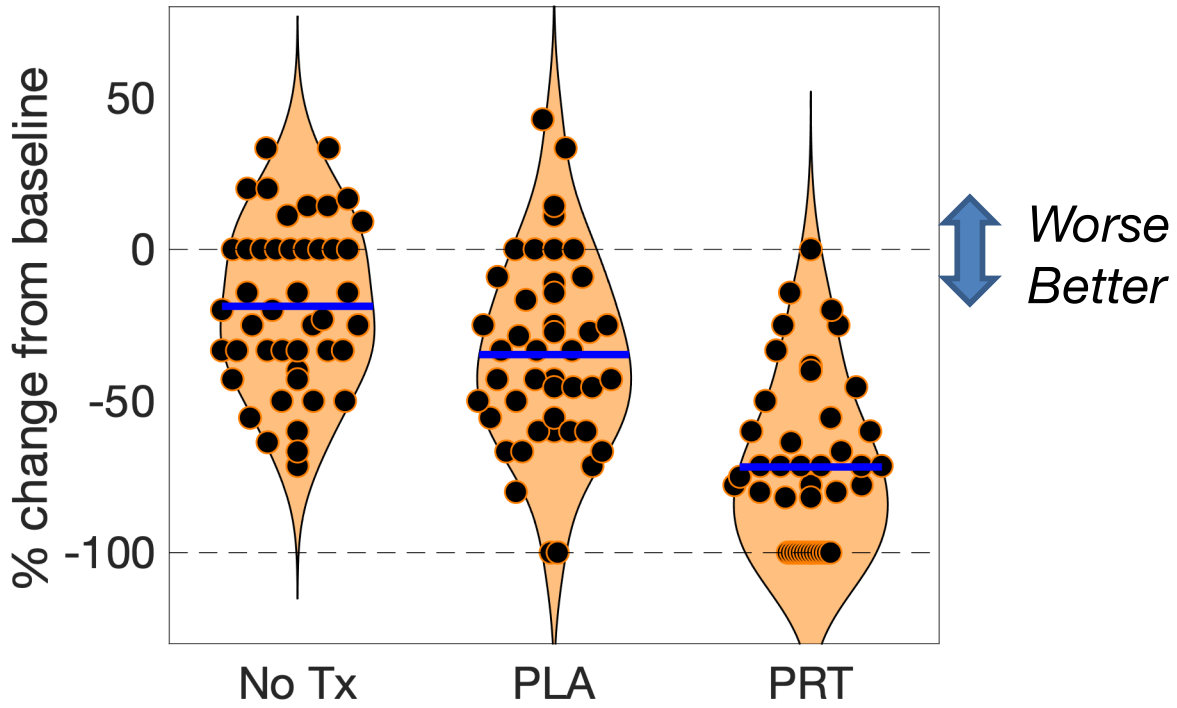
Pain percent change from baseline



	No Tx	PLA	PRT
Avg % improved:	-19%	-35%	-72%

Ashar et al., under review

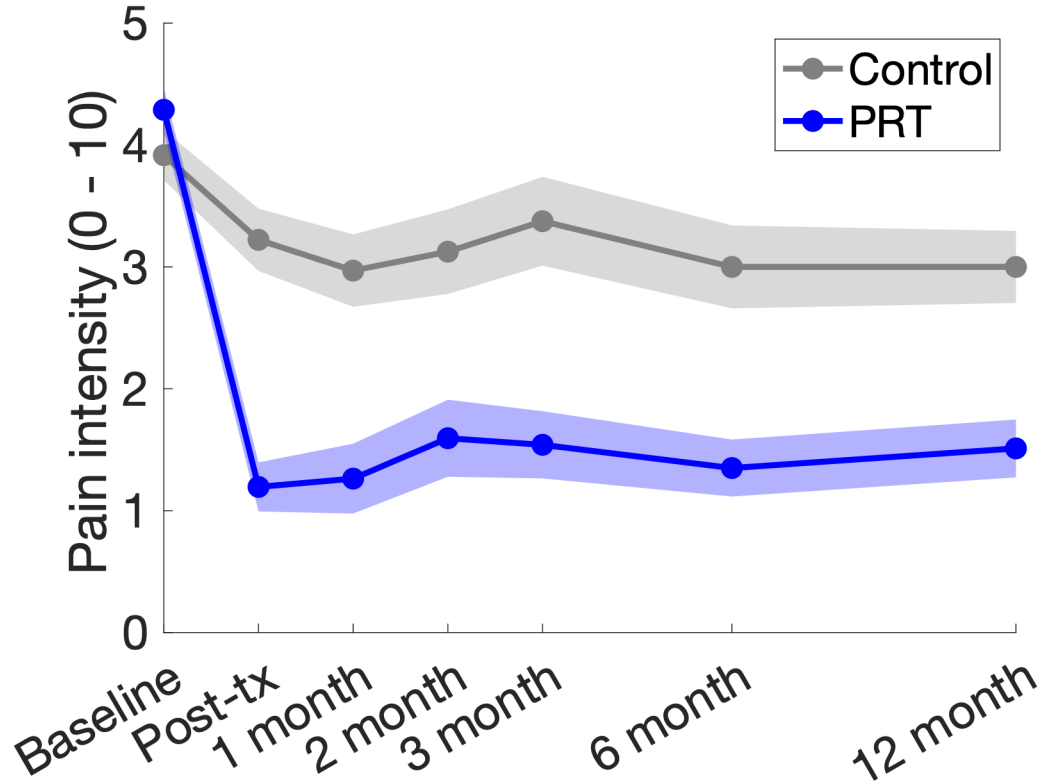
Pain percent change from baseline



"Pain free or nearly pain free": 0 or 1 pain at post-treatment

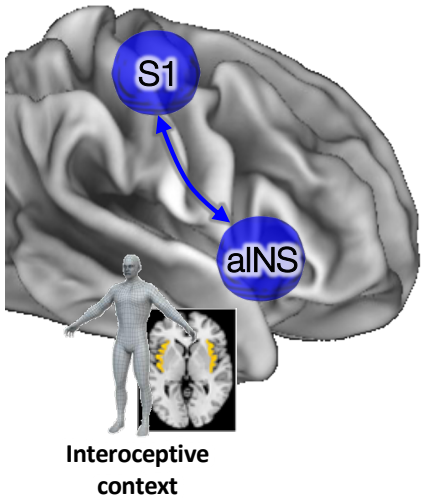
Ashar et al., under review

Benefits persist at 12-month followup

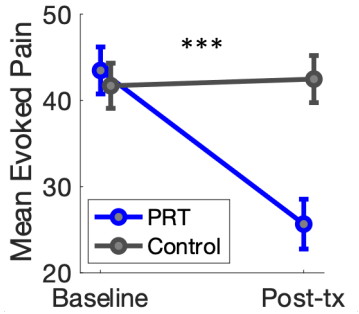


Ashar et al., under review

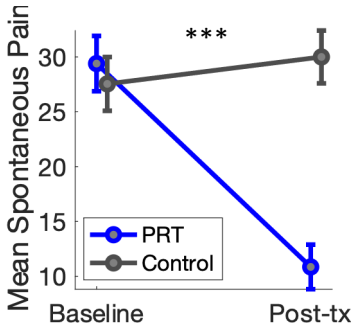
Effects of PRT on brain construction of pain

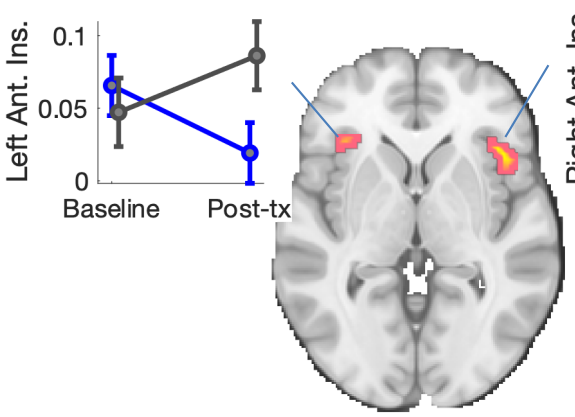


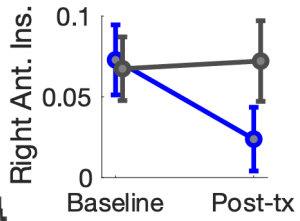
Evoked Pain



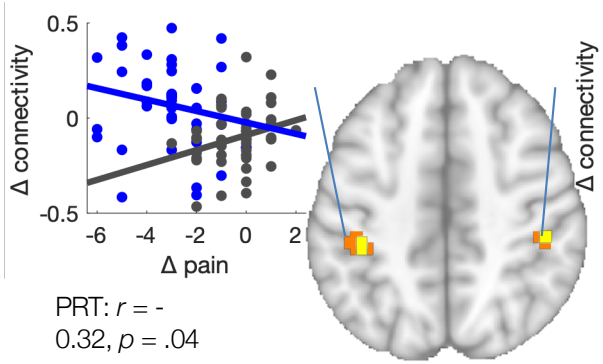
Spontaneous Pain





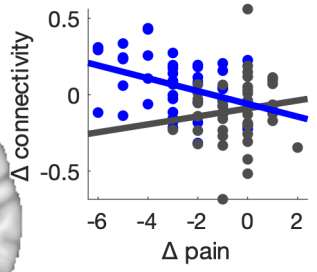


z = 0



PRT: r = -0.32, p = .04

z = 46



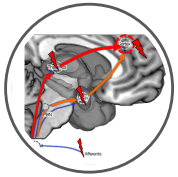
PRT: r = -0.38, p = .02

Changes with biobehavioral treatment

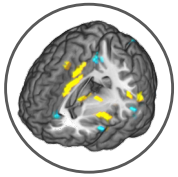


- Reverse pain-promoting narrative
- Sustained reinterpretation of sensation and pain over time
- Normalize somatic sensations; can experience without fear
- Renewed activities

Summary



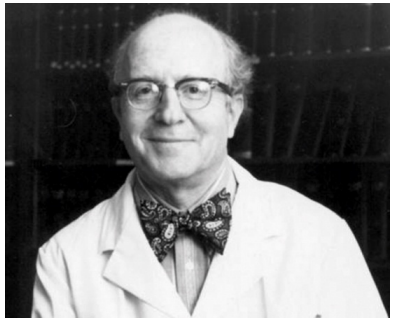
Nociceptive pain and
beyond



Self in context:
Brain systems for conceptual thought



A psycho-behavioral intervention



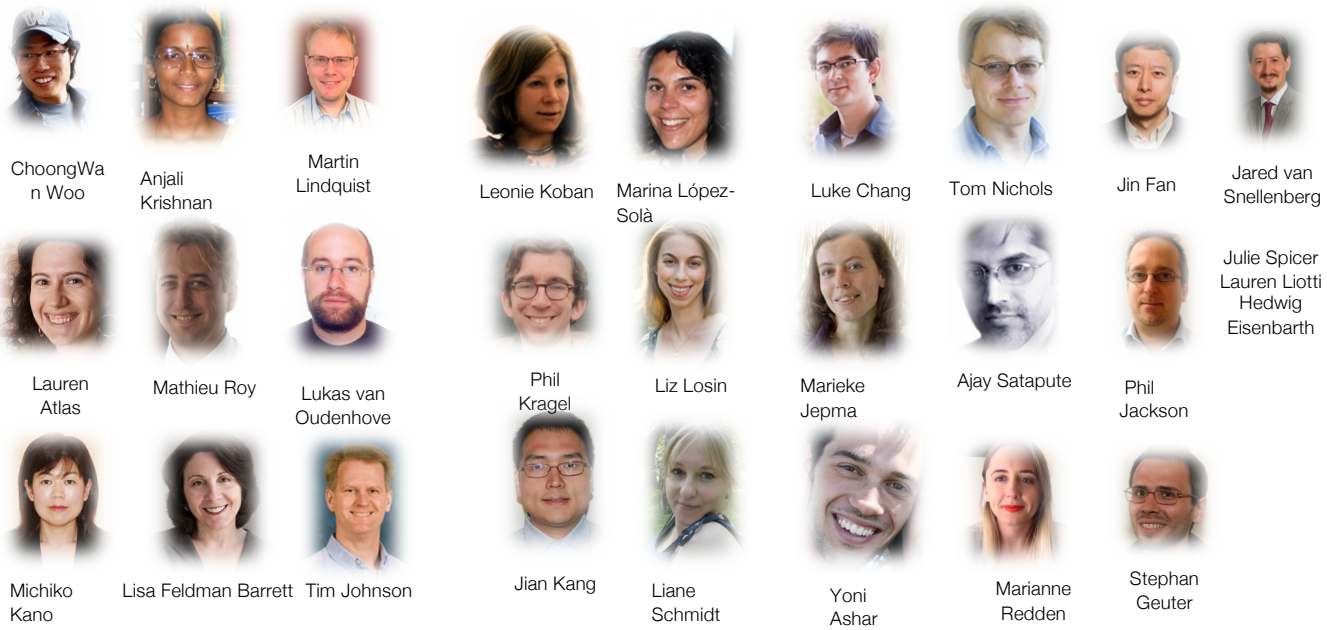
"In spite of this importance of pain, it is astonishing how little we understand pain, but how confident we are of our knowledge of pain."

George Engel

Cognitive and Affective Neuroscience Lab Members



Collaborators and Former Lab Members



Chronic back pain team



NIH National Institutes of Health

PPDA Psychophysiologic Disorders Association

RSNA Radiological Society of North America

Foundation for the Science of the Therapeutic Encounter



Funding Sources

National Institutes of Health

NIH National Institute of Mental Health

NIDA National Institute on Drug Abuse

NSF

U.S. Army

NIH National Cancer Institute

John Templeton Foundation
Supporting Science · Investing in the Big Questions

Brain & Behavior Research Foundation
Awarding NARSAD Grants

FNSNF Swiss National Science Foundation

DFG Deutsche Forschungsgemeinschaft

Catalan government
Mind, Brain, Body and Health Network

Code: shared on https://github.com/canlab . *Papers, etc.* : wagerlab.colorado.edu