

Psychological Mechanisms of Pain and Analgesia

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Disclosures

- GW Pharmaceuticals—Consultant
- Parallel—Investigator-initiated grant

Agenda

- Our mental life (thoughts, emotions, & behaviors) is a neural experience
 - “Behind every thought there is a neuron.”
 - “Any man could, if he were so inclined, be the sculptor of his own brain.”
- Relationship of pain psychological symptoms to pain
 - Impacts on treatment
 - Effects on pain of treating psychological symptoms and psychiatric conditions

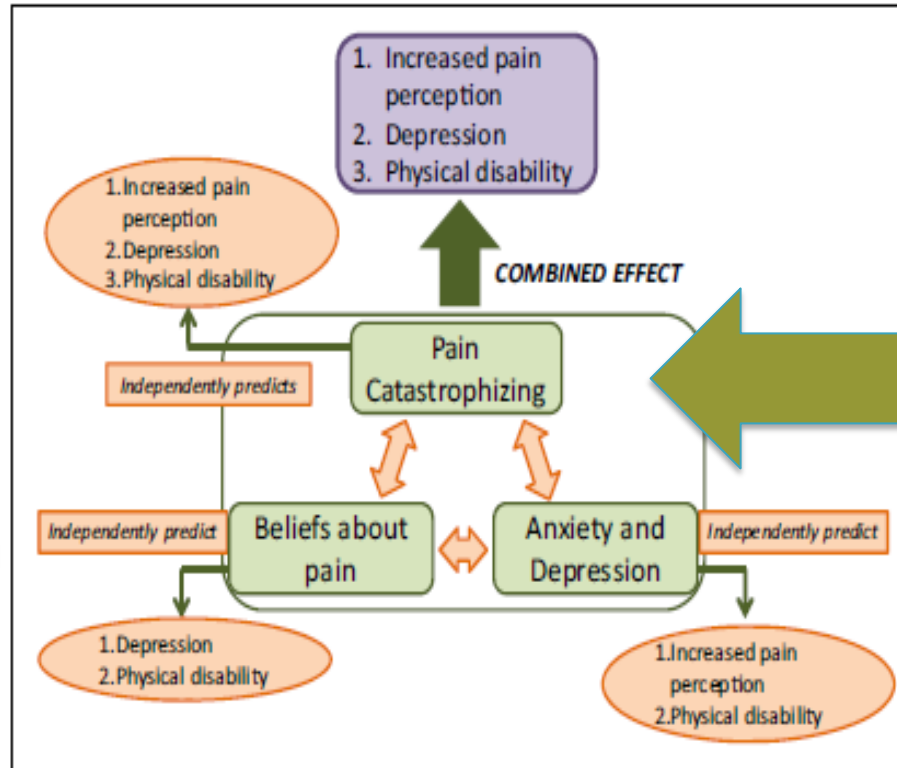
What is Negative Affect?

AKA...Negative Valence Disorders

20% of CLBP patients have a co-morbid depression or anxiety disorder
--Edwards RR, Wasan AD, et. al., *J Pain*, 2016

Affect=Thoughts
emotions, and
behavior

Pain
Catastrophizing=
Negative
thoughts about
pain

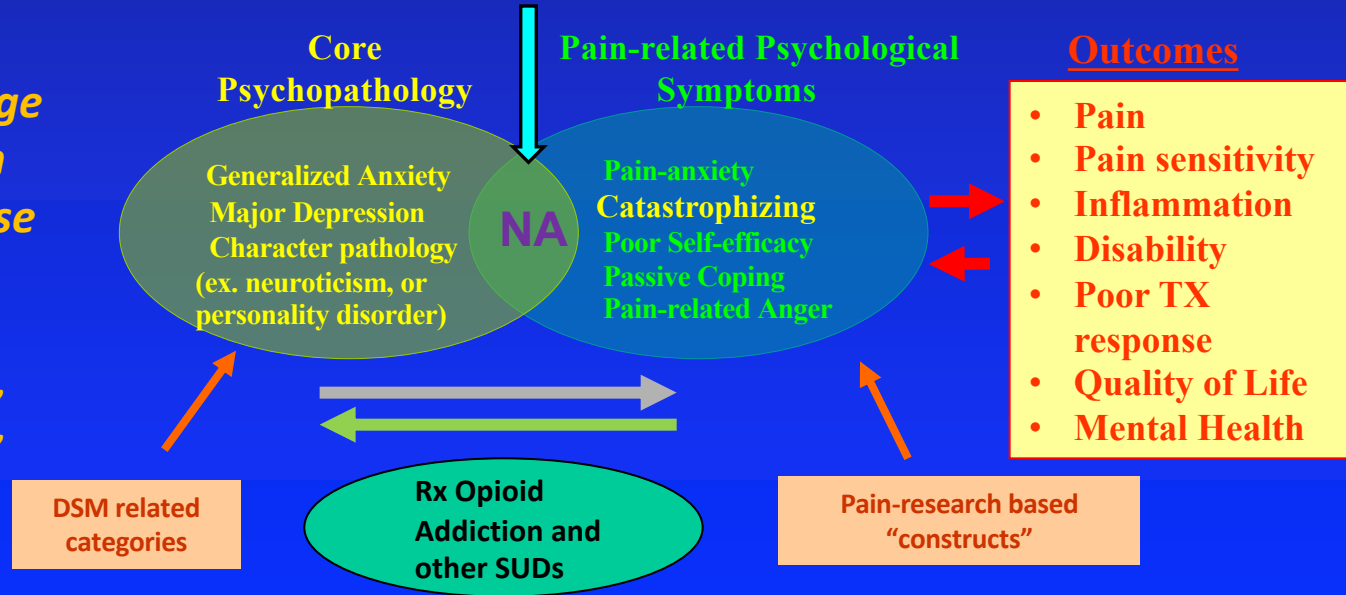


Common Psychiatric Symptoms in Patients with Pain can be Described as Negative Affective Disorders

Correlations of .60-.70 between these categories= Negative Affect, AKA Negative Valence

*In a broad range
of chronic pain
conditions these
relationships
hold true*

Ryan and McGuire,
Brit J Health Psych,
2016

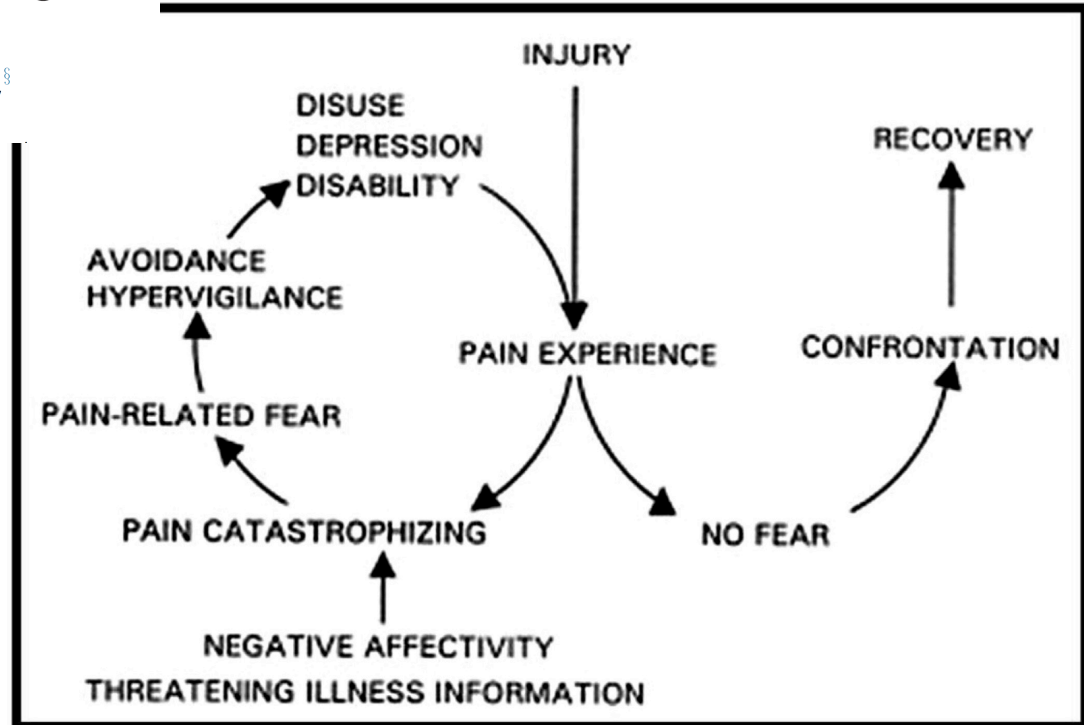


Redrawn and adapted from Wasan AD and Alpay M, "Pain and the Psychiatric Comorbidities of Pain," in *Comprehensive Clin. Psychiatry*, 2nd Ed., 2016, Elsevier Pub.

The Role of Psychosocial Processes in the Development and Maintenance of Chronic Pain



Robert R. Edwards,^{*} Robert H. Dworkin,[†] Mark D. Sullivan,[‡] Dennis C. Turk,[§] and Ajay D. Wasan[¶]



ICD 11 Taxonomy of Chronic Pain—Nociplastic Pain and IASP

- **Nociceptive Pain:** Pain perception transmitted from ‘intact’ nervous systems pathways.
 - Fracture pain, routine postoperative pain
- **Neuropathic Pain:** Pain as a consequence of a disease or lesion to the nervous system
 - Diabetic peripheral neuropathy
- **Nociplastic Pain:** Pain that arises from altered nociceptive function
 - Fibromyalgia
 - Neuropathic process amplifying a nociceptive process (burning or expanded joint pain of OA)

PAIN®

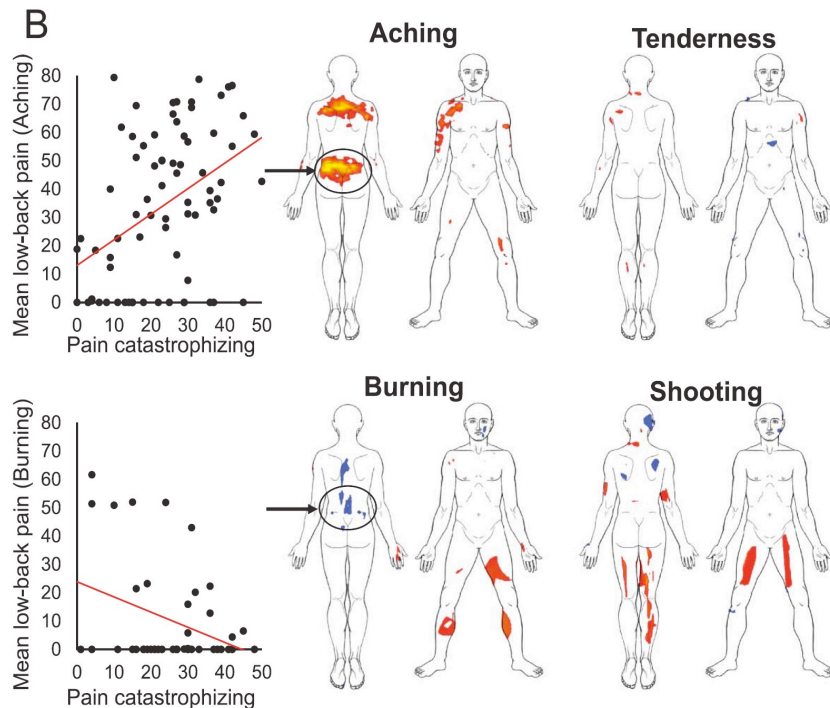
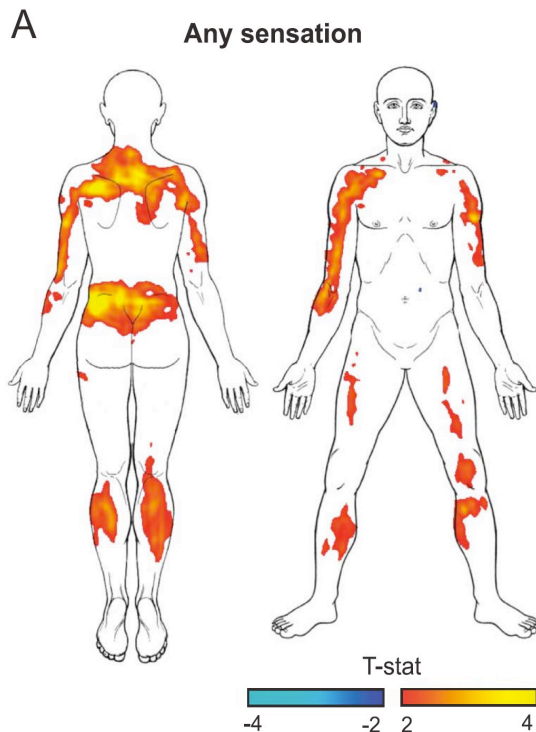
Recently introduced definition of “nociplastic pain” by the International Association for the Study of Pain needs better formulation

Nociplastic pain: Pain that (1) arises from altered nociception despite no (2) clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or (3) evidence for disease or lesion of the somatosensory system causing the pain (IASP Taxonomy 2017).

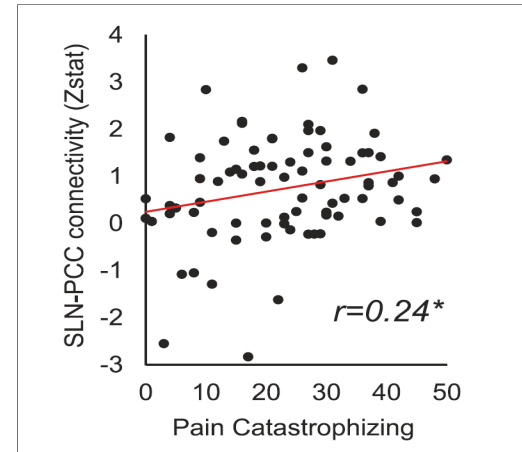
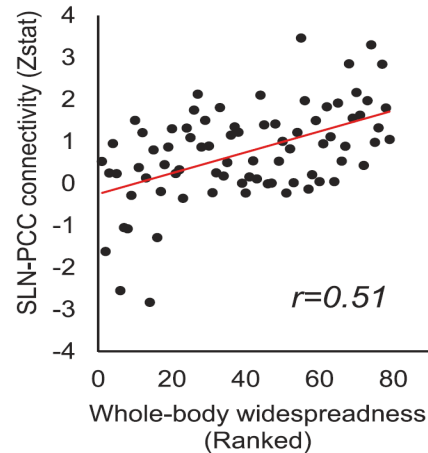
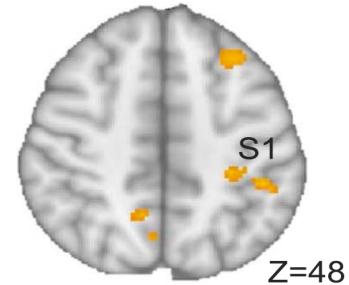
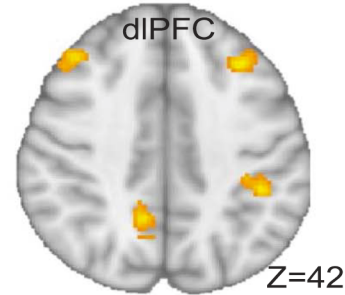
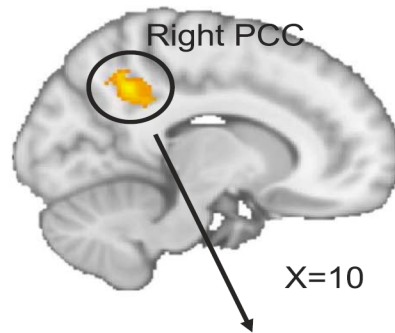
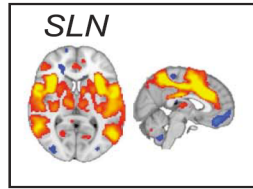
A picture is worth a thousand words: linking fibromyalgia pain widespreadness from digital pain drawings with pain catastrophizing and brain cross-network connectivity

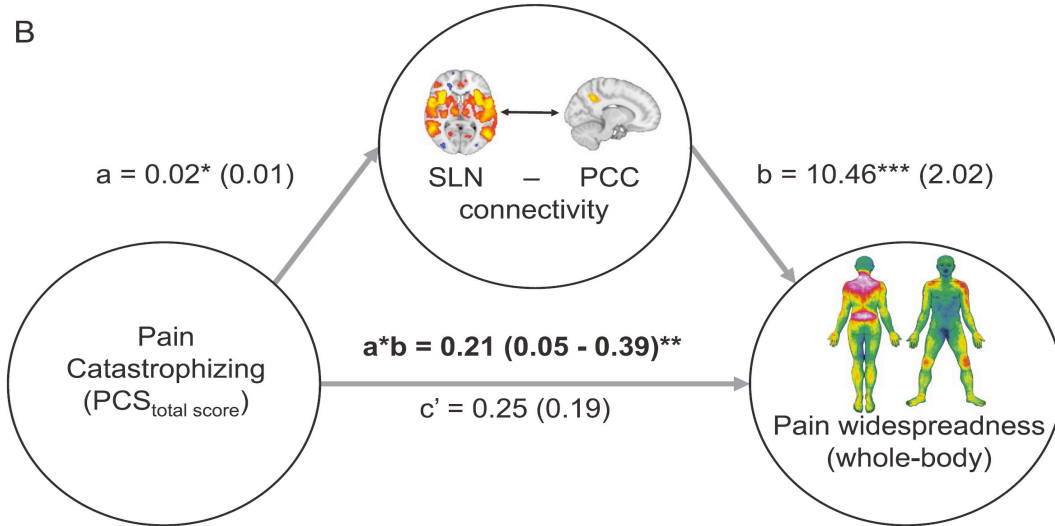
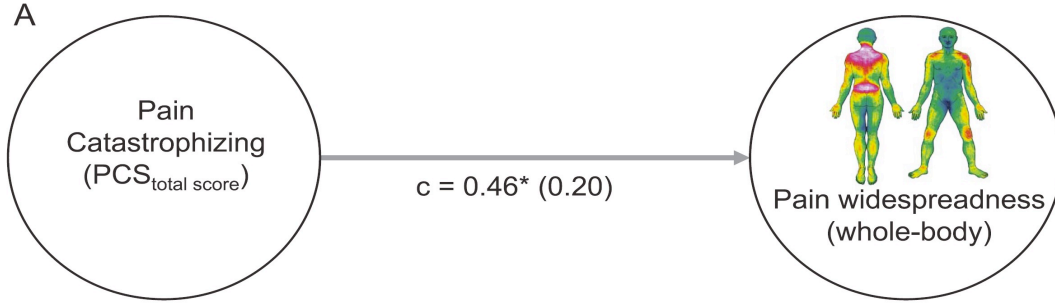
Dan-Mikael Ellingsen^{a,b,c,*}, Florian Beissner^d, Tawfik Moher Alsady^d, Asimina Lazaridou^e, Myrella Paschall^e, Michael Berry^c, Laura Isaro^e, Arvina Grahl^c, Jeungchan Lee^c, Ajay D. Wasan^f, Robert R. Edwards^g, Vitaly Napadow^{c,e}

N=79

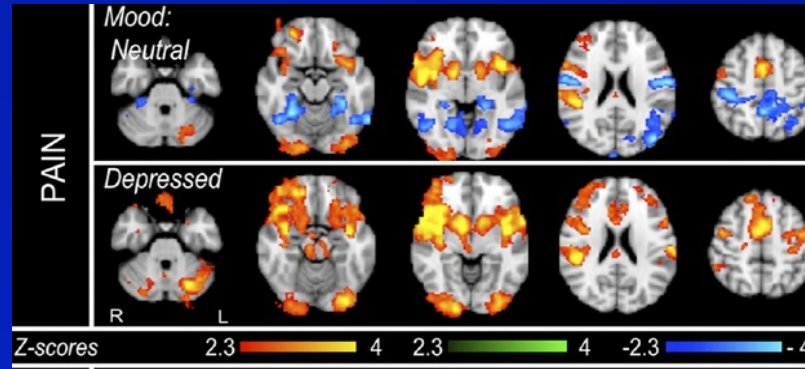


Association between Salience Network (SLN) connectivity and pain widespreadness

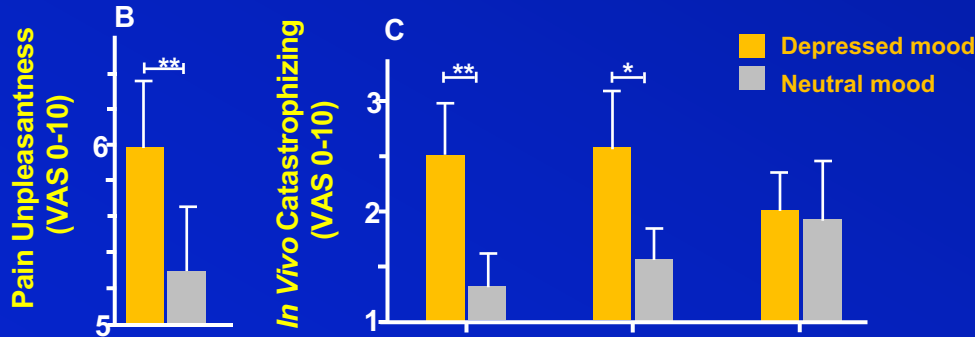




Depressed Mood and Pain



* $P < 0.05$. ** $P < 0.01$.



* $P < 0.05$. ** $P < 0.01$.

N = 20 healthy subjects.

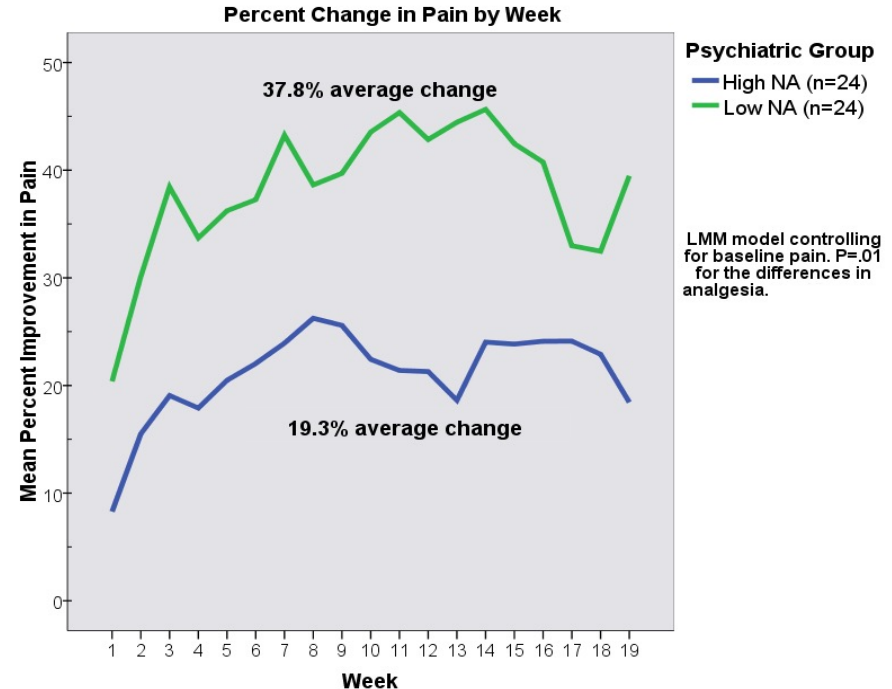
VAS = visual analog scale.

Berna C, et. al. *Biol Psychiatry*. 2010;67:1083-1090.

Magnification Rumination Helplessness

Wasan AD, et. al., “Psychiatric Comorbidity Is Associated Prospectively with Diminished Opioid Analgesia and Increased Opioid Misuse in Patients with Chronic Low Back Pain,” *Anesthesiology*, 2015

- N=55 patients with CLBP, Hi and Lo negative affect (depression + anxiety symptoms)
- Prescribed opioids over 5 months, with the prescriber blinded to group
- Tracked pain daily
- 8% rate of opioid misuse in the Low group
- 38% misuse rate in the High group
- **MISUSE—MAPS ONTO a MILD OUD DX**



Depression and Prescription Opioid Misuse Among Chronic Opioid Therapy Recipients With No History of Substance Abuse

Alicia Grattan, MD¹

Mark D. Sullivan, MD, PhD¹

Kathleen W. Saunders, JD²

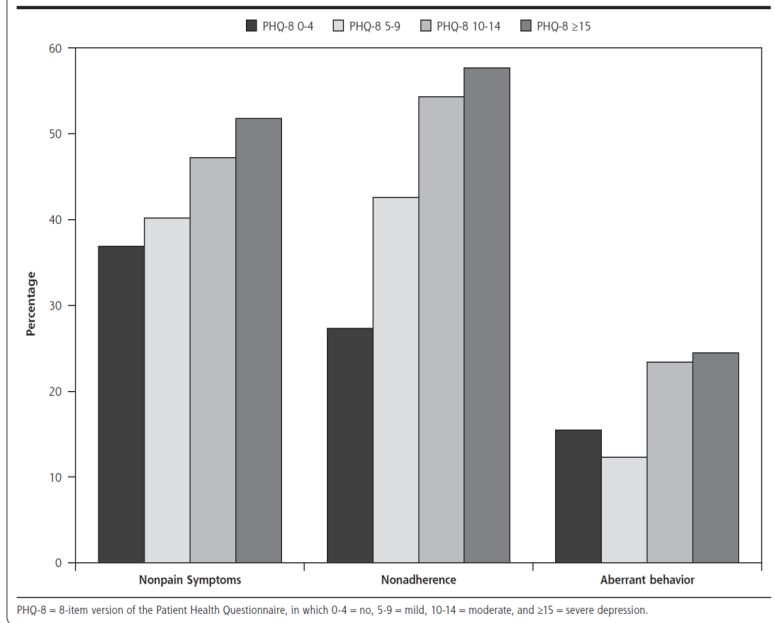
Cynthia I. Campbell, PhD, MPH³

Michael R. Von Korff, ScD²



Ann Fam Med 2012;10:304-311.

- Evaluated 1334 chronic pain patients prescribed opioids chronically
- Self report of misuse, such as self-medicating non-pain, increasing doses, or obtaining opioids from others
- Patients with major depression 2X as likely to misuse opioids
- Most commonly by self-increasing their dose

Figure 1. Percentage of weighted positive misuse in relationship to depression score.

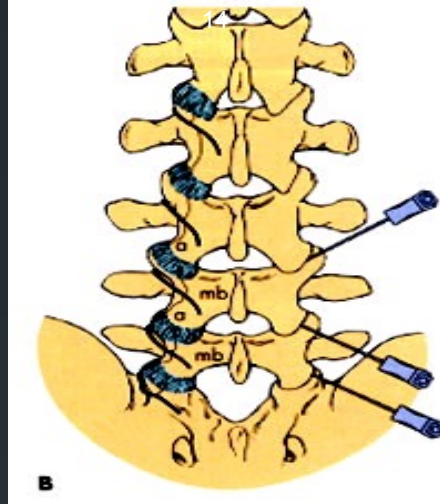
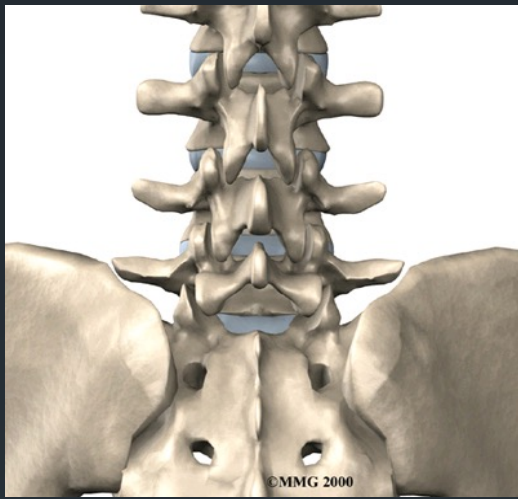


Negative Affect–Related Factors Have the Strongest Association with Prescription Opioid Misuse in a Cross-Sectional Cohort of Patients with Chronic Pain *Pain Medicine*, 21(2), 2020, e127–e138

Gadi Gilam , PhD,* John A. Sturgeon, PhD,[†] Dokyoung S. You, PhD,* Ajay D. Wasan, MD, MSc,[†] Beth D. Darnall , PhD,* and Sean C. Mackey, MD, PhD*

- N=1193, pain clinic sample

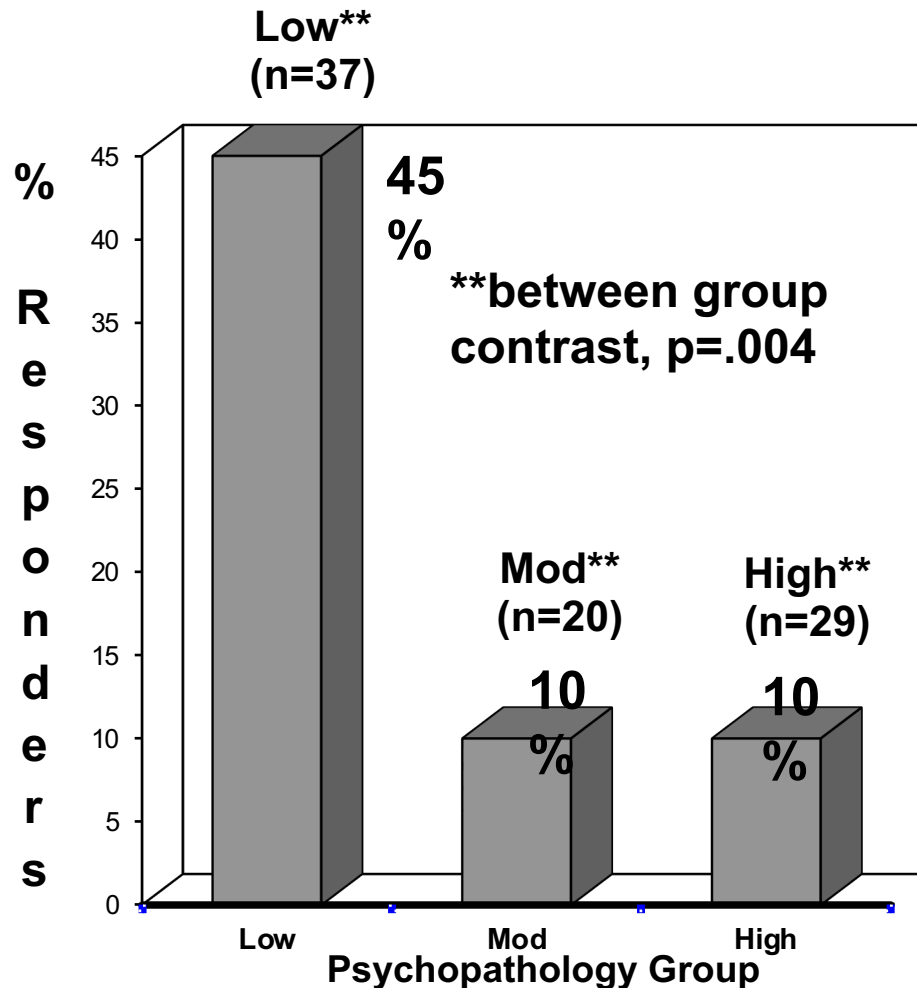
Facet Syndrome and Therapeutic Medial Branch Blocks



- Axial low back or neck pain—with concordant PE
- MRI or CT findings of facet arthropathy
- Positive bone scan predicts positive response with MBB
- Effectiveness= Improvement in pain and function

Percent of
Patients with
at least 30%
improve-
ment

AD Wasan, et.
al, *BMC MSK
Disorders*, 2009



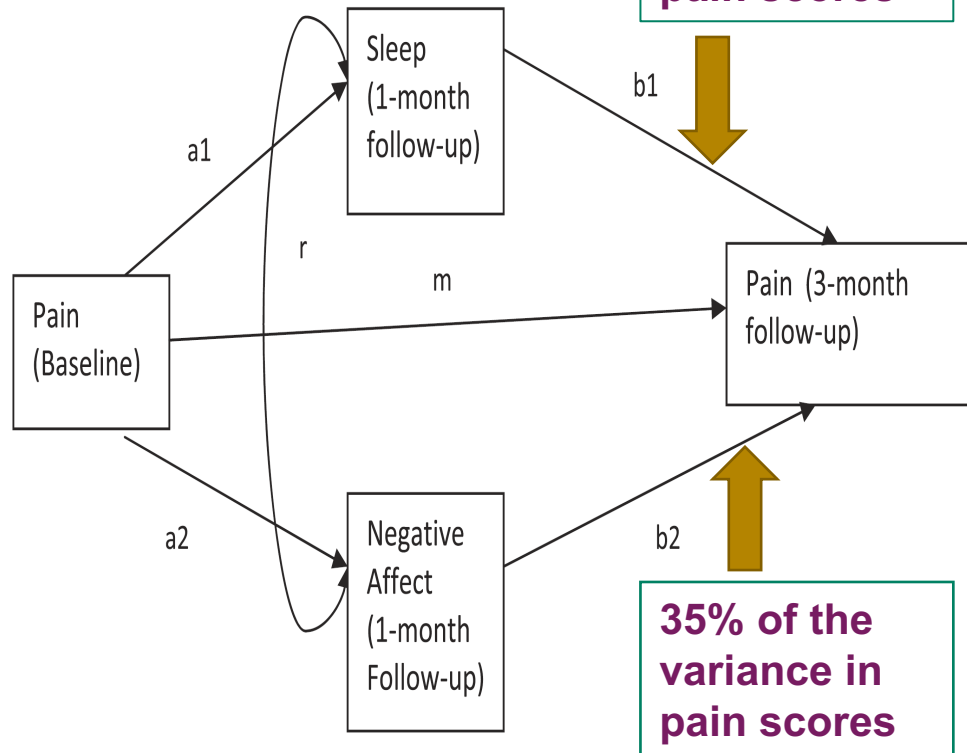
Similar findings
in patients
undergoing
spine surgery
or epidural
steroid
injections

ORIGINAL ARTICLE

Negative Affect and Sleep Disturbance May Be Associated With Response to Epidural Steroid Injections for Spine-Related Pain

Jordan F. Karp, MD,^{a,b} Lan Yu, PhD,^a Janna Friedly, MD,^c Dagmar Paul A. Pilkonis, PhD^a

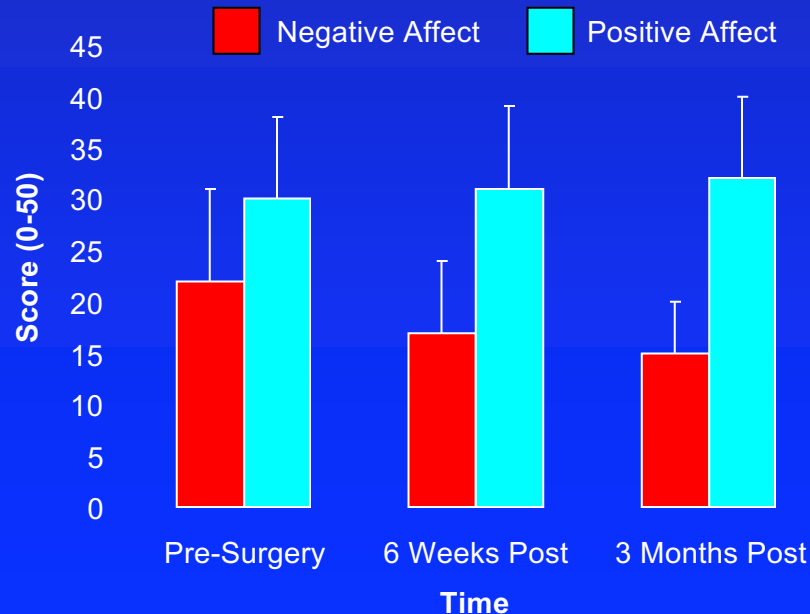
- 160 patients with ESI's or TFESI's
- PROMIS scores at baseline, 1 month and 3 month follow up



Positive Affect

Examining the role of positive and negative affect in recovery from spine surgery

Caryn L. Seebach^a, Matthew Kirkhart^b, Jeffrey M. Lating^b, Stephen T. Wegener^c, Yanna Song^d,
Lee H. Riley III^e, Kristin R. Archer^{f,*}



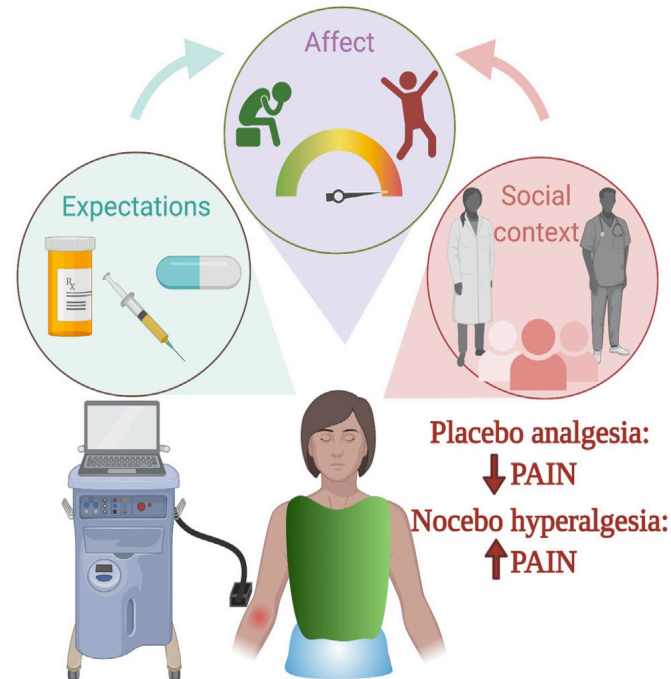
141 patients treated by spine surgery for lumbar or cervical degeneration. Affect was measured with the PANAS. Negative affect decreased post-surgery while positive affect remained constant. Linear regression analyses found that 6-week positive affect predicted functional status at 3 months following surgery.

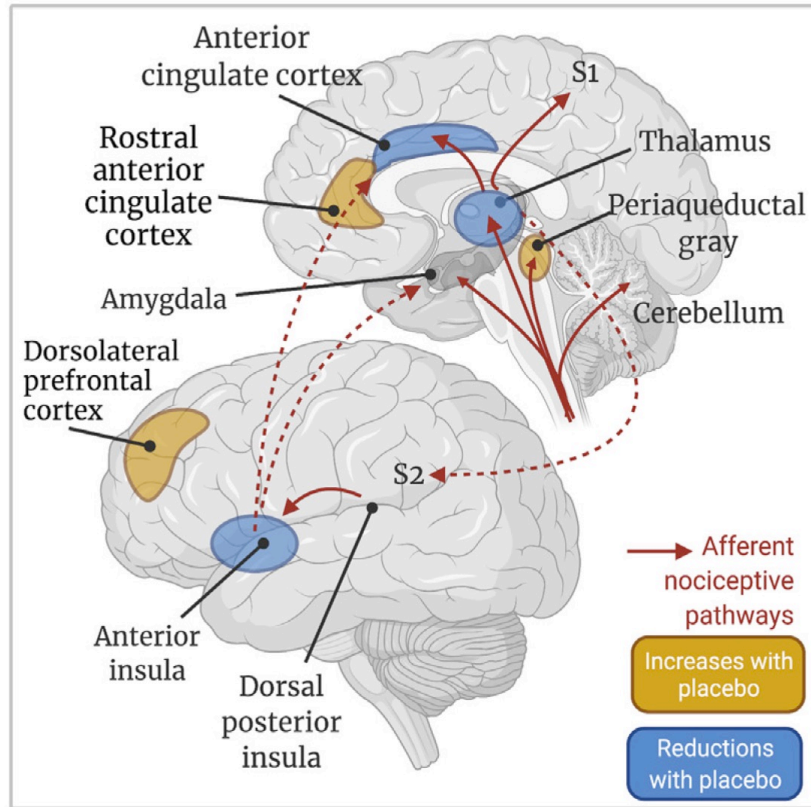
Review

A social affective neuroscience lens on
placebo analgesiaLauren Y. Atlas^{1,2,3,*}

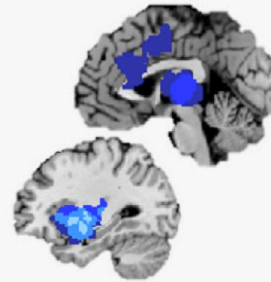
Key figure

Expectations, affect, and social context shape pain and lead to placebo analgesia or nocebo hyperalgesia

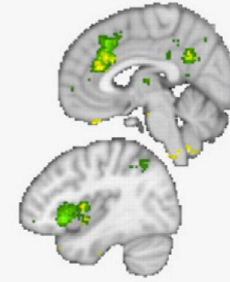




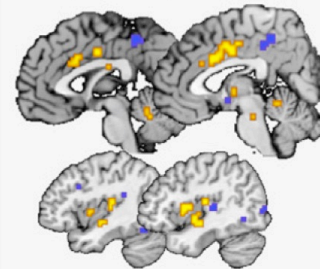
Placebo-induced reductions



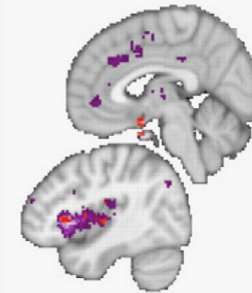
Salience network



Neurologic pain signature



Interoception



Trends in Cognitive Sciences



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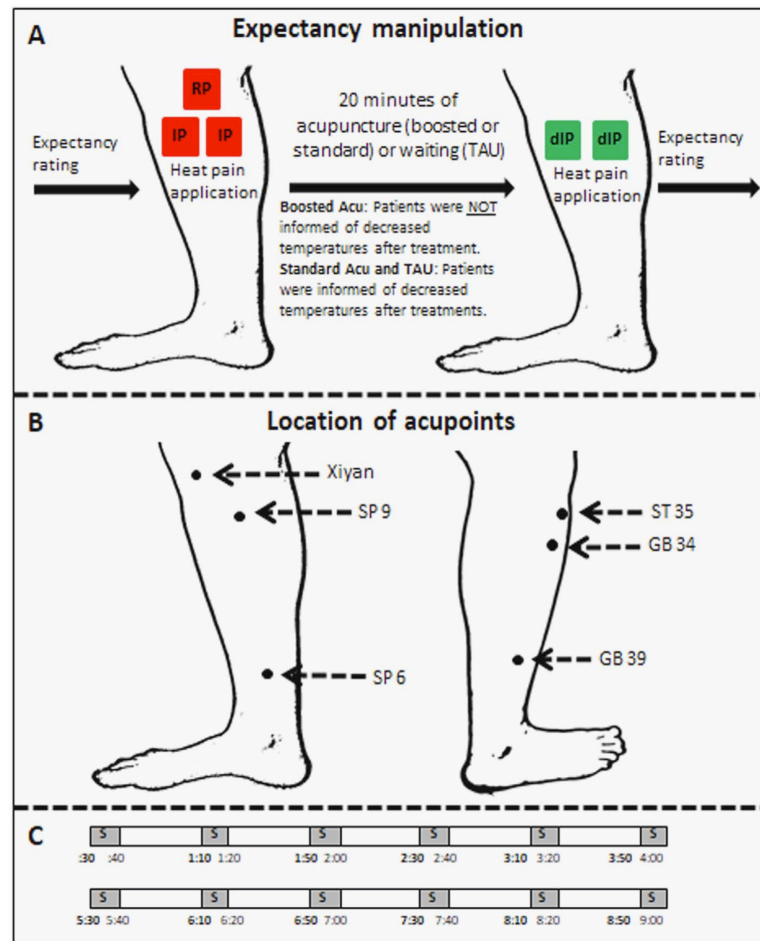
journal homepage: www.elsevier.com/locate/ynicl

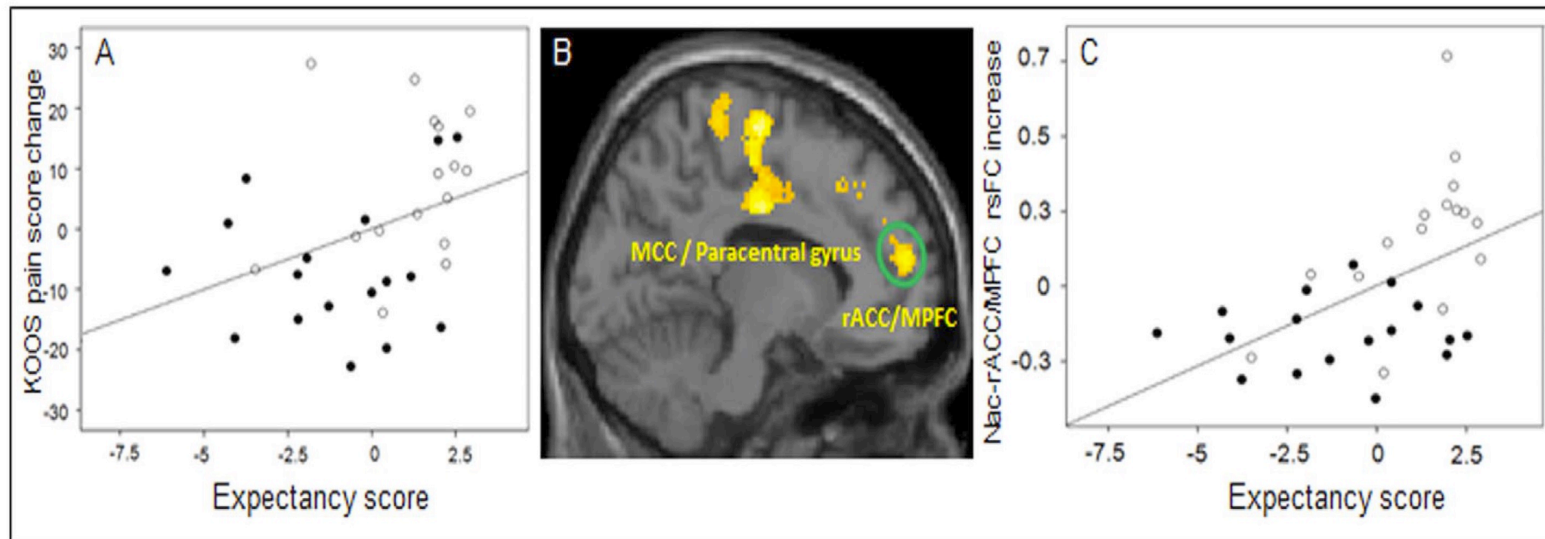
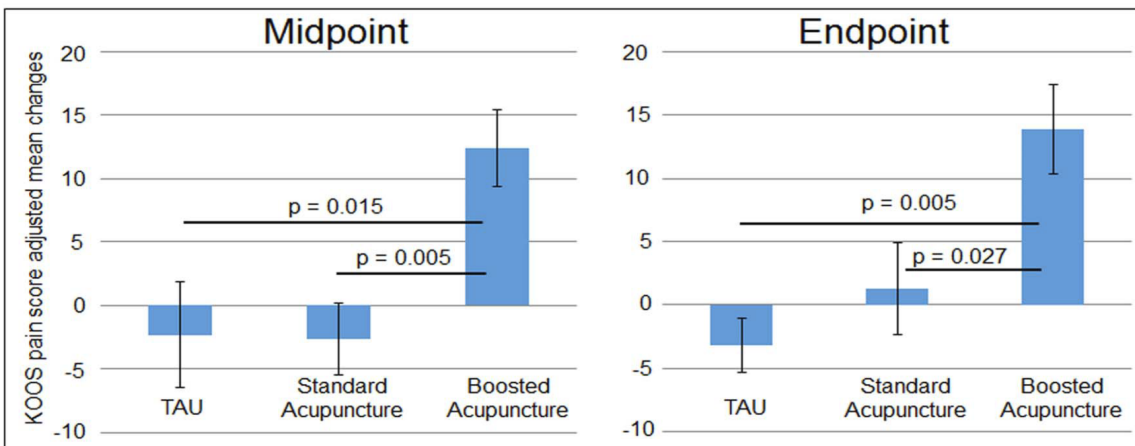


Enhancing treatment of osteoarthritis knee pain by boosting expectancy: A functional neuroimaging study

Jian Kong^{a,b,*}, Zengjian Wang^a, Jaclyn Leiser^a, Domenic Minicucci^a, Robert Edwards^{c,d}, Irving Kirsch^e, Ajay D. Wasan^{f,g}, Courtney Lang^a, Jessica Gerber^b, Siyi Yu^a, Vitaly Napadow^b, Ted J. Kaptchuk^e, Randy L. Gollub^{a,b,e}

- 74 patients with knee OA
- Treated with acupuncture
- Expectations for acupuncture relief manipulated by response to heat pain after an Acup. TX at start of TX
- 3 groups: boosted acup, std acup, wait list control
- 8 sessions of acupuncture
- FMRI brain at 1st and 6th treatment session in acup groups





Thank You!

I have been blessed with terrific colleagues!

- University of Pittsburgh
 - Ben Alter
 - Jim Ibinson
 - Trent Emerick
- Brigham and Women's Hospital/
Harvard Medical School
 - Robert Edwards
 - Srdj Nedeljkovic
 - Robert Jamison
 - Jeff Katz
- MGH Martinos Center/HMS
 - Marco Loggia
 - Vitaly Napadow
 - Randy Gollub
 - Jian Kong



Thank You!