Cognitive aspects of acute and chronic pain: 10 advances in 10 years

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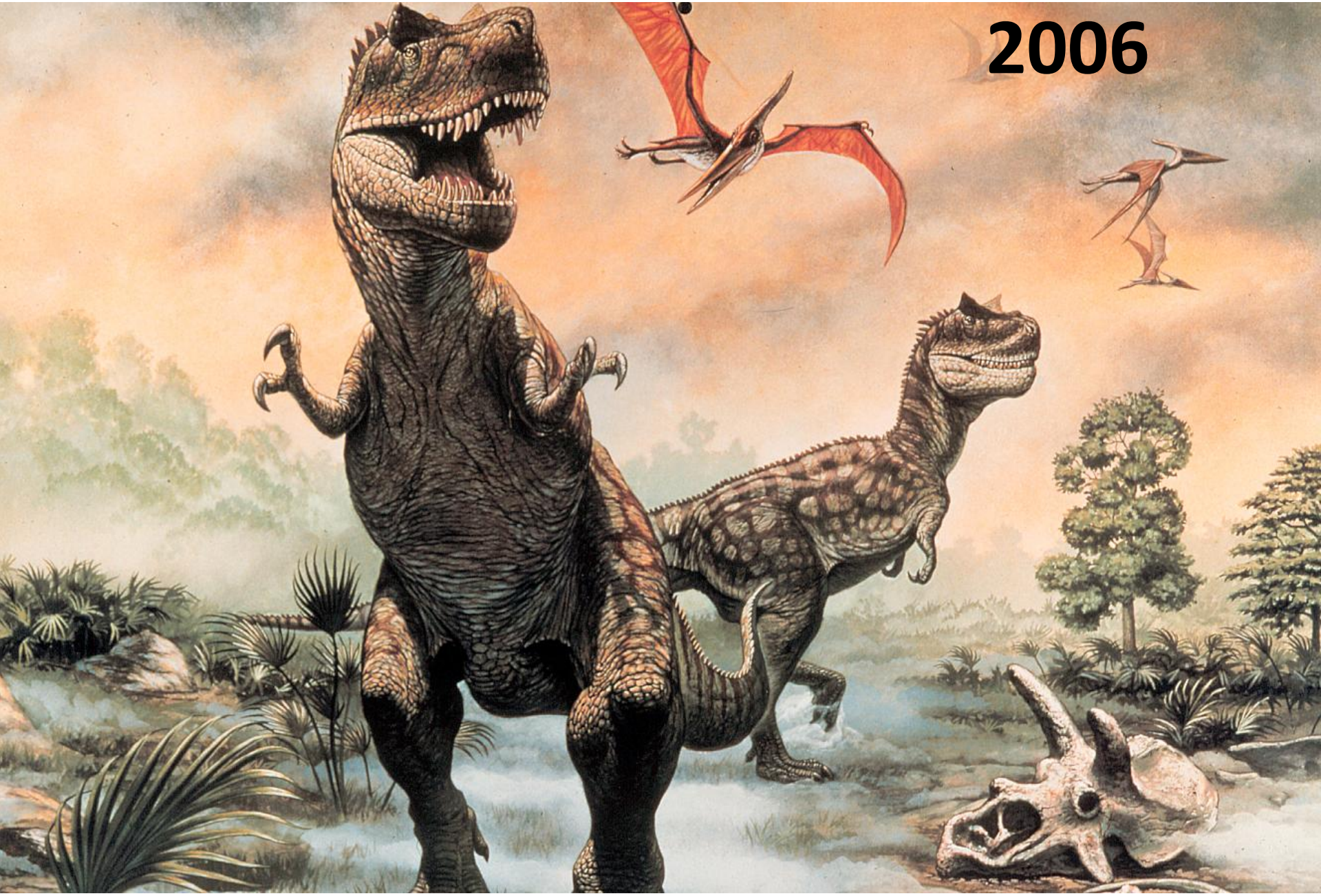
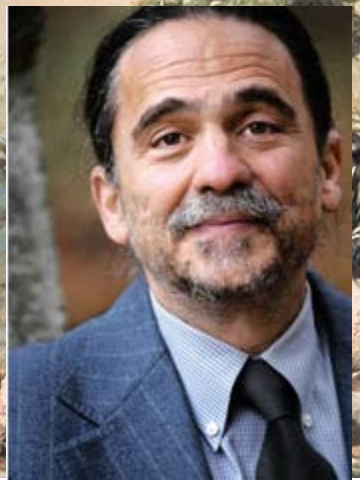
CENTER TO ADVANCE CHRONIC PAIN RESEARCH

NIH Pain Consortium Symposium, Bethesda MD, May 26, 2015

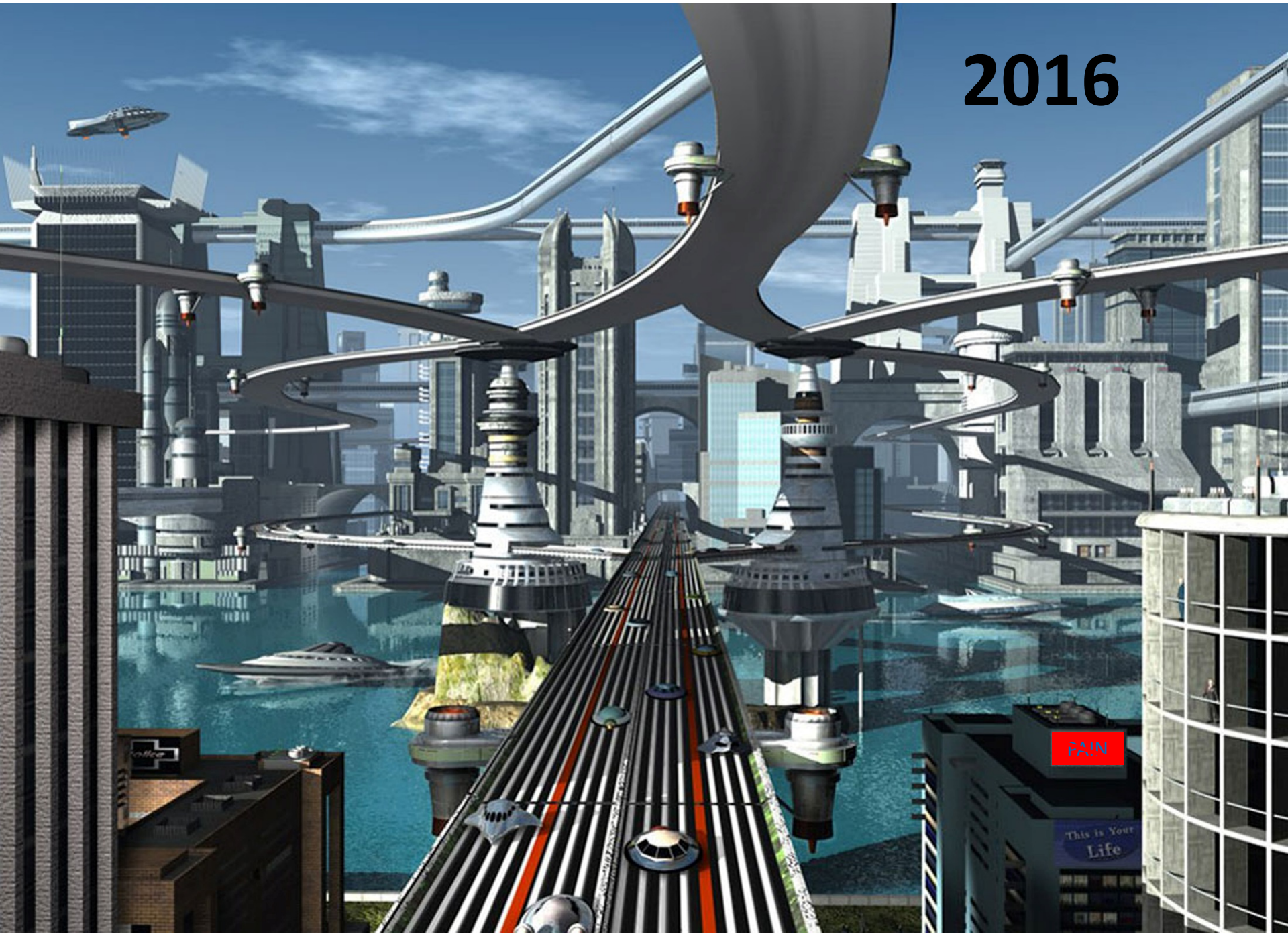
A retrospective …


2006

2006



And a look ahead …


2016
PAIN
This is Your Life

Back in 2006…

IV. COGNITIVE AND EMOTIONAL ASPECTS OF PAIN Moderator: Ray Dionne

Cognitive Factors That Enhance Pain Processing

Jennifer Haythornthwaite

Roger Fillingim

The Placebo Effect: New Insights

Ted Kaptchuk

Individual Differences in Pain and Analgesia: Genes, Gender, and Ethnicity

Catastrophizing:
Cognitive/affective response to pain

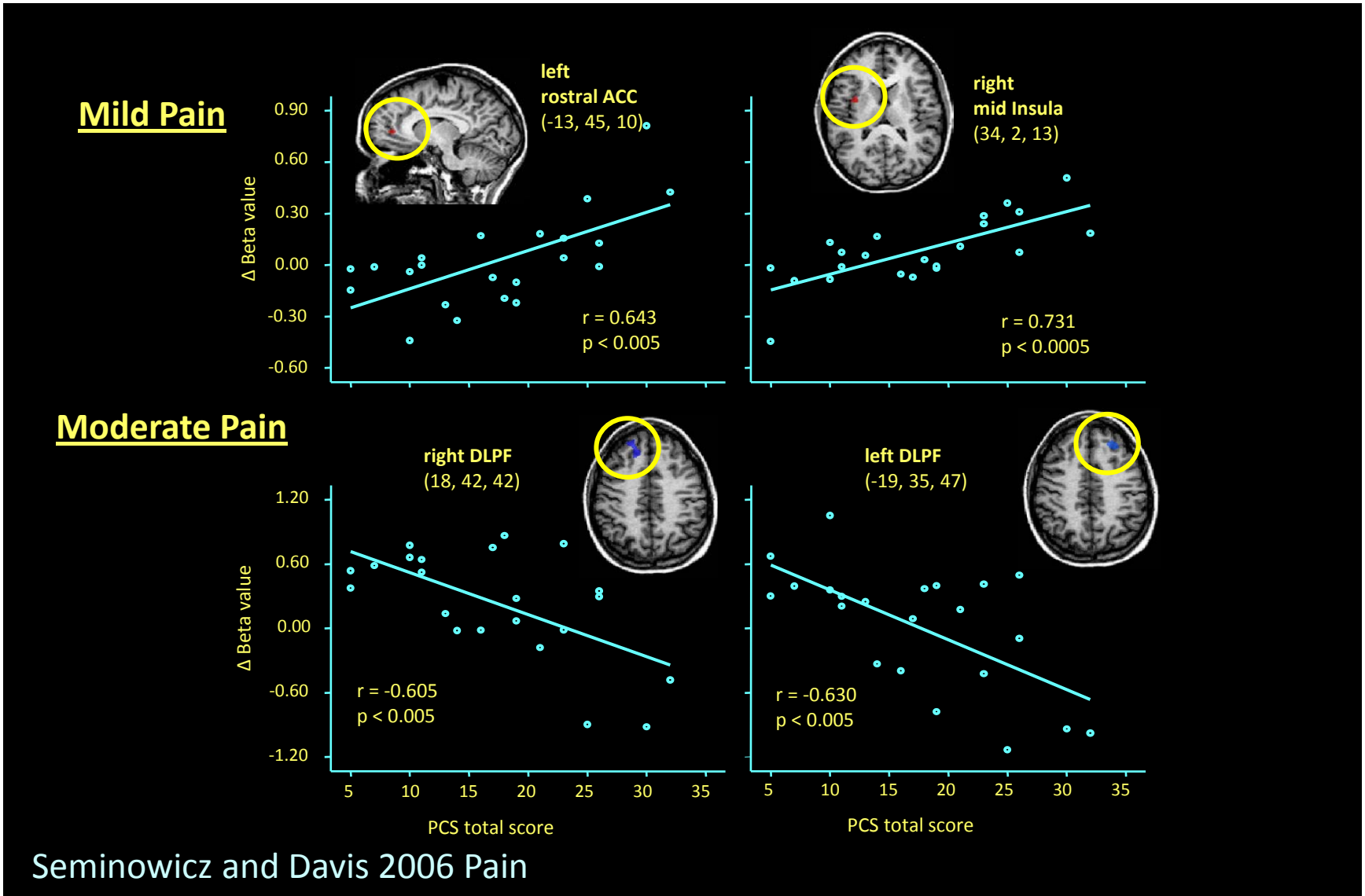
- Negative Emotions
  - Anxiety, Depression, Rumination
  - "I worry about whether it will end"
- Attention to pain
  - Magnification, Exaggeration, Hypervigilance
  - "I can't seem to keep it out of my mind"
- Beliefs about pain
  - Threat, Helplessness, Pessimism
  - "I become afraid that the pain will get worse"

Slide courtesy of Jennifer Haythornthwaite, presented at 2006 NIH Pain Consortium meeting

2006: What are the neural correlates of pain catastrophizing in healthy subjects?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

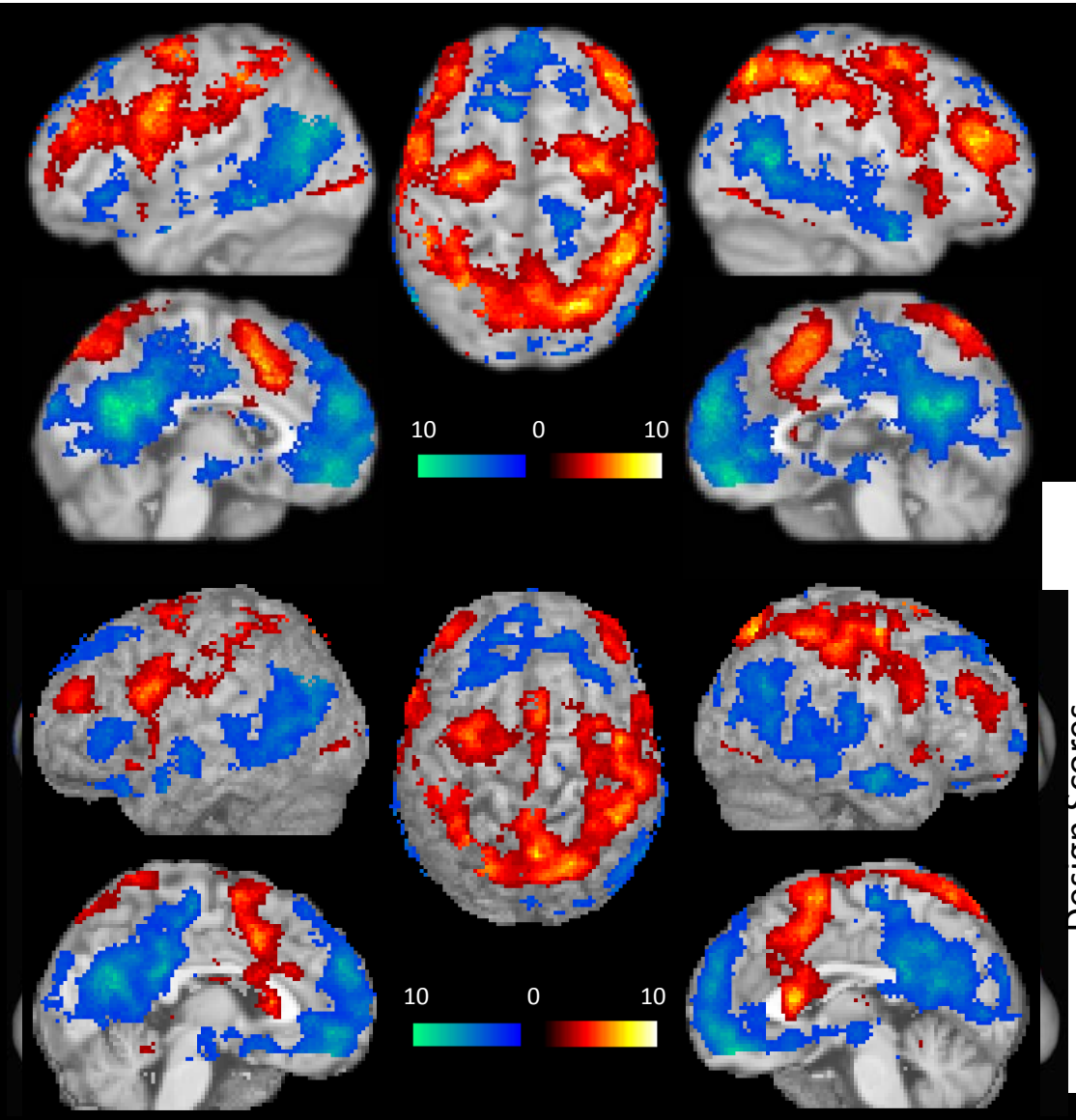
Individual differences: pain catastrophizing

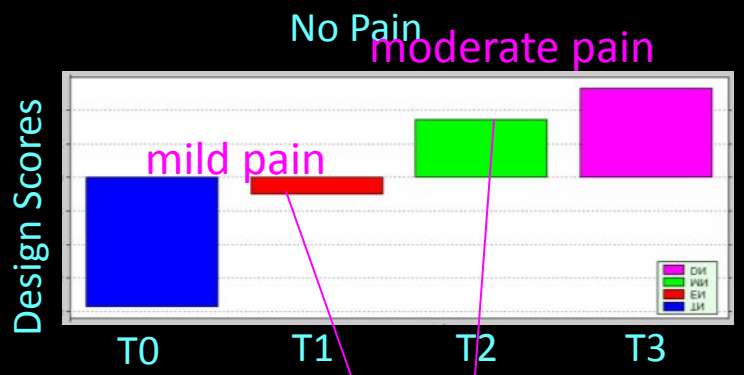


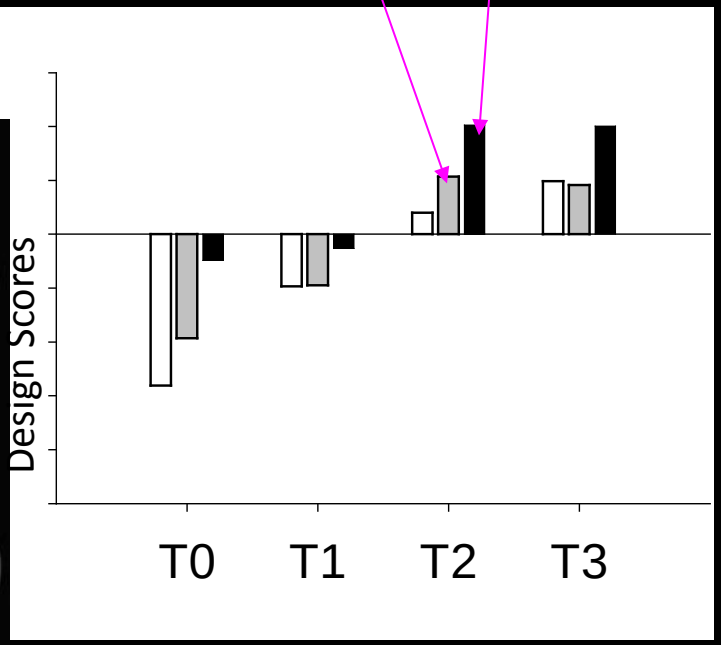
Seminowicz and Davis 2006 Pain

2007: Is pain a cognitive load?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015





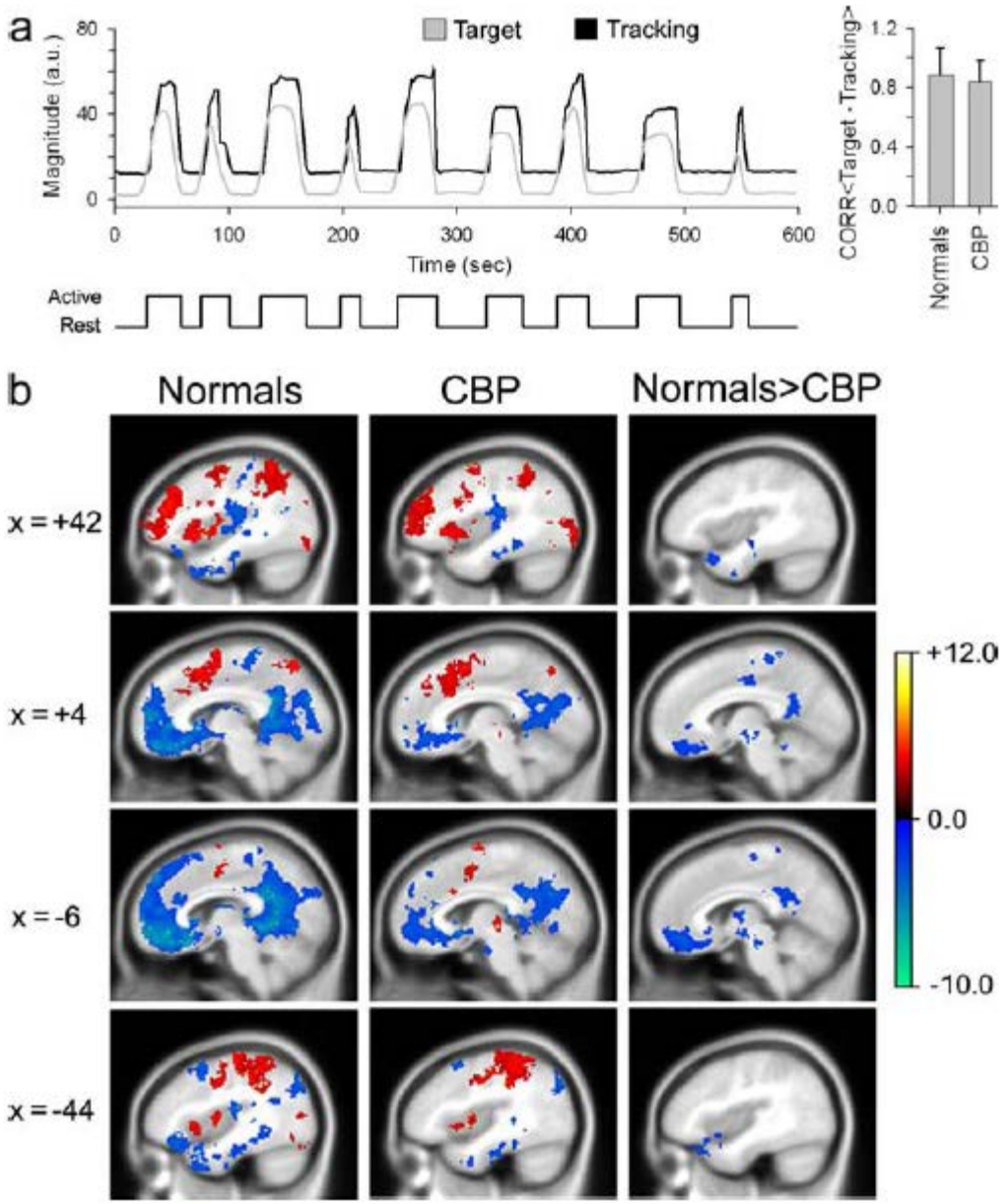


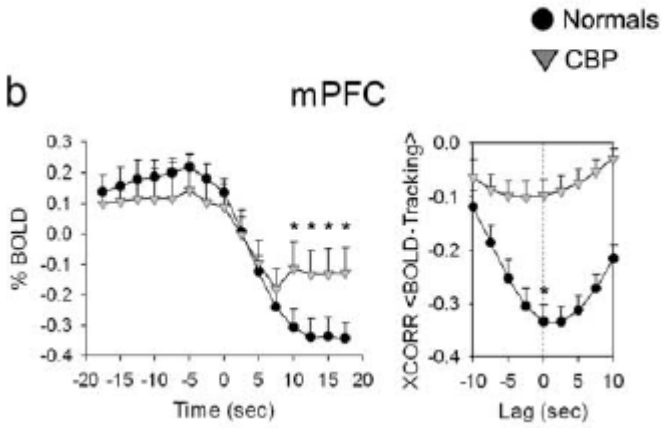
Seminowicz and Davis 2007 J Neurophysiol

2008: are cognitive networks disrupted in chronic pain?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Beyond Feeling: Chronic Pain Hurts the Brain, Disrupting the Default-Mode Network Dynamics



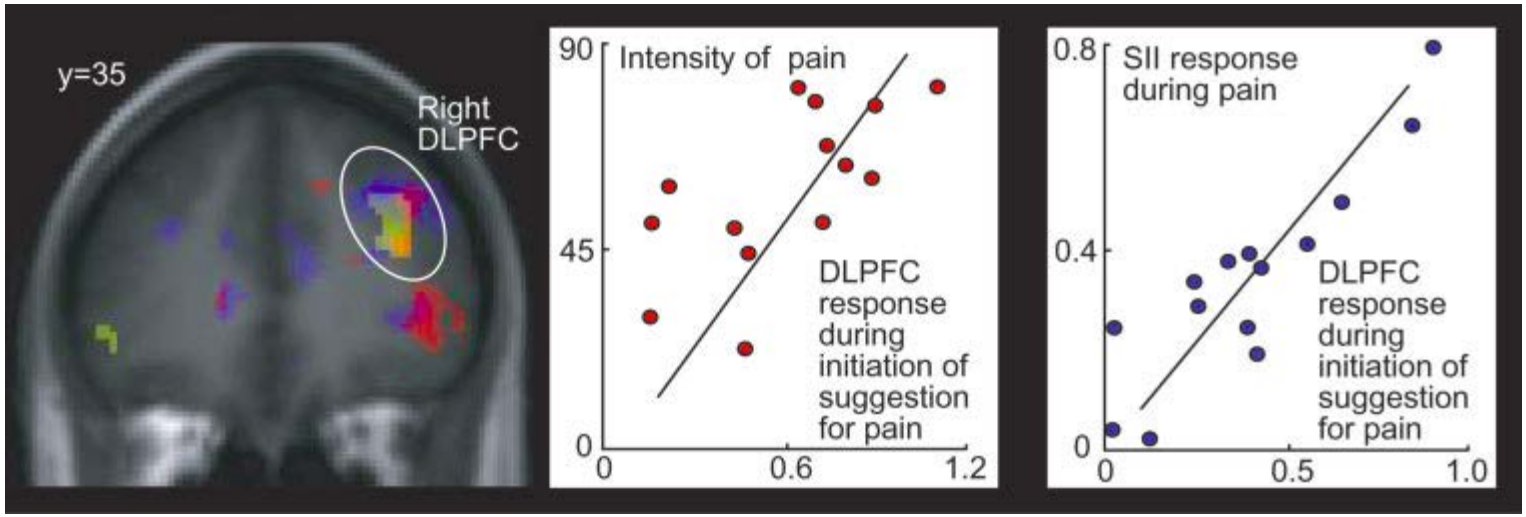


Baliki et al., 2008 JNeurosci

2009: what drives attention-related pain modulation?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Strength of prefrontal activation predicts intensity of suggestion-induced pain

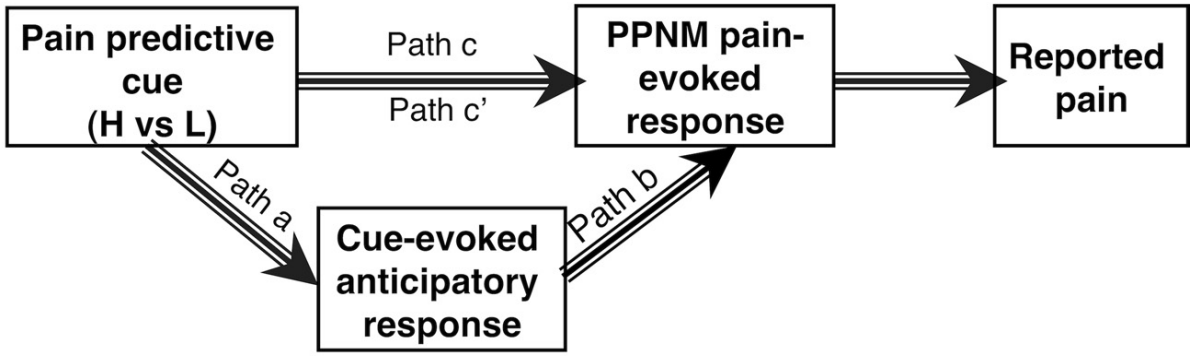


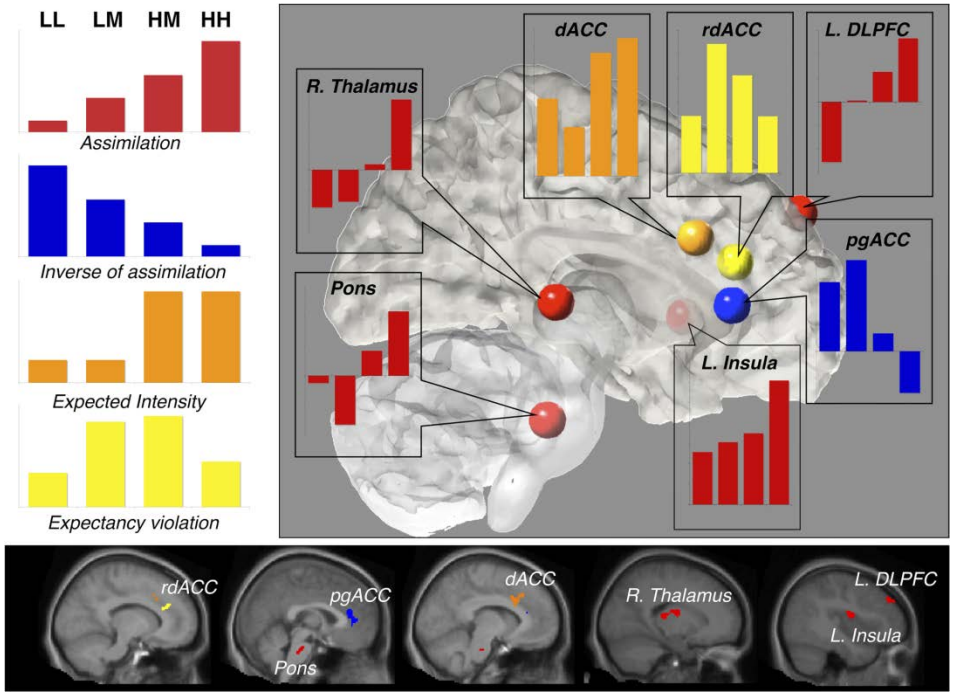
Raij et al. 2009 Hum Brain Mapp

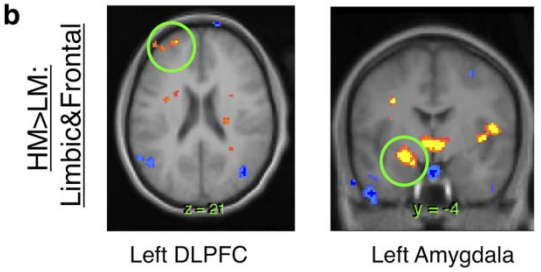
2010: what brain regions mediate the pain experience?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Brain mediators of predictive cue effects on perceived pain







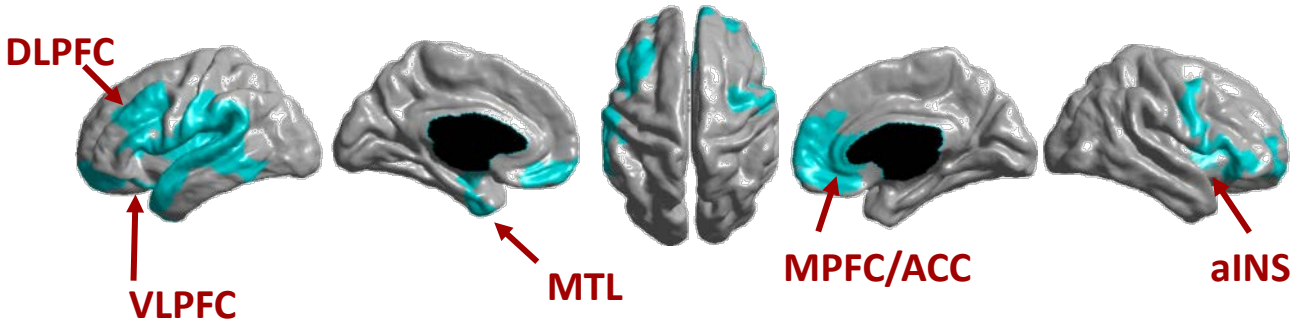
Atlas et al. 2010 J Neurosci

2011: can treatment reverse abnormal cognitive-related activity in chronic pain?

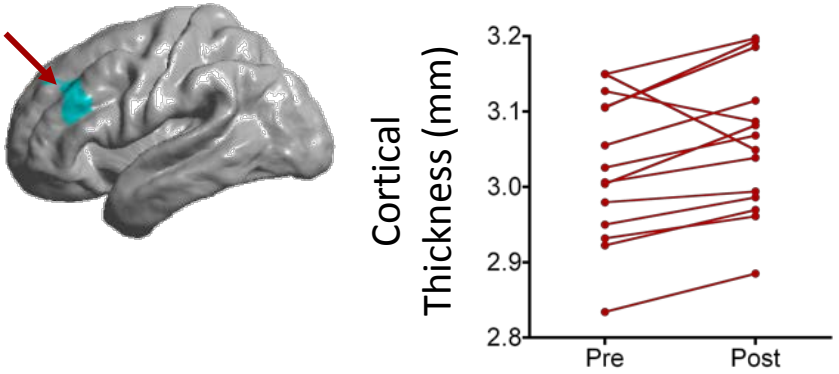
2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Treatment reverses left DLPFC GMV loss

Patients
vs.
controls

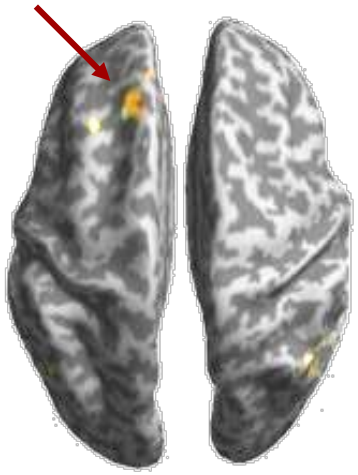


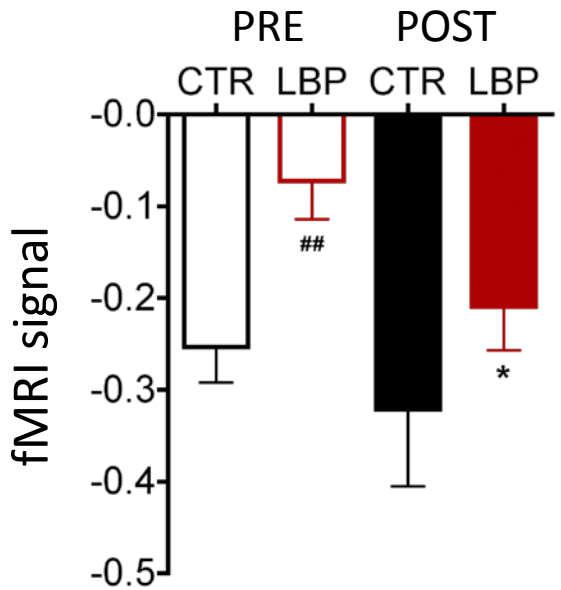
Patients
pre-Tx vs. post-Tx

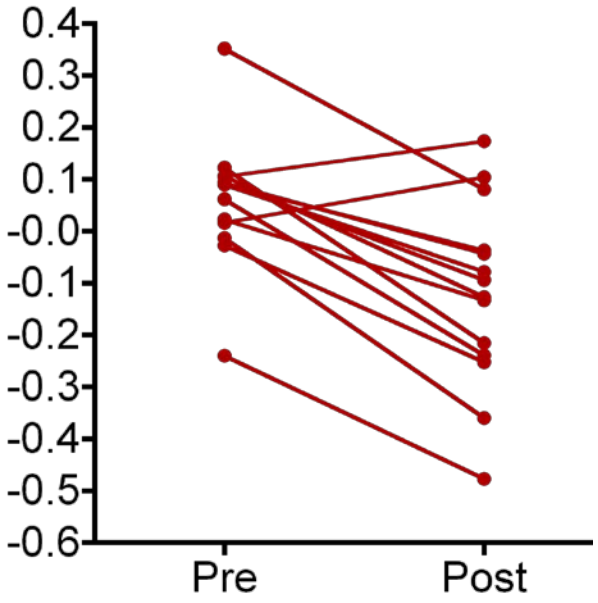


Seminowicz et al. 2011 J Neurosci

Left DLPFC has abnormal activity in CLBP, normalizes with treatment





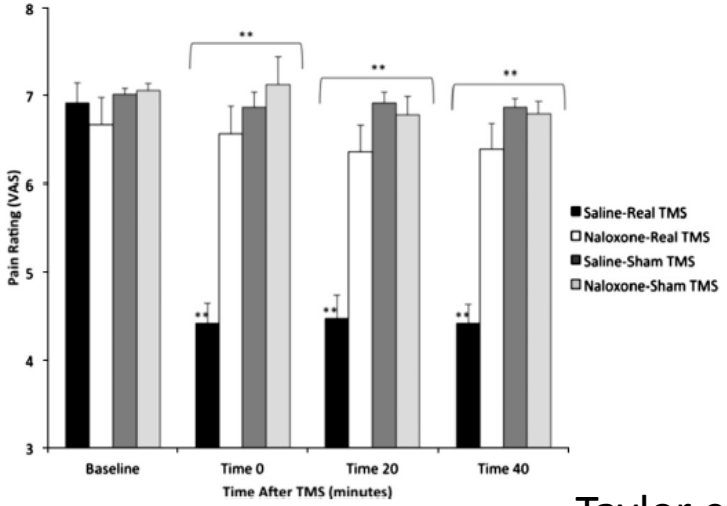


Seminowicz et al. 2011 J Neurosci

2012: can we modulate activity in the left DLPFC and affect pain?

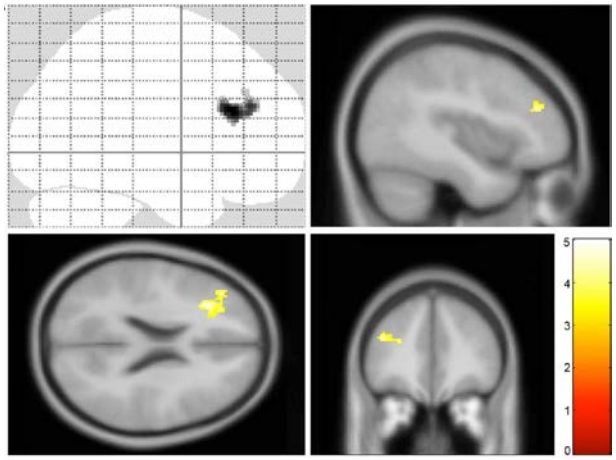
2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Endogenous opioids mediate left DLPFC rTMS-induced analgesia



Taylor et al., 2012 Pain

Mindfulness meditation engages left DLPFC

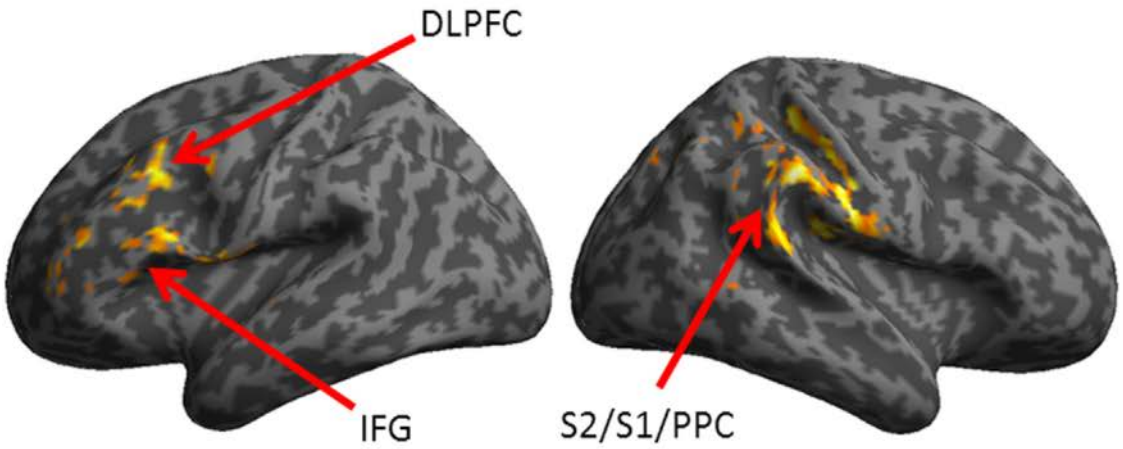


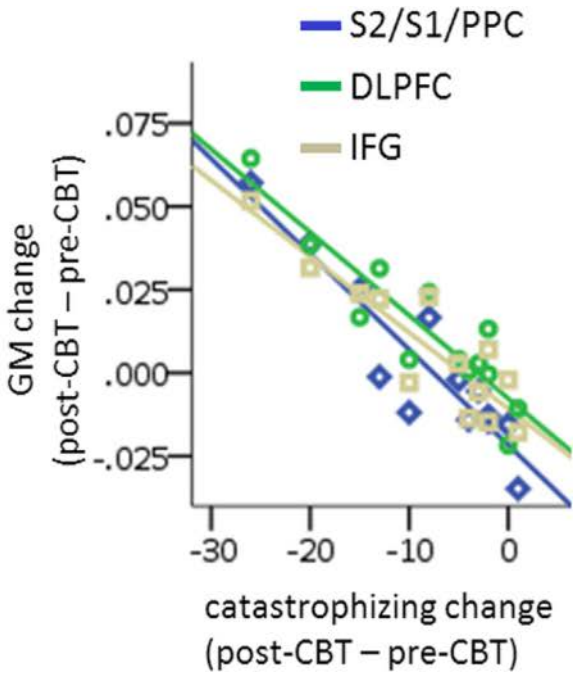
Allen et al. 2012 J Neurosci

2013: are there catastrophizing-related treatment effects?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

CBT for chronic pain: reduced catastrophizing, increased gray matter



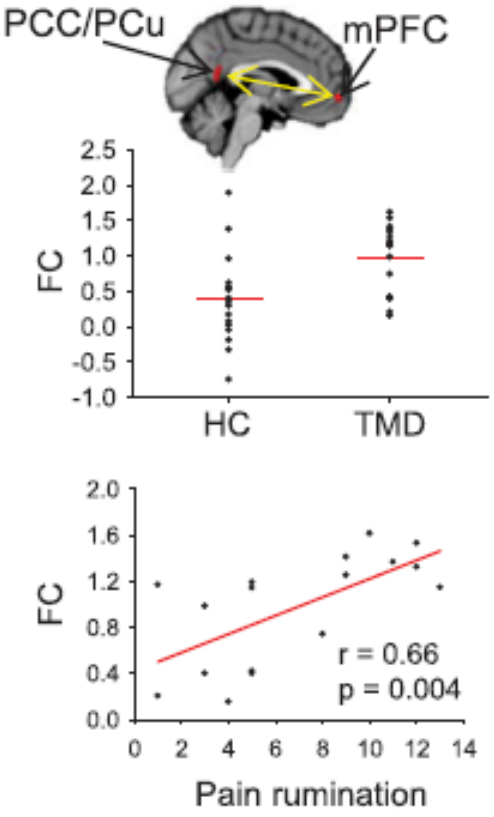


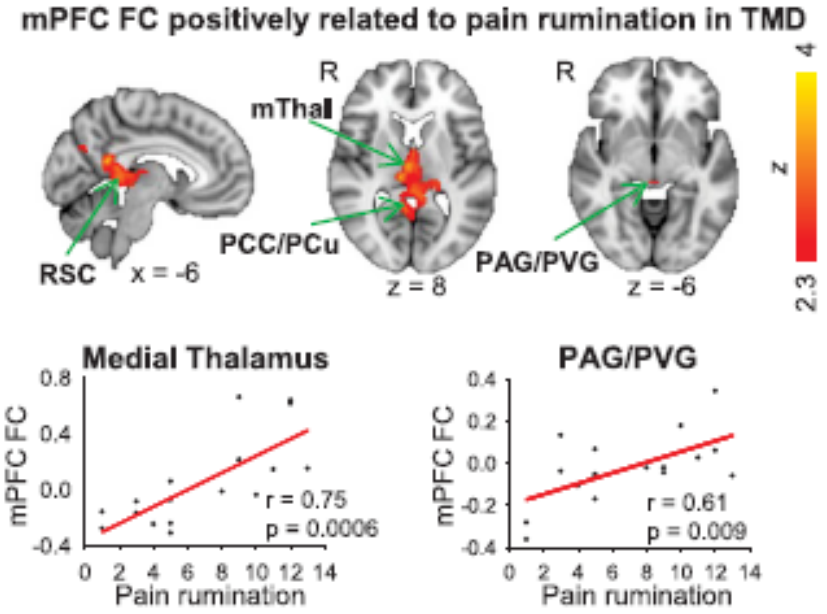
Seminowicz et al., 2013 J Pain

2014: does catastrophizing (rumination) disrupt cognitive networks in chronic pain patients?

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Enhanced default mode connectivity in chronic pain is associated with pain rumination



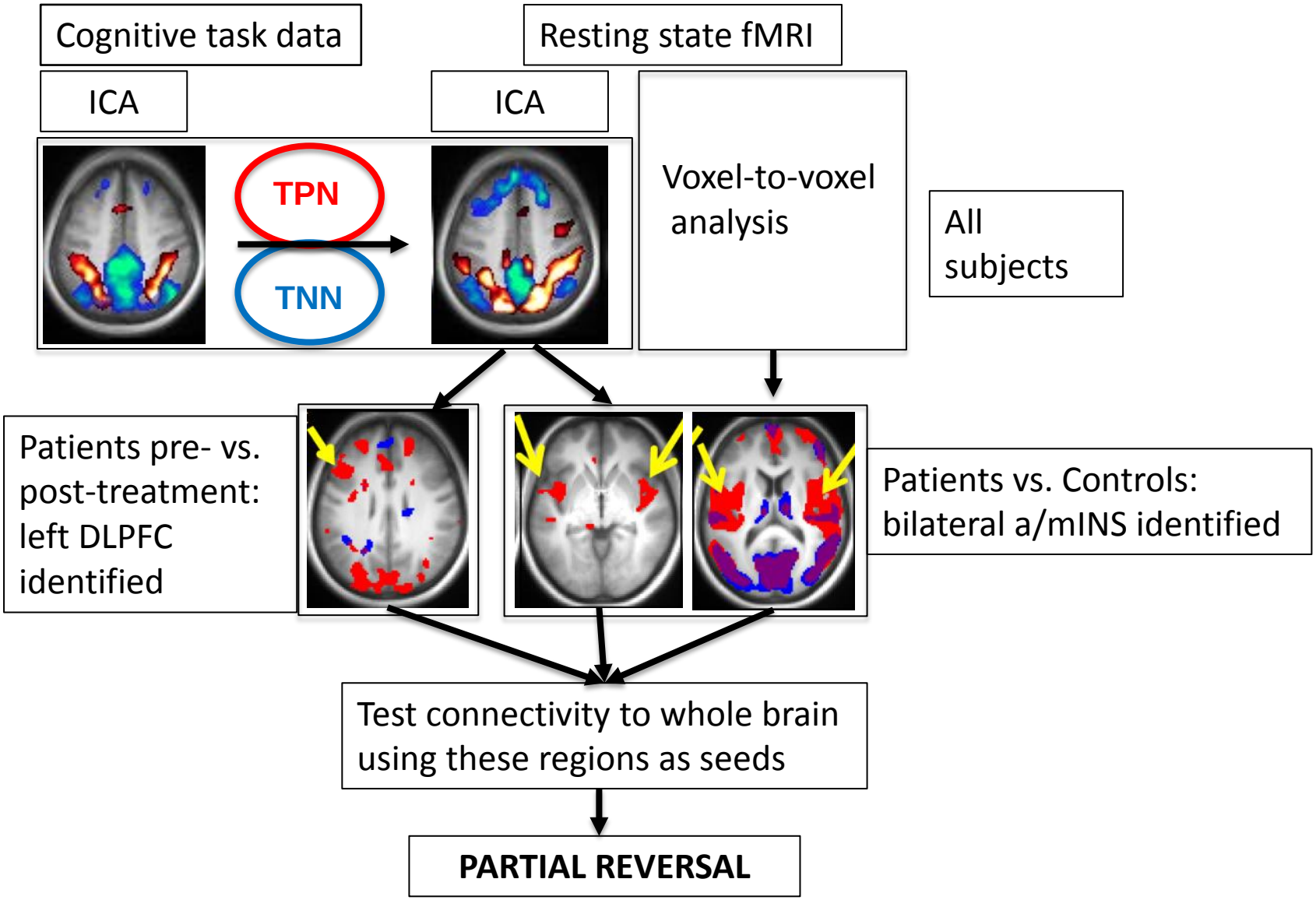


Kucyi et al. 2014 J Neurosci

2015: can we restore cognitive network function with treatment?

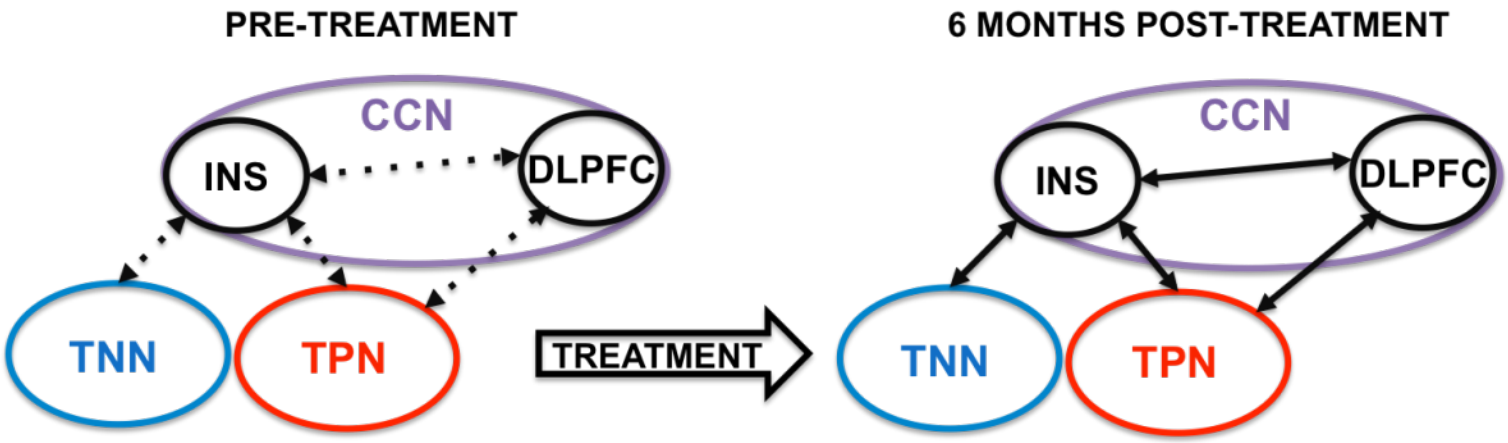
2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

Cognitive networks in chronic low back pain



Čeko et al, 2015 Hum Brain Mapp

Hypothesized cognitive network dysfunction in CLBP



Čeko et al, 2015 Hum Brain Mapp

Summary 2006-2015

- Catastrophizing affects pain-related activity
- Pain has a cognitive load that affects cognitive network function
- Left DLPFC might be a particularly good target

The future?
Three newish trends

1. Shift to limbic circuits (Baliki et al 2012, Hashmi et al 2013)
2. Maladaptive stress (Borsook et al 2012)
3. Refinement of treatment targets

2006 2007 2008 2009 2010 2011 2012 2013 2014 2015

1: Development of chronic pain

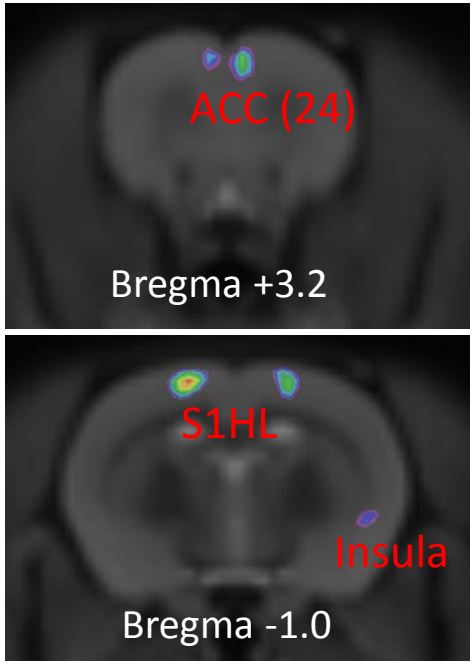
2: Treatment

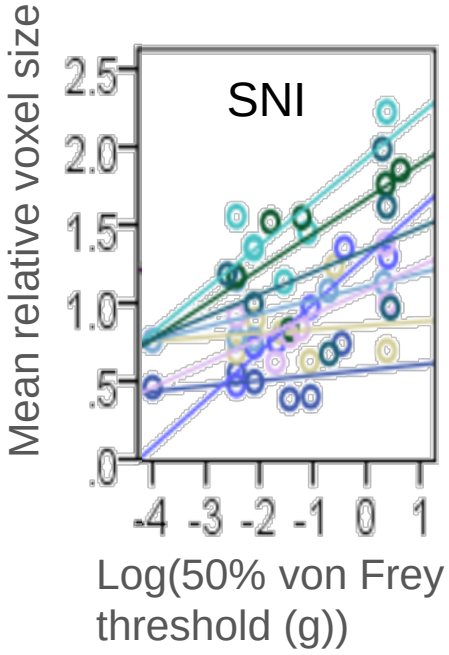
3. Disease-related vs ongoing pain

1. Shift to limbic circuits

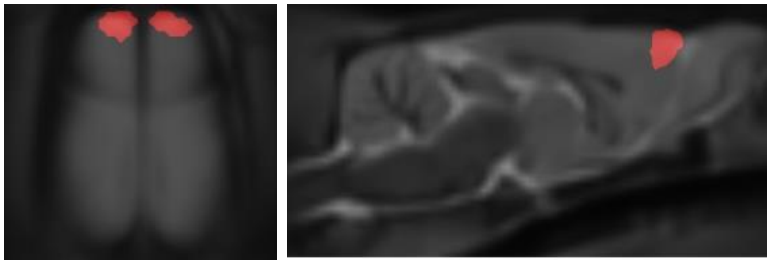
Gray matter changes in sensory- and affective-related brain regions

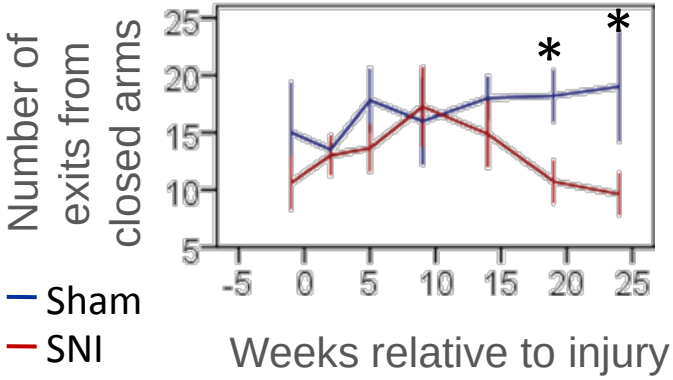
Hyperalgesia





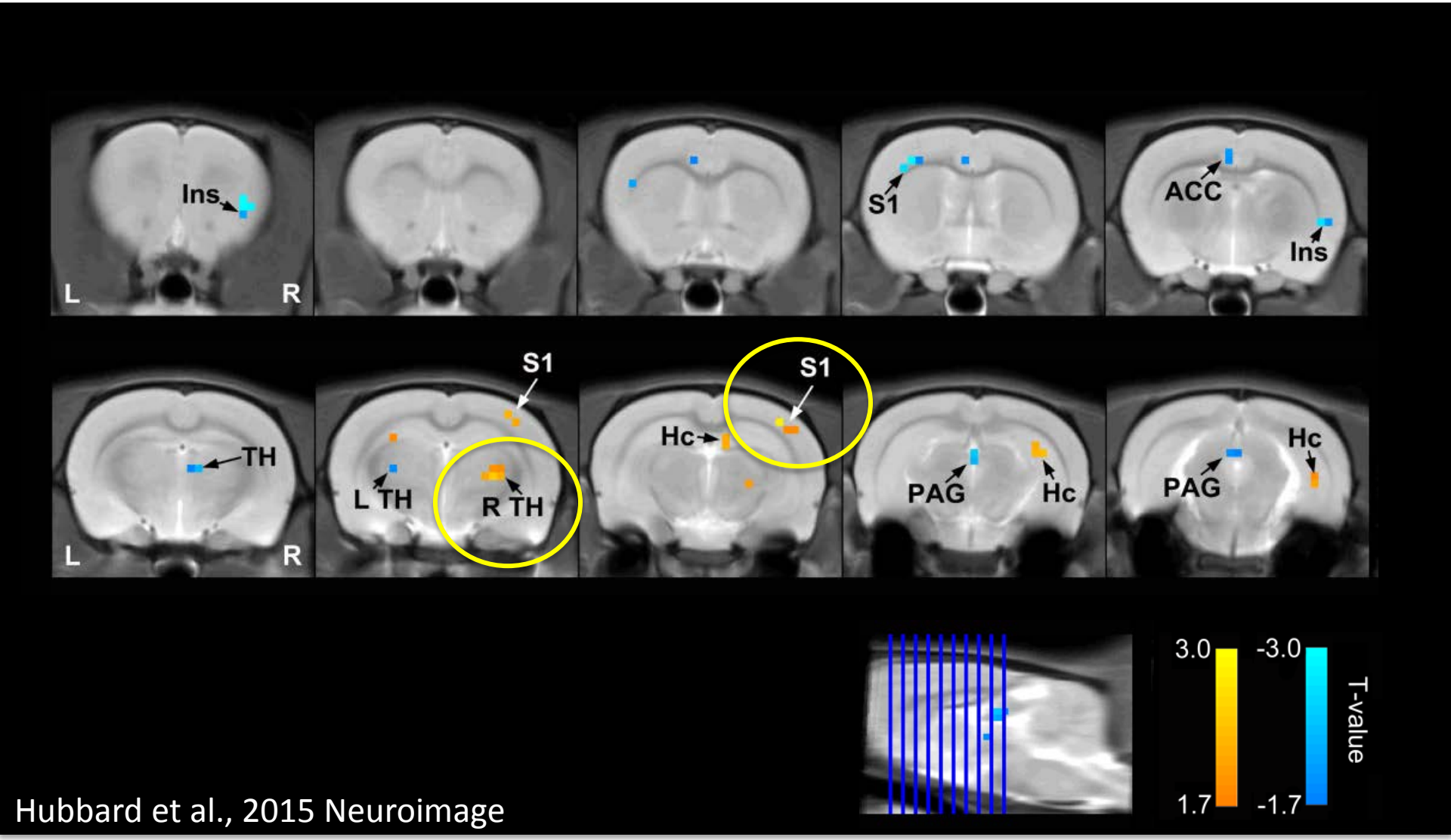
Anxiety





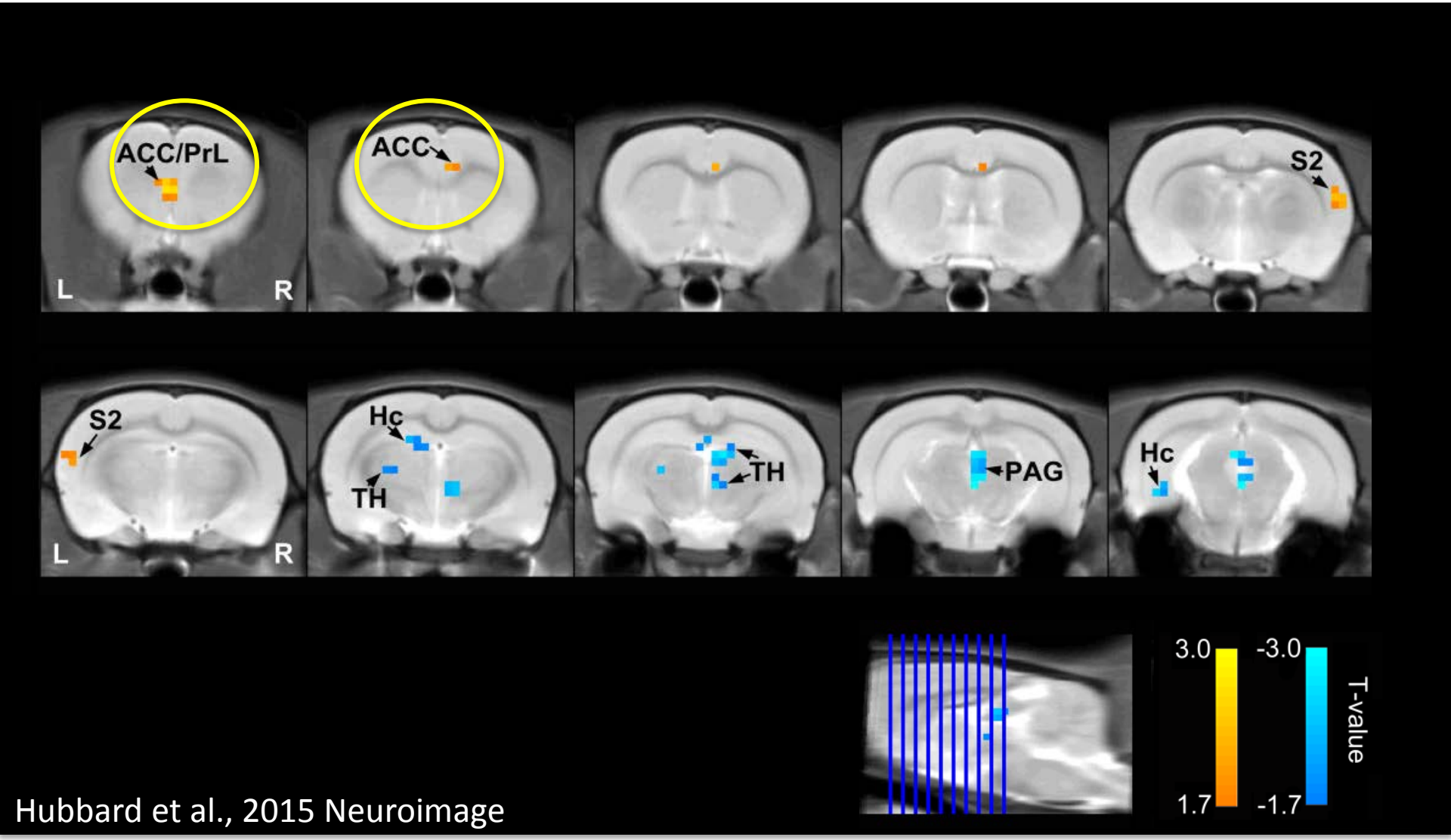
Seminowicz et al., 2009 Neuroimage

SNI > SHAM – **EARLY** (4 wks post-injury)



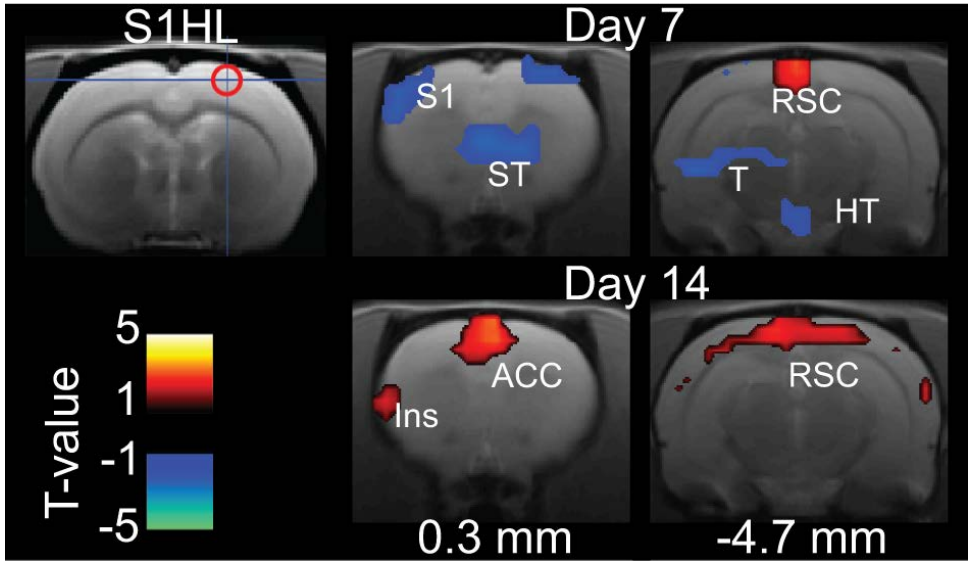
Hubbard et al., 2015 Neuroimage

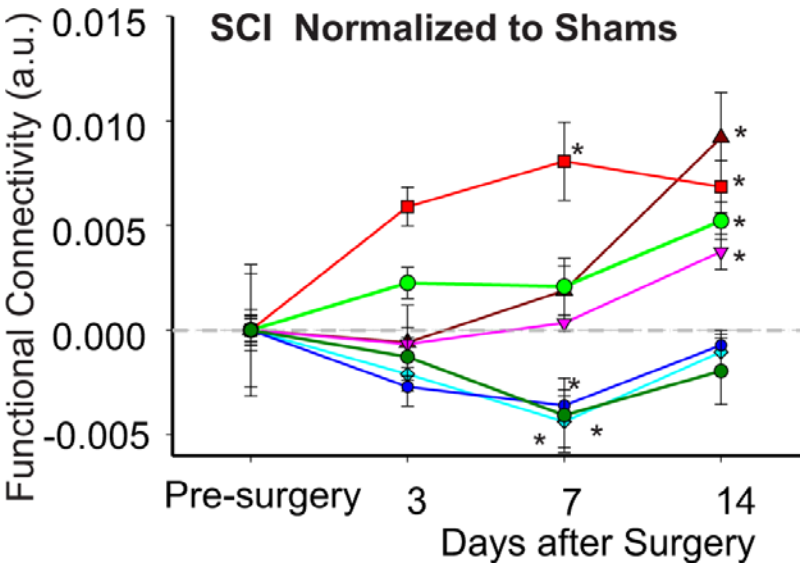
SNI > SHAM – **LATE** (20 wks post-injury)



Hubbard et al., 2015 Neuroimage

Spinal cord injury pain model: S1(hind limb) resting state connectivity

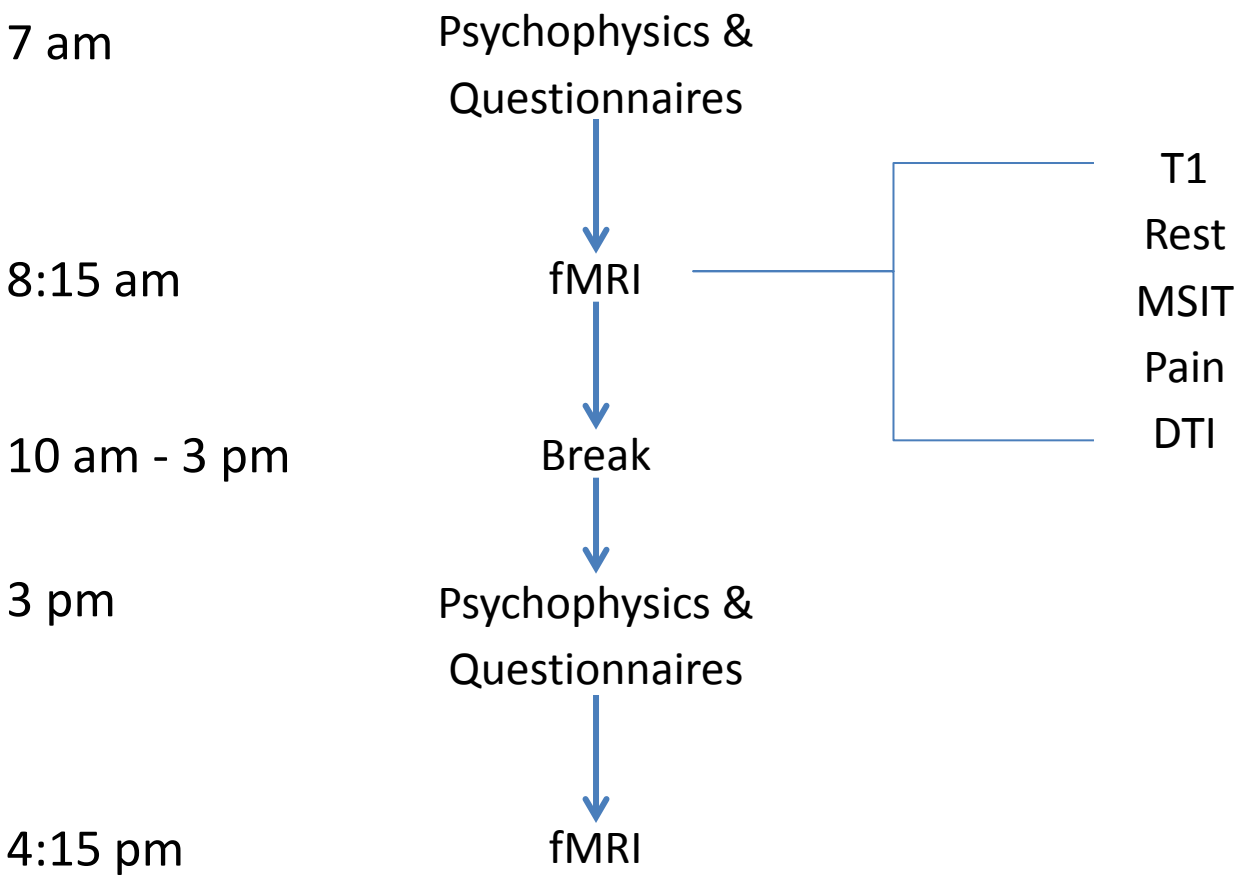




Seminowicz et al. 2012 J Neurosci

2. Maladaptive stress

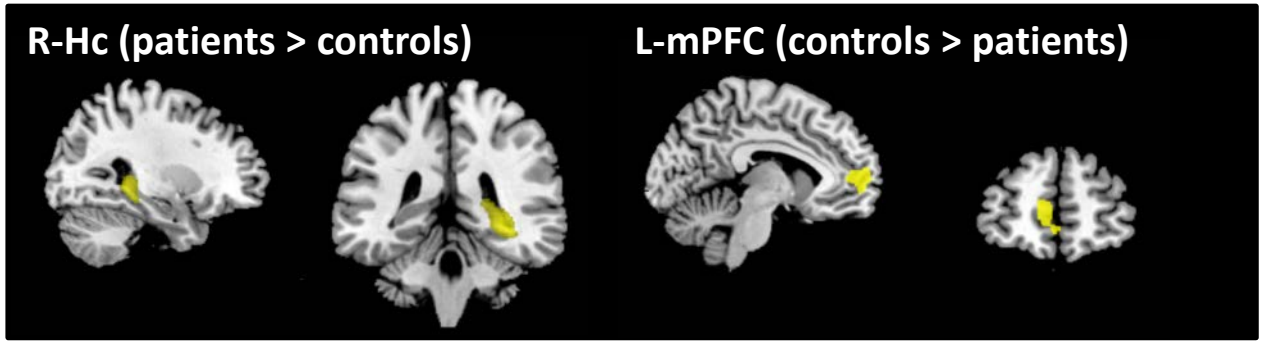
Burning Mouth Syndrome



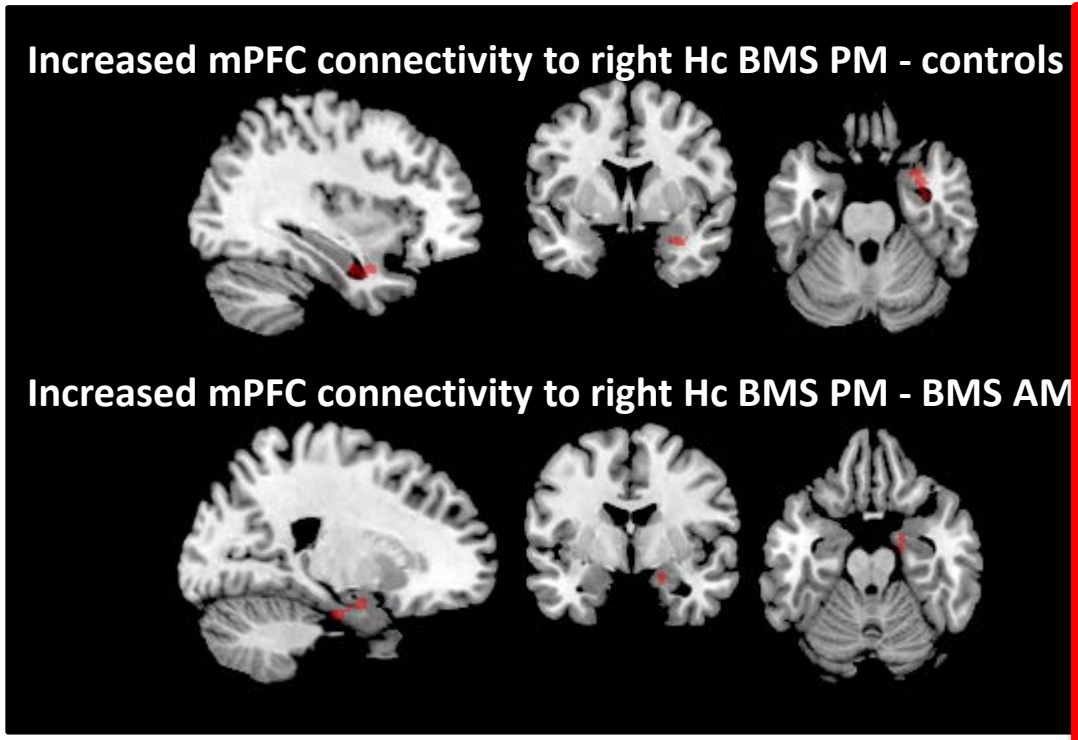
Khan et al, 2014 Pain

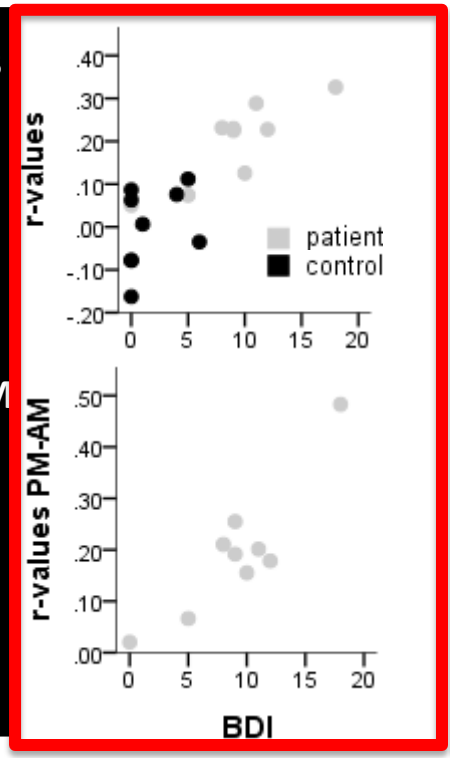
Burning Mouth Syndrome

Gray matter volume



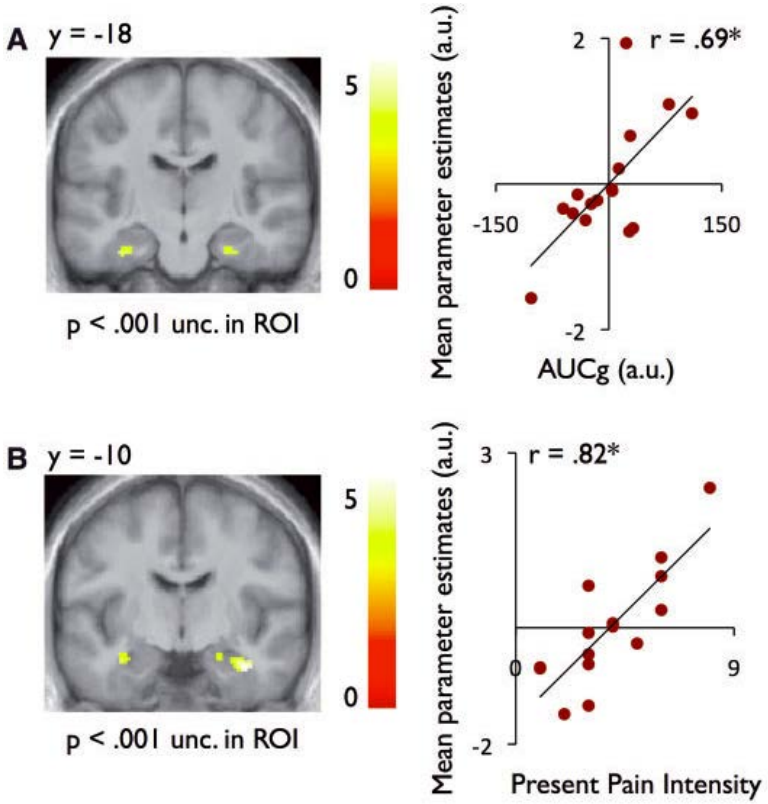
Resting state connectivity





Khan et al, 2014 Pain

Hippocampus in chronic pain: maladaptive stress



Vachon-Presseau et al., 2013 Brain

DLPFC

aMCC

MPFC

aINS

NAc

hippocampus

PAG

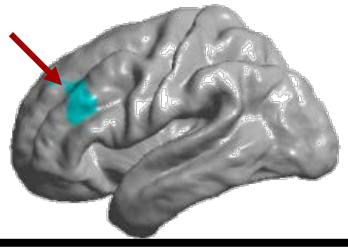
medial thalamus

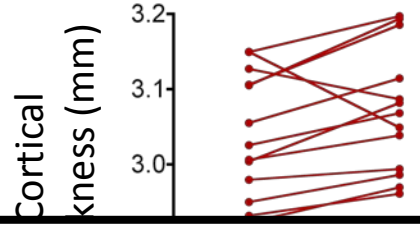
3. Refinement of treatment targets

- A good target:
  - Does something when you hit it
  - Doesn’t move
  - Might not always do what you expect

Treatment normalizes left DLPFC anatomy and function

Patients
pre-Tx vs. post-Tx

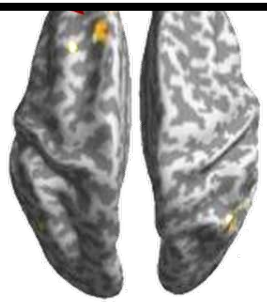


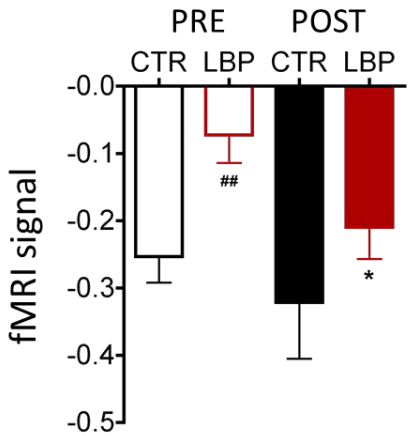


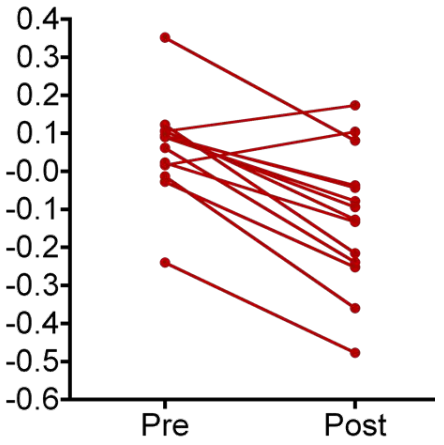
Int J Oral Maxillofac Surg. 2015 May 12. pii: S0901-5027(15)00146-0. doi: 10.1016/j.ijom.2015.04.008. [Epub ahead of print]

Daily left prefrontal repetitive transcranial magnetic stimulation for medication-resistant burning mouth syndrome.

Umezaki Y[1], Badran BW[2], Gonzales TS[3], George MS[4].

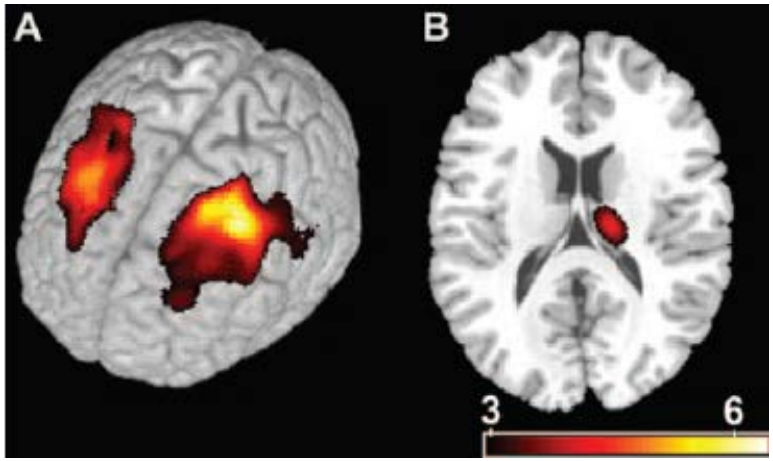






Seminowicz et al. 2011 J Neurosci

Left DLPFC in CLBP

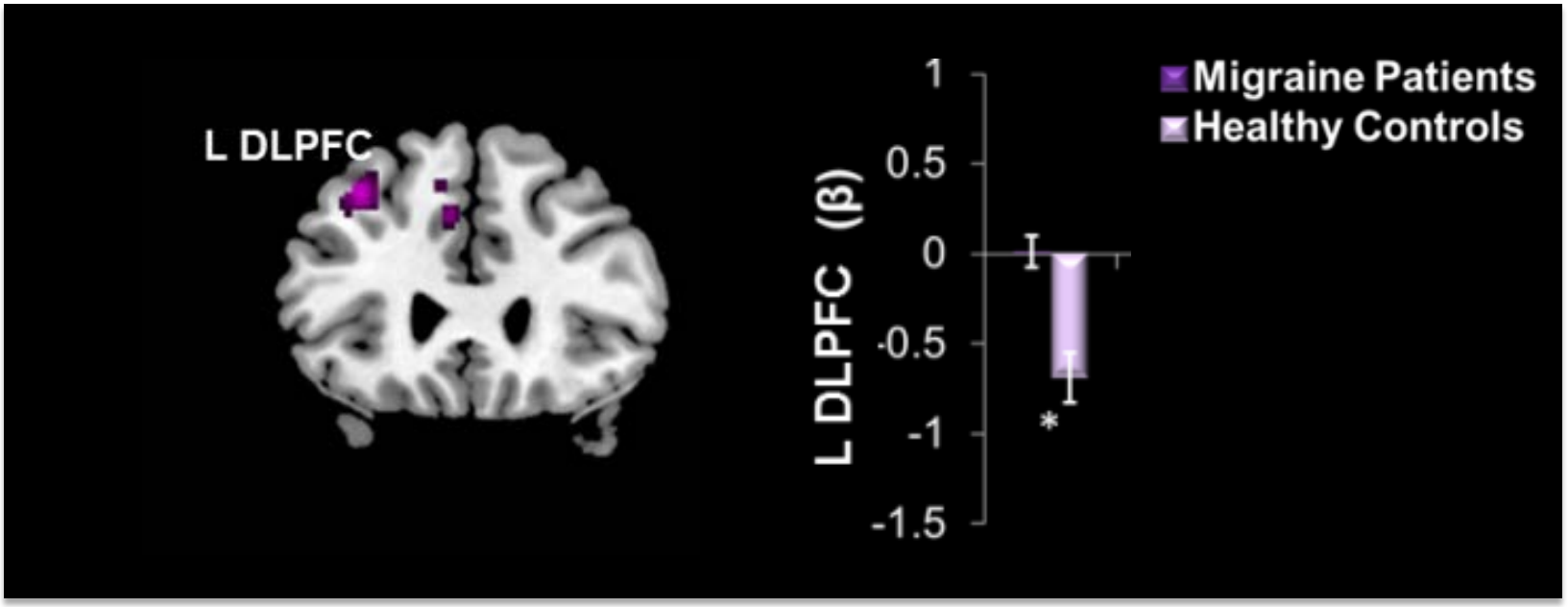


Apkarian et al 2004 JNeurosci

Chronic pain disorder	Reference	Thal	BG	S1	S2	IC	ACC	MCC	M1	PFC	Brainstem	Other
CBP	Apkarian et al., 2004	↓								↓ dlPFC		
	Schmidt-Wilcke et al., 2006	↑	↑ putamen	↓						↓ dlPFC		↓ pTL, TL
	Buckalew et al., 2008											↓ PPC
	Seminowicz et al., 2011			↓		↓	↓			↓ vlPFC, dlPFC, OFC		↑ MTL

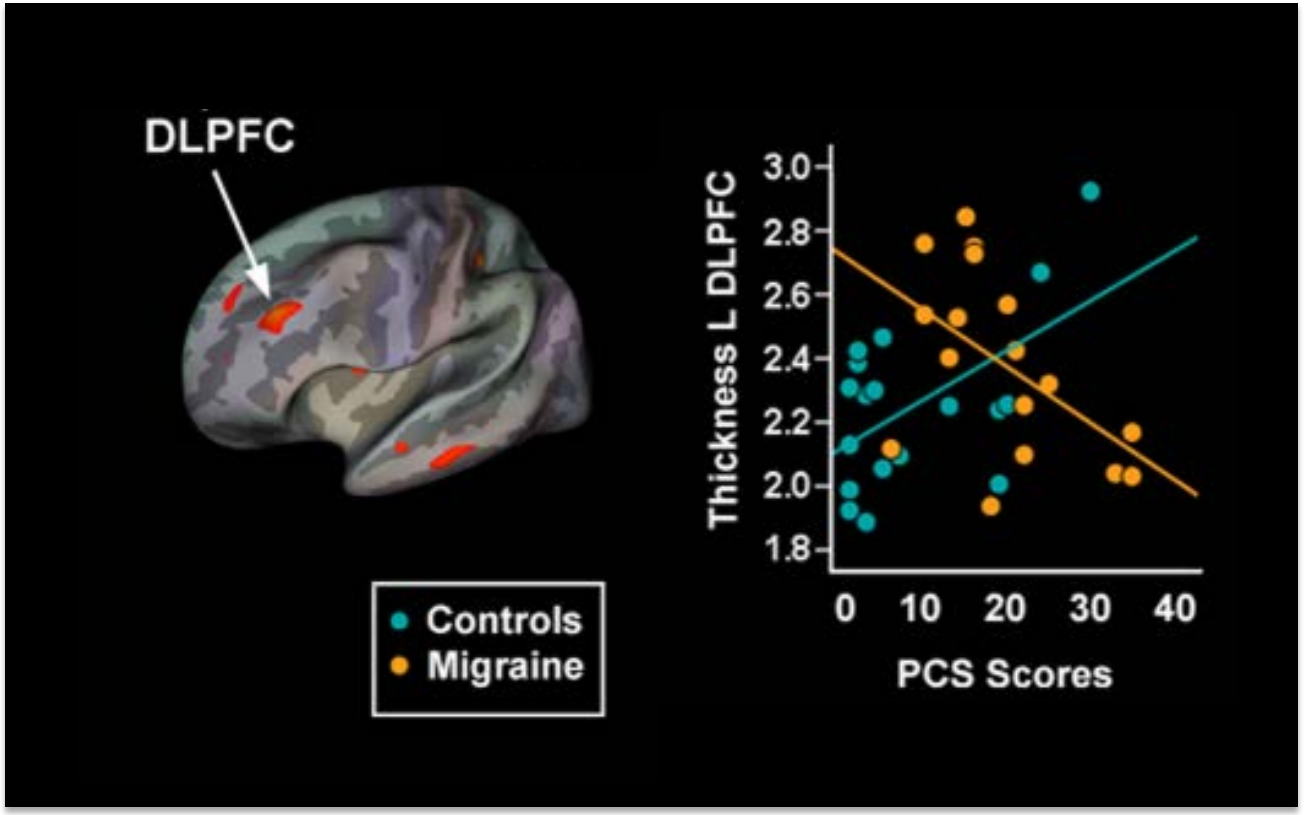
Davis & Moayedi 2012 J Neuroimmune Pharmacol

Enhanced left DLPFC cognitive-related activity in migraine



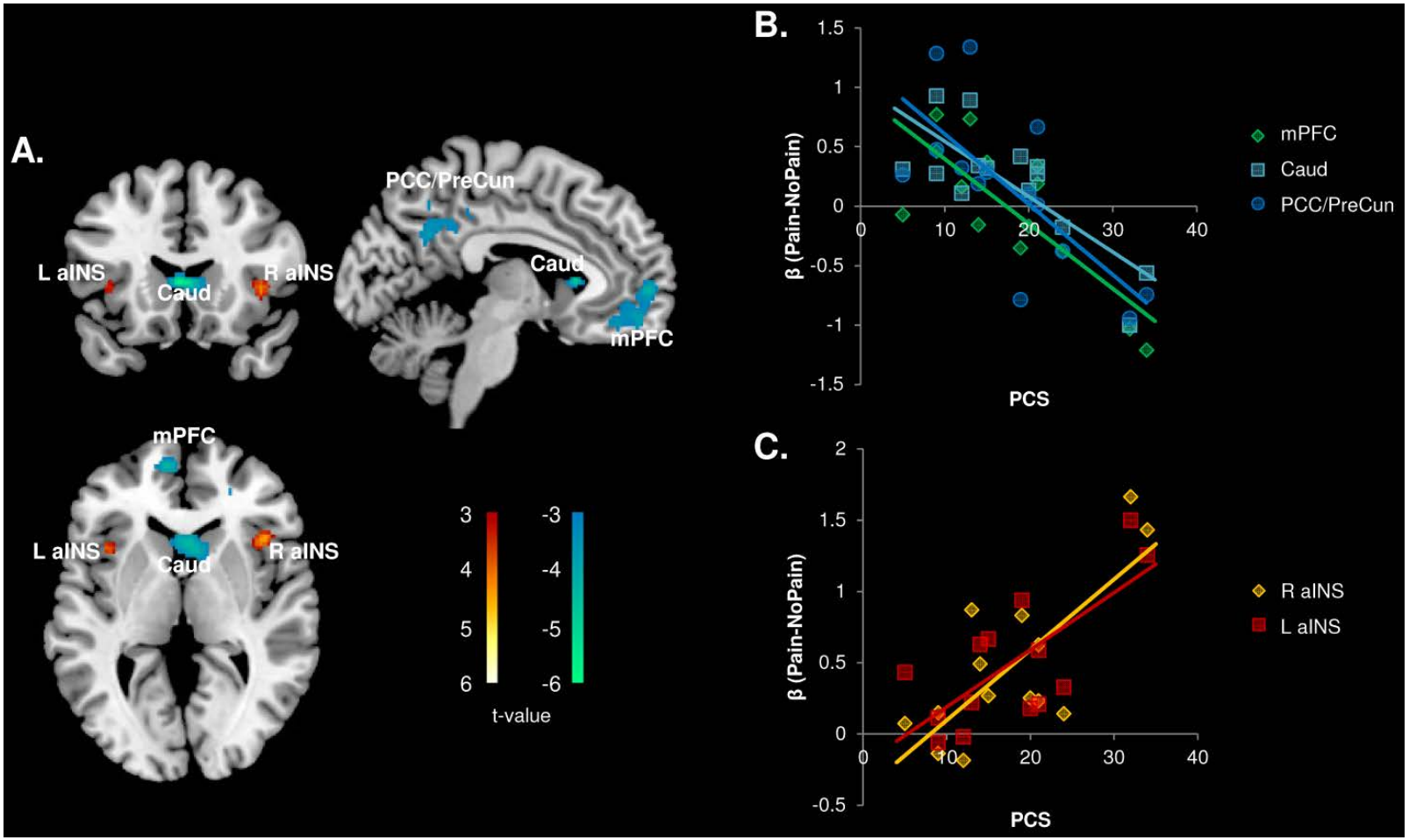
Mathur et al., 2015 Neuroimage: Clin

Catastrophizing related to structural differences



Hubbard et al. 2014 eNeuro

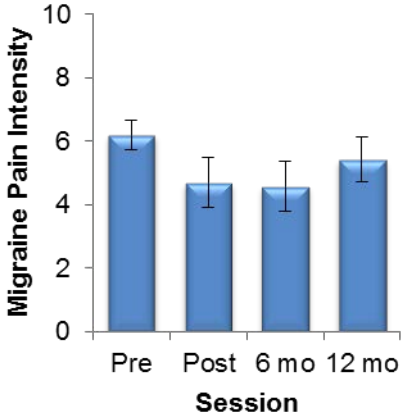
Catastrophizing related to pain-related brain activity



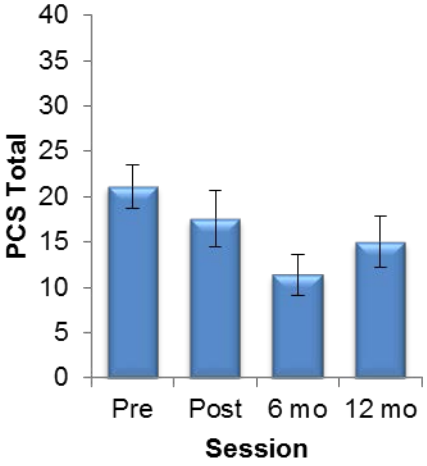
Mathur et al., in prep

Effectiveness of mindfulness for migraine

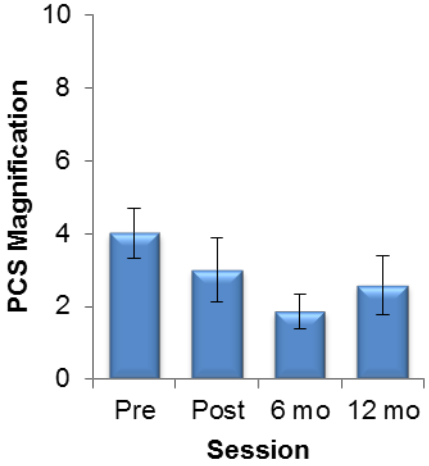
Migraine Pain month (omnibus LMM p=.01)



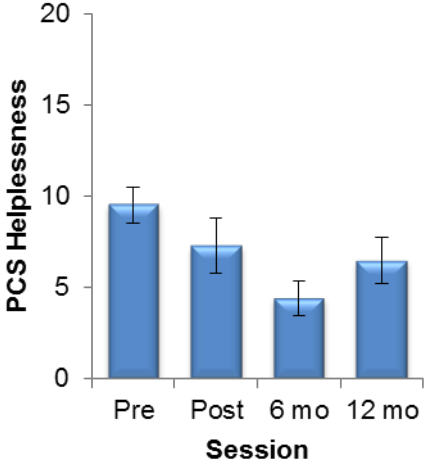
PCS Total
(omnibus LMM p=.07)



PCS magnification
(omnibus LMM p=.02)



PCS helplessness
(omnibus LMM p=.008)



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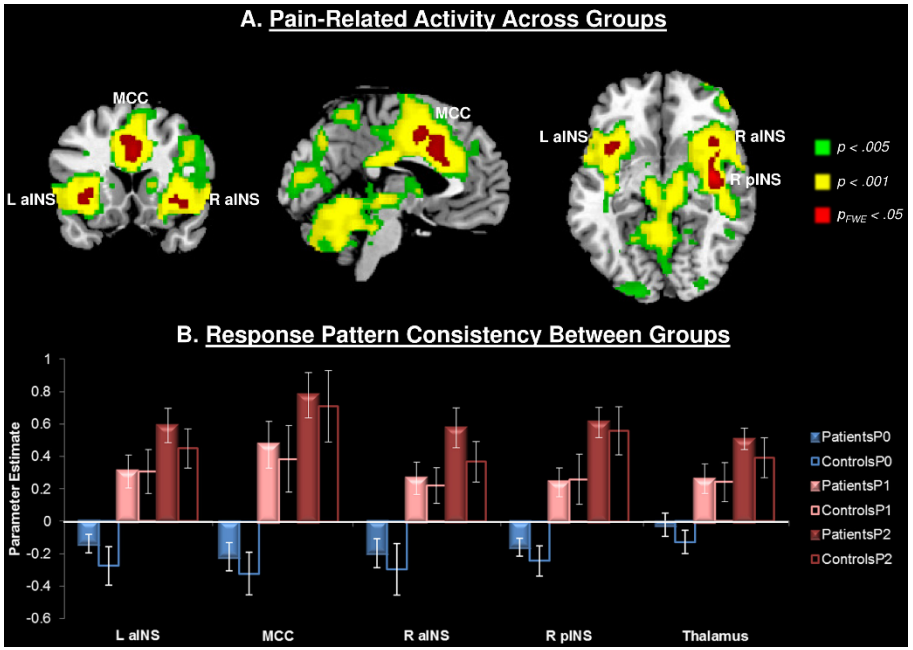
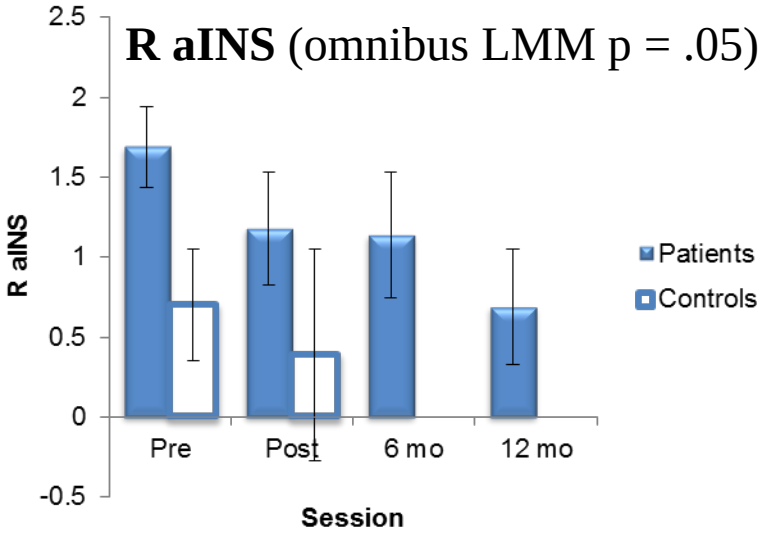
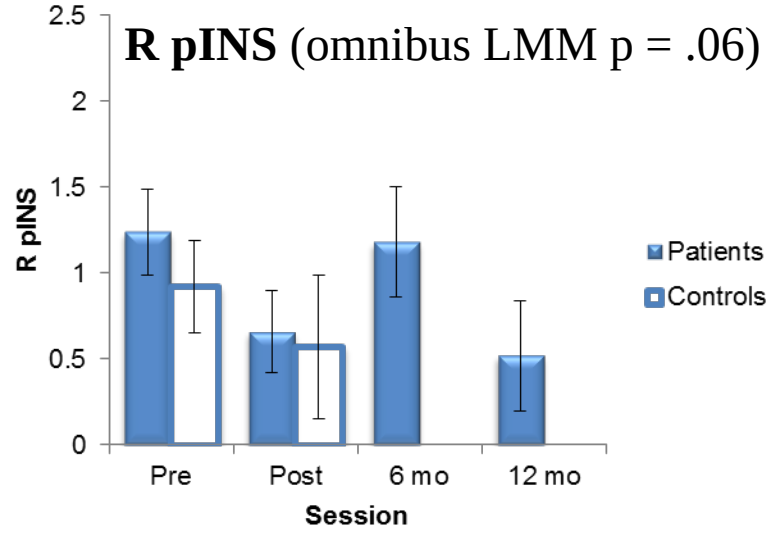
Reduction in pain-related activity?







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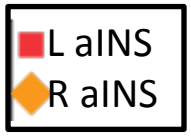
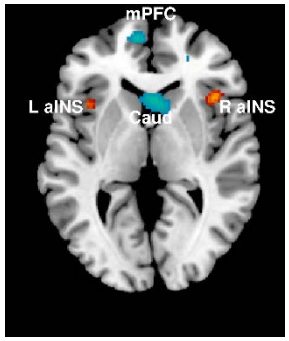
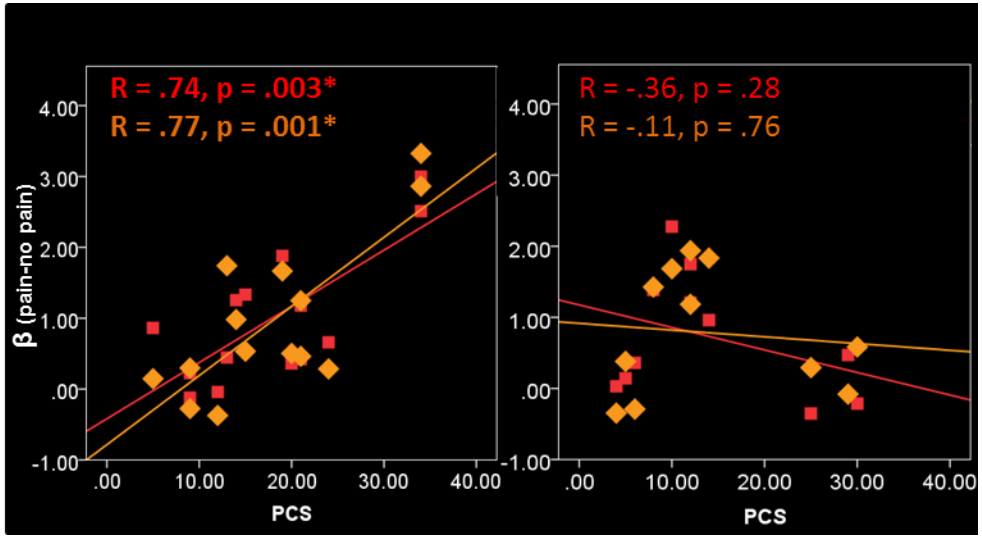
Change in relationship between pain catastrophizing and pain-related activity







Mathur et al., in prep

The future?

1. Shift to limbic circuits
   - Can we prevent the shift?
2. Maladaptive stress
   - Can we break the cycle?
3. Refinement of treatment targets
   - Can we use it for individualized medicine?

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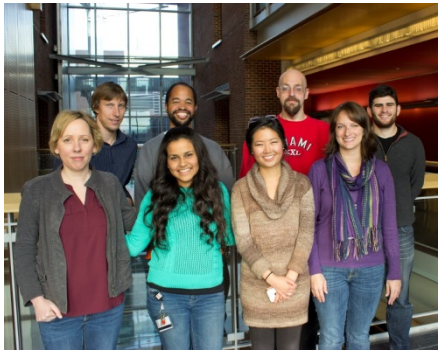

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