



# John J. Bonica Lectureship

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# Disclosures

- NIH funding supported much of the work I will describe
- No other disclosures



# Objectives: Pain-related suffering

# Catastrophizing triggered by pain



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

# Pain Catastrophizing Develops Early

- Data suggest that CAT develops early in healthy people
  - We see CAT in children and adolescents



CAT is a risk factor that  
people bring to acute pain

## Catastrophizing: a predictive factor for postoperative pain

Reenam S. Khan<sup>a</sup>, Kamran Ahmed, M.R.C.S.<sup>a,\*</sup>, Elizabeth Blakeway, M.A., M.B.B.S.<sup>a</sup>,  
Petros Skapinakis, M.P.H., Ph.D.<sup>b</sup>, Leo Nihoyannopoulos, B.Sc.<sup>a</sup>,  
Kenneth Macleod, F.R.C.A.<sup>c</sup>, Nick Sevdalis, M.S., Ph.D.<sup>a</sup>,  
Hutan Ashrafian, B.Sc., M.R.C.S.<sup>a</sup>, Michael Platt, F.R.C.A., F.F.P., M.R.C.A.<sup>c</sup>,  
Ara Darzi, F.R.C.S., F.A.C.S., K.B.E.<sup>a</sup>, Thanos Athanasiou, Ph.D., F.E.T.C.S.<sup>a</sup>

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# Objectives

- Review findings on the effects of pain catastrophizing on various pain outcomes
- Identify pathophysiological mechanisms linking pain catastrophizing to clinical outcomes
- Discuss recent controversies and misconceptions about pain catastrophizing

# Objectives

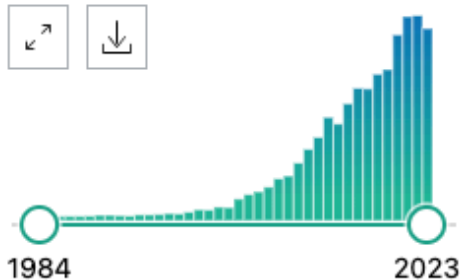
- Review findings on the effects of pain catastrophizing on various clinical outcomes

MY NCBI FILTERS 

4,939 results

Page 1 of 494

RESULTS BY YEAR



TEXT AVAILABILITY

[Neural correlates of central \*\*pain\*\* sensitization in chronic low back \*\*pain\*\*: a resting-state fMRI study.](#)

1

Cite

Fan N, Chen J, Zhao B, Liu L, Yang W, Chen X, Lu Z, Wang L, Cao H, Ma A.

Share

*Neuroradiology*. 2023 Dec;65(12):1767-1776. doi: 10.1007/s00234-023-03237-3. Epub 2023 Oct 26.

PMID: 37882803

PURPOSE: The objective of this study is to explore the neural correlates of **pain** sensitization in patients with chronic low back **pain** (cLBP). ...Furthermore, mediation analyses were performed to investigate the path association between brain alterations and **pain** ...



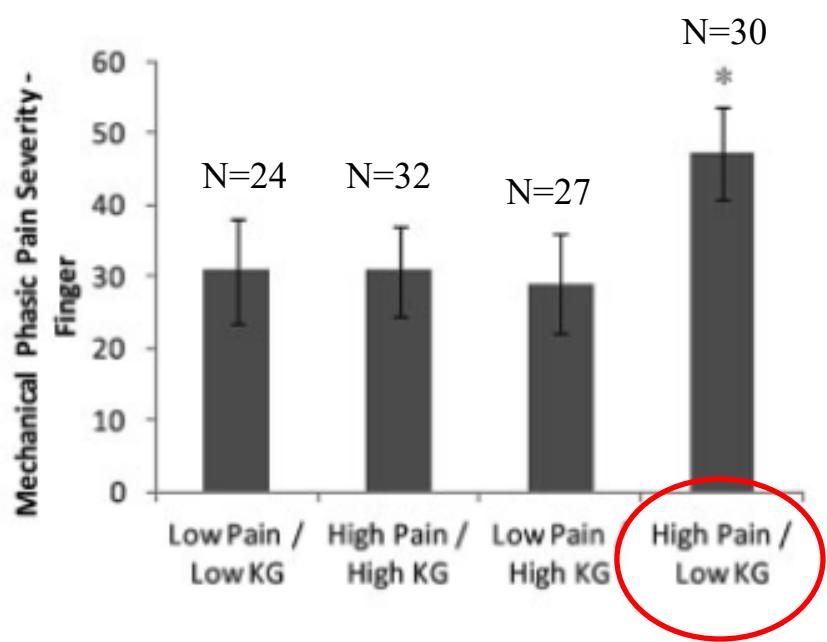
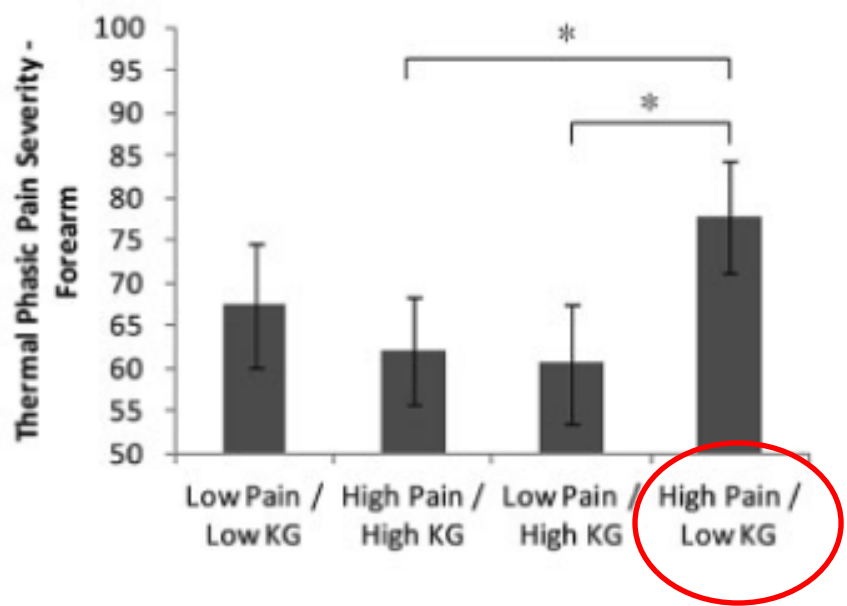
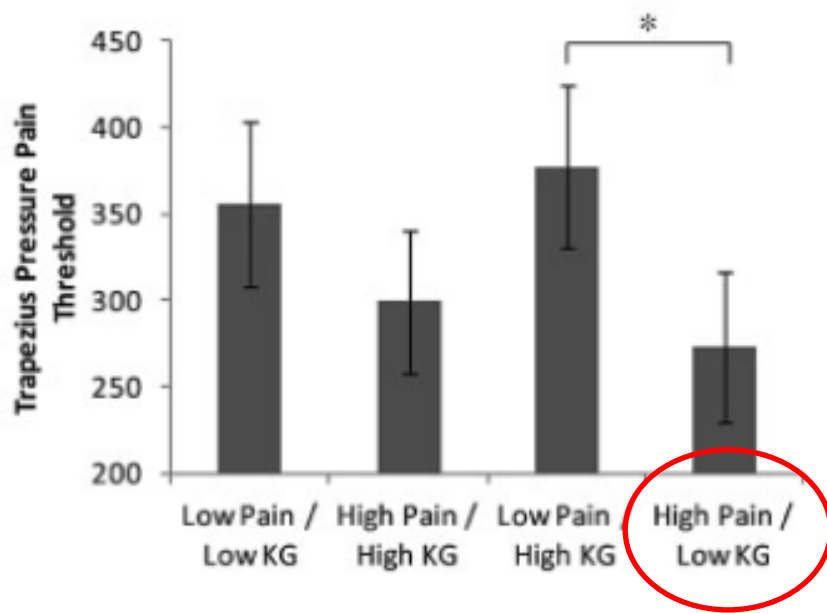
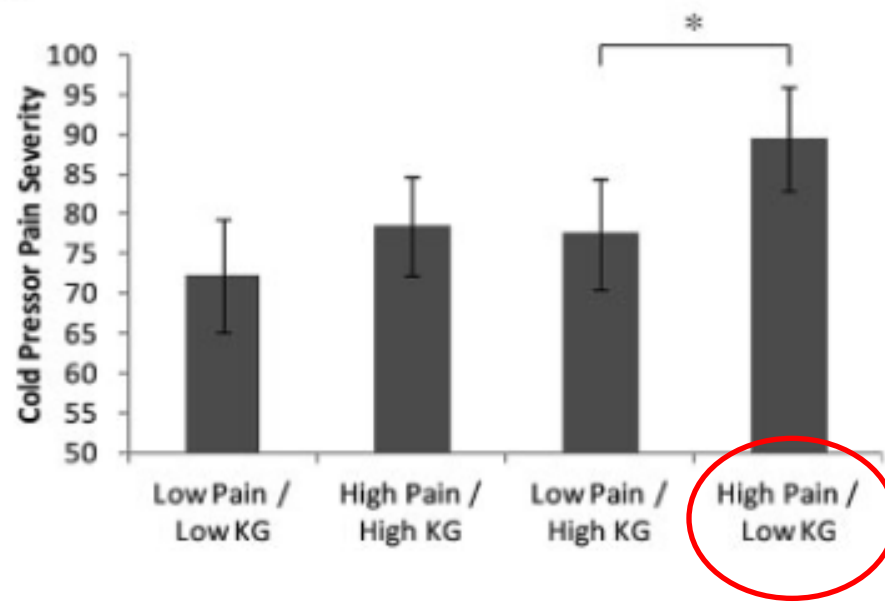
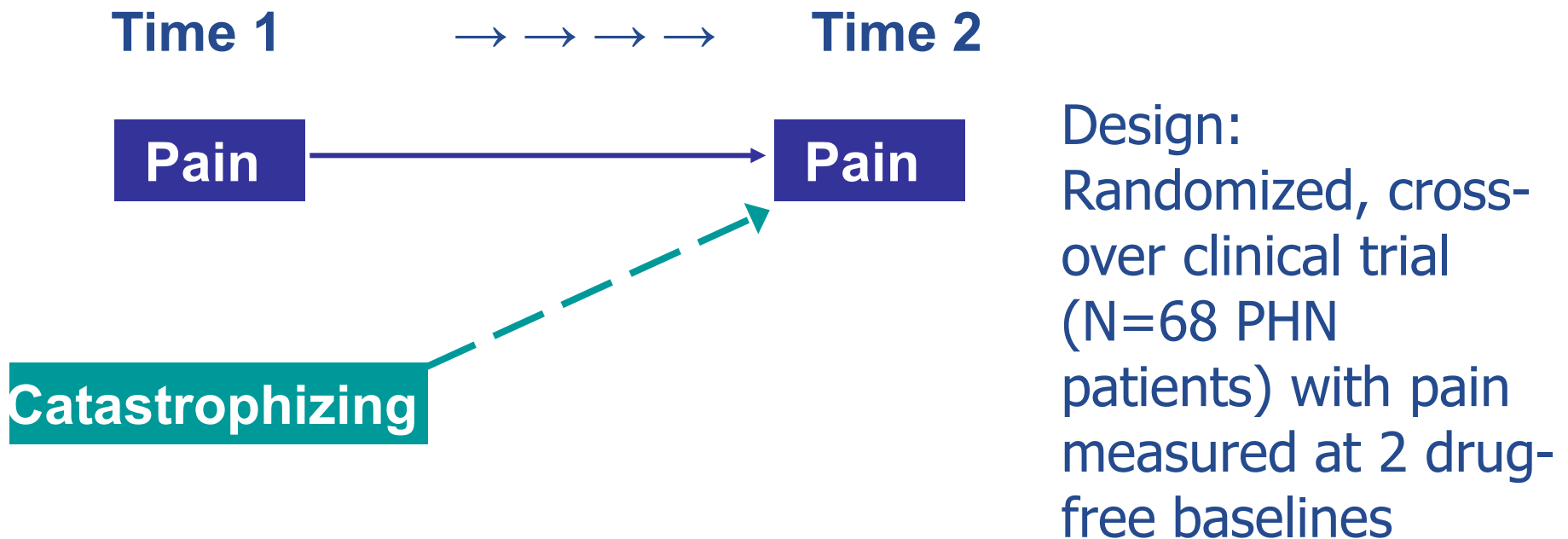
**A****B****C****D**

Figure 2 from Finan et al., *Arthritis & Rheumatism*, 2013, 65: 363-372

# Catastrophizing predicts persistence of pain<sup>1,2,3</sup>



Catastrophizing at Time 1 predicted pain at 8 weeks (Time 2), beyond the effects of pain at Time 1<sup>1</sup>

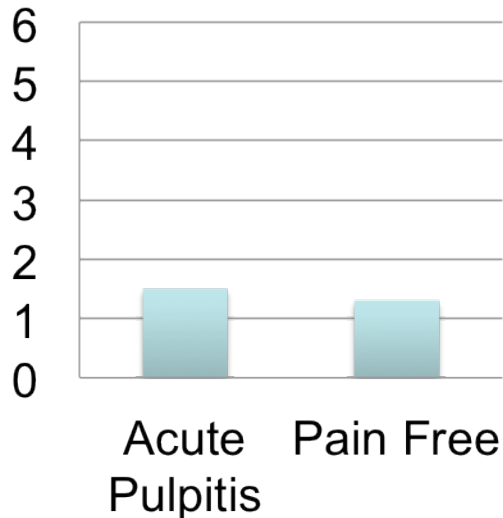
<sup>1</sup>Haythornthwaite et al. Pain coping strategies play a role in the persistence of pain in PHN. *Pain*, 2003, 106:453.

<sup>2</sup> Keefe et al., Coping with rheumatoid arthritis pain: Catastrophizing as a maladaptive strategy. *Pain*, 1989, 37: 51

<sup>3</sup> Edwards et al., Catastrophizing and depressive symptoms ... total knee replacement. *Pain Res Manage*, 2009, 14: 307

# Pain Catastrophizing

- Stable over relatively short periods of time (weeks or months)

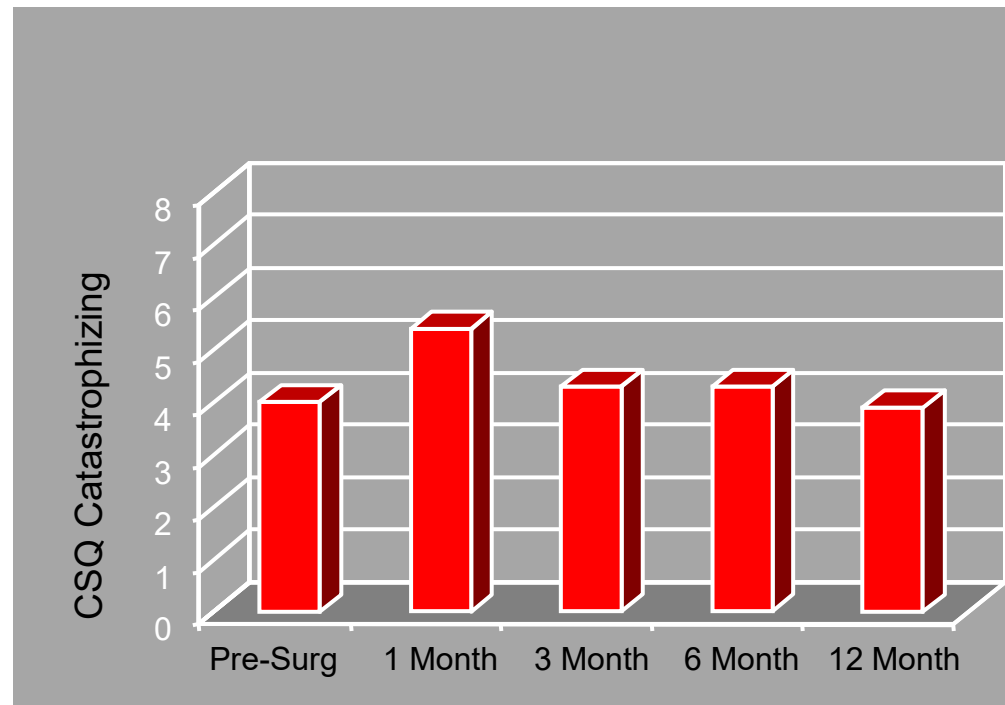


Healthy adults presenting with acute pulpitis

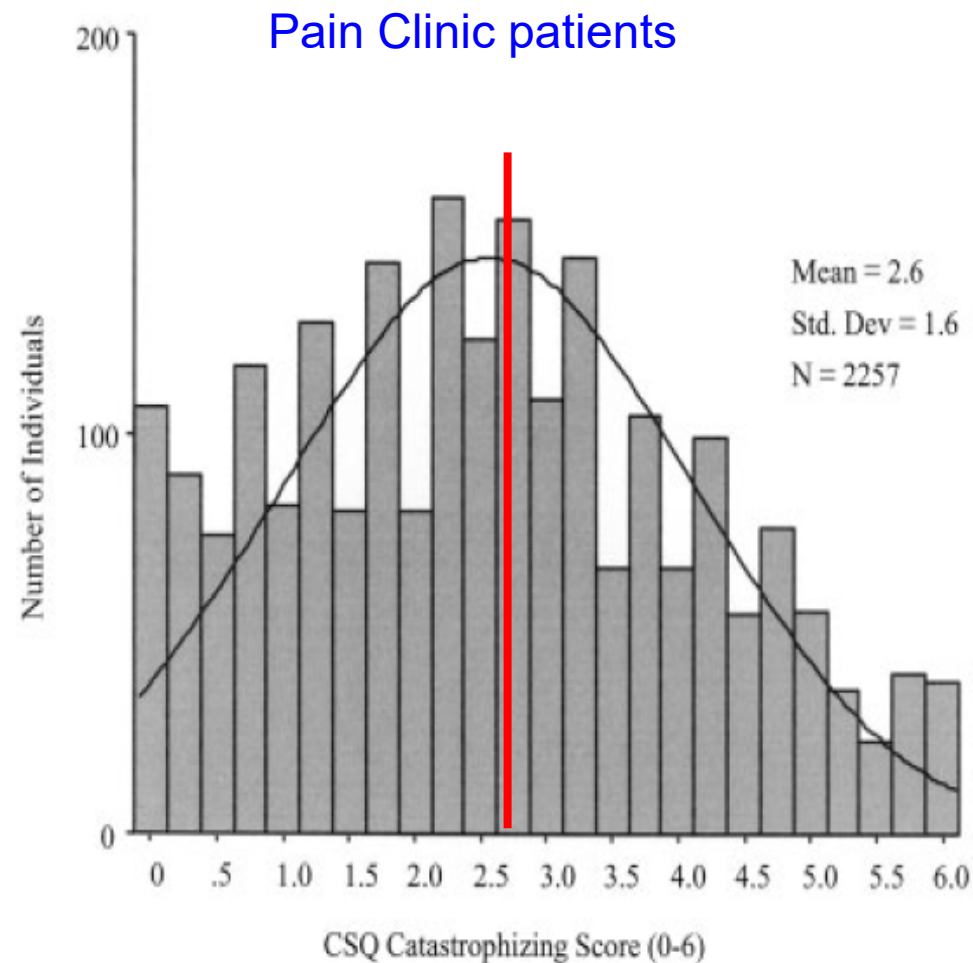
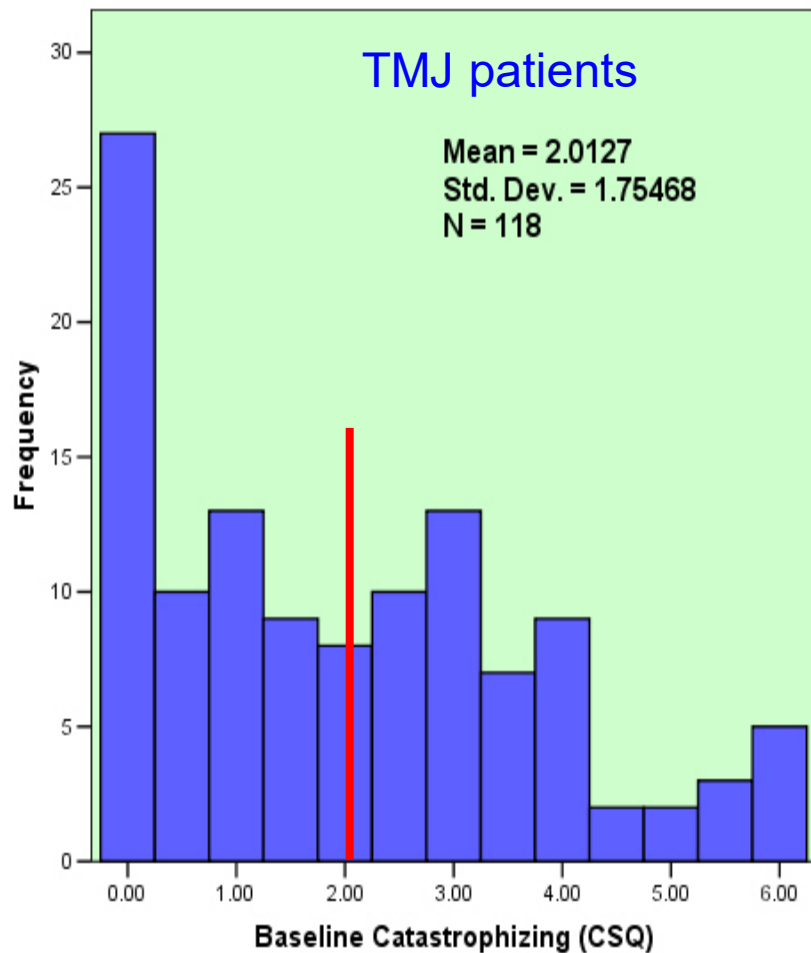
# Pain Catastrophizing

- Stable over relatively short periods of time (weeks or months)

Seniors undergoing  
TKA

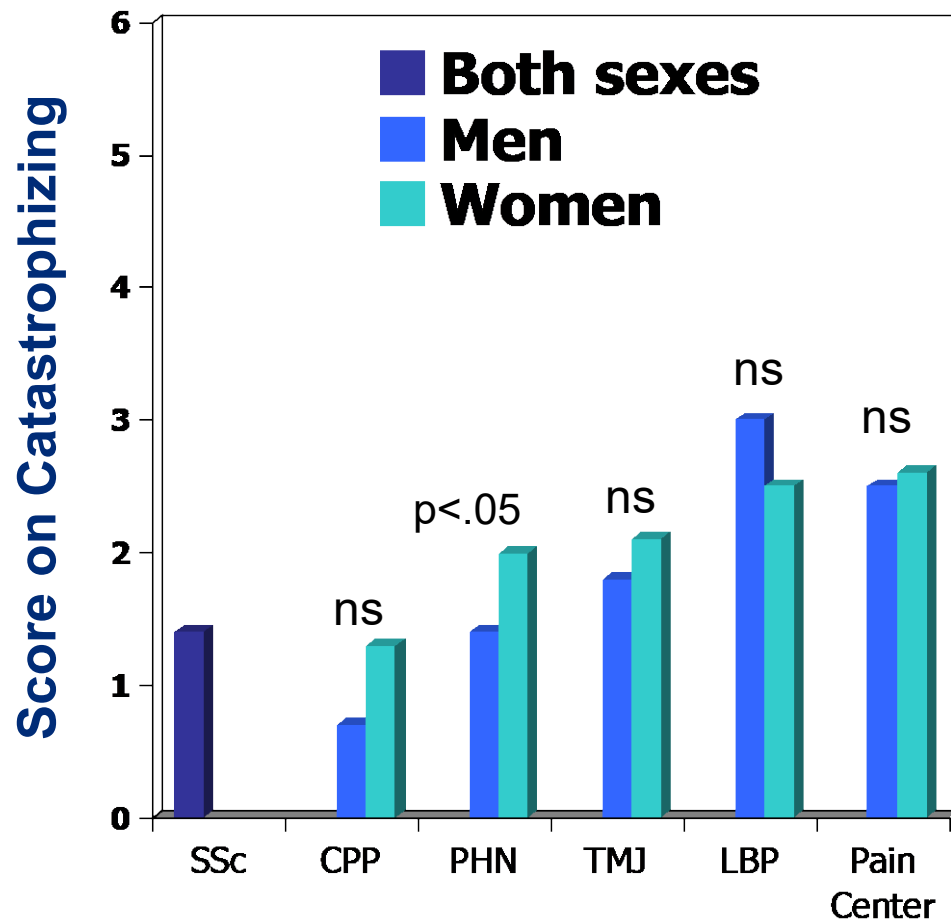


# Pain Catastrophizing





•There is some indication that catastrophizing scores increase with clinical severity/clinical setting of evaluation

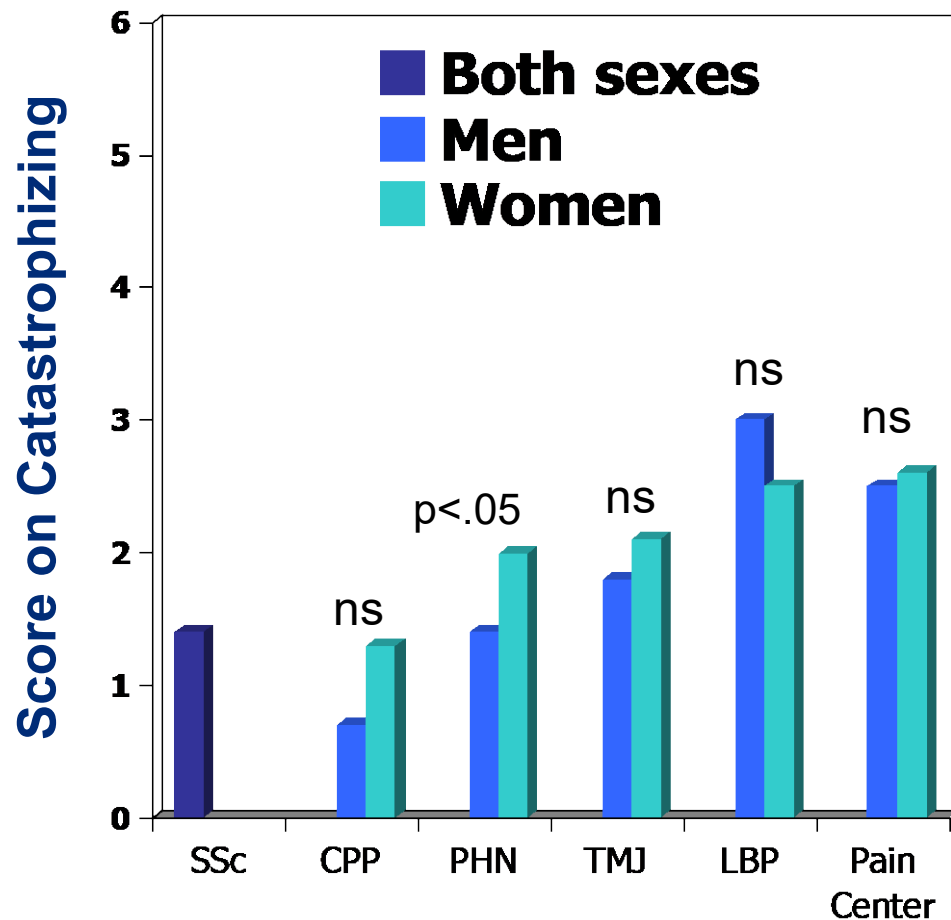


**SSc:** Edwards et al., *Clin J Pain*, 2006, 22: 639; **CPP& LBP:** Heinberg et al., *Pain*, 2004, 108:88; **PHN:** Haythornthwaite et al., *Pain*, 2003, 106: 453; **Pain Center:** Buenaver et al., *Pain*, 2007, 127: 34 **TMJ:** R01 DE13906 (NIH/NIDCR)



- There is some indication that catastrophizing scores increase with clinical severity/clinical setting of evaluation

- Is this related to **duration of pain**: as pain endures, does catastrophizing increase?

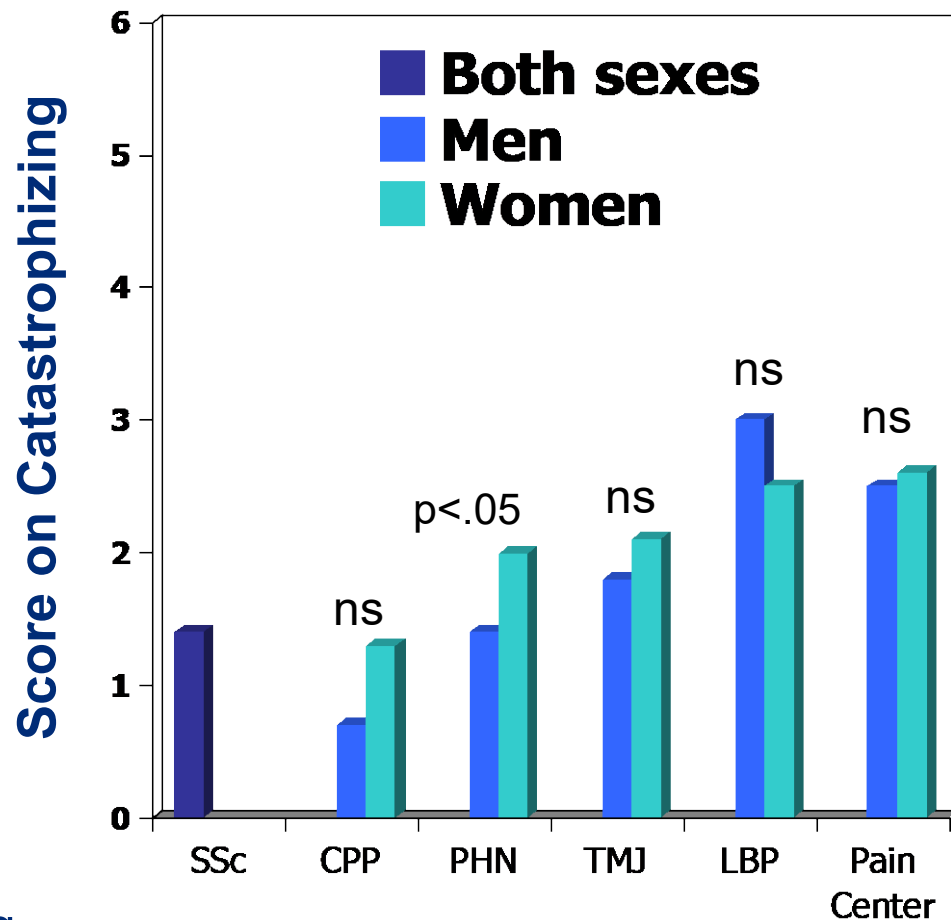




- There is some indication that catastrophizing scores increase with clinical severity/clinical setting of evaluation

- Is this related to duration of pain: as pain endures, does catastrophizing increase?

- Is this a **selection process**: do patients with more catastrophizing fail treatment?





# (Trait) Pain Catastrophizing

- Trait Catastrophizing (When I feel pain....)
  - Stable over relatively short periods of time

# (Trait) Pain Catastrophizing

- Trait Catastrophizing
  - Stable over relatively short periods of time
  - Modest prediction of clinical pain outcomes
    - Magnitude varies across clinical samples



# (Trait) Pain Catastrophizing

Time 1



Time 2

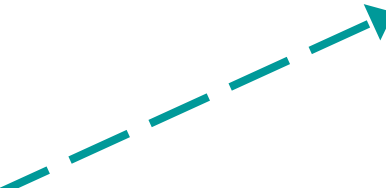
Pain



Pain

**Total of  
31% of the  
variance in  
Time 2 pain**

**Catastrophizing**



**Only 6% for CAT**

Design: Randomized, cross-over clinical trial (N=68 PHN patients) with pain measured at 2 drug-free baselines

<sup>1</sup>Haythornthwaite et al. Pain coping strategies play a role in the persistence of pain in PHN. *Pain*, 2003, 106:453.

<sup>2</sup> Keefe et al., Coping with rheumatoid arthritis pain: Catastrophizing as a maladaptive strategy. *Pain*, 1989, 37: 51

# (Trait) Pain Catastrophizing

Table 4

Final model for BPI Pain Severity at 6 months after surgery

| Pre-Operative Parameter         | Estimate | 95% Confidence Limits | P-value |
|---------------------------------|----------|-----------------------|---------|
| BPI Pain Severity Pre-Surgery   | 0.12     | -0.01 0.26            | 0.07    |
| State PCS (Walking) Pre-Surgery | 0.06     | -0.009 0.13           | 0.09    |
| PCS Total Pre-Surgery           | 0.02     | 0.002 0.05            | 0.04    |
| Opioid Use Pre-Surgery          | 1.18     | 0.20 2.16             | 0.02    |
| Sleep Efficiency Pre-Surgery    | -0.03    | -0.07 -0.007          | 0.02    |
| Other Chronic Pain Pre-Surgery  | 0.78     | 0.18 1.39             | 0.01    |
| Painful Areas Pre-Surgery       | 0.16     | 0.04 0.29             | 0.01    |
| PROMIS Anxiety Pre-Surgery      | 0.07     | 0.02 0.12             | 0.006   |
| NEO Agreeableness Pre-Surgery   | -0.07    | -0.12 -0.02           | 0.002   |

Cohort study of 248 patients undergoing Total Knee Arthroscopy Followed out to 6 mos Post-surgery.

30% pain  $\geq$  3 at 6 mos

# Objectives

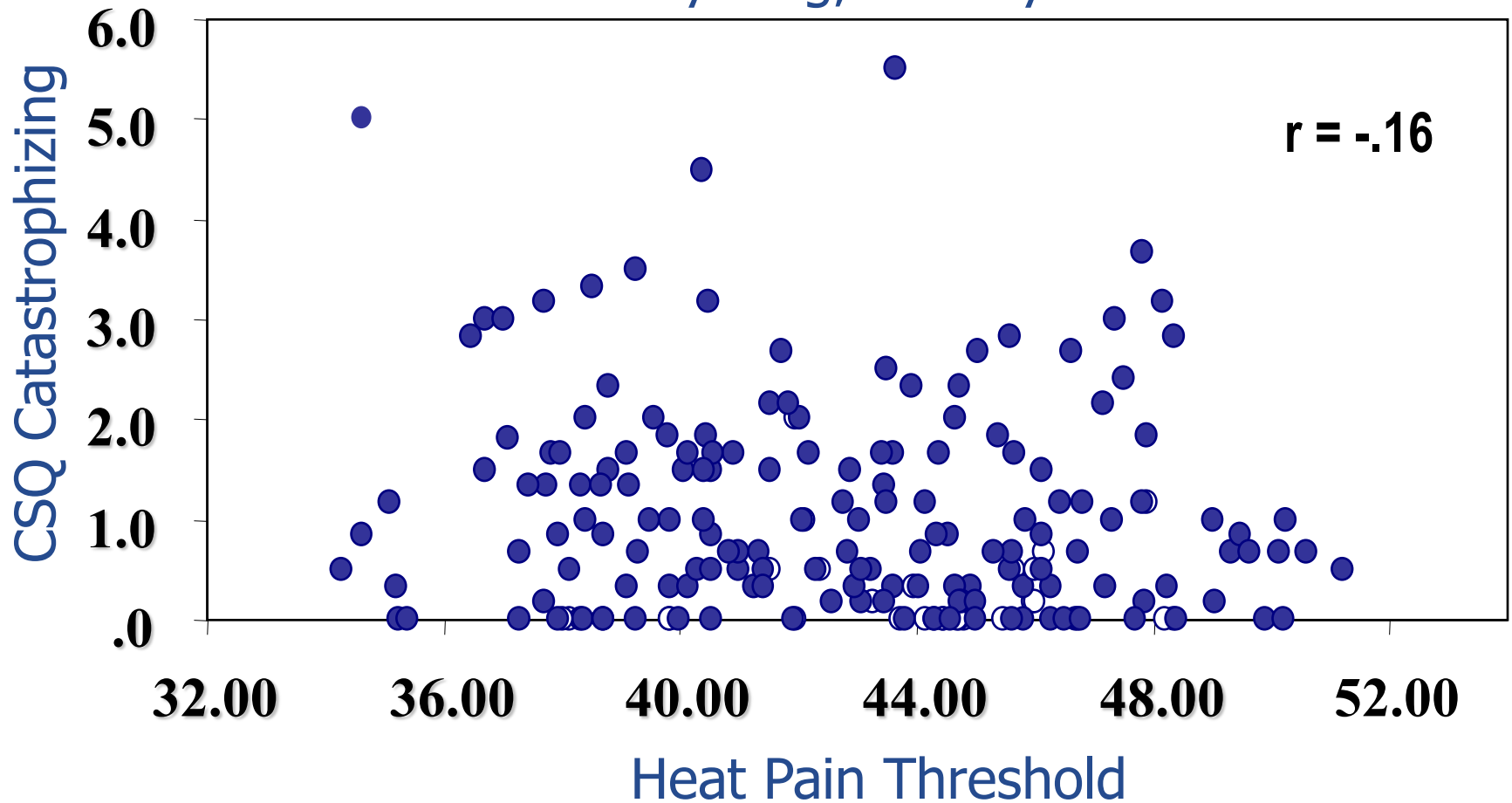
- Review recent findings on the effects of pain catastrophizing on various clinical outcomes
- Identify pathophysiological **mechanisms** linking pain catastrophizing to clinical outcomes

# (Trait) Pain Catastrophizing

- Trait Catastrophizing
  - Stable over relatively short periods of time
  - Modest correlation to pain
    - Magnitude varies across clinical samples
    - No/inconsistent association with various measures of pain sensitivity in healthy volunteers

# (Trait) Pain Catastrophizing

Male and female young, healthy adults : N=198



# Trait AND Situational

- Situational Catastrophizing (Specific thoughts in specific situation)
  - typically reflecting on distinct experience of pain (e.g., QST experience)
  - or can be obtained through daily diaries and relate to CAT that day



# Trait AND Situational

- Situational Catastrophizing (Specific thoughts in specific situation)
  - typically reflecting on distinct experience of pain (e.g., QST experience)
  - or can be obtained through daily diaries and relate to CAT that day

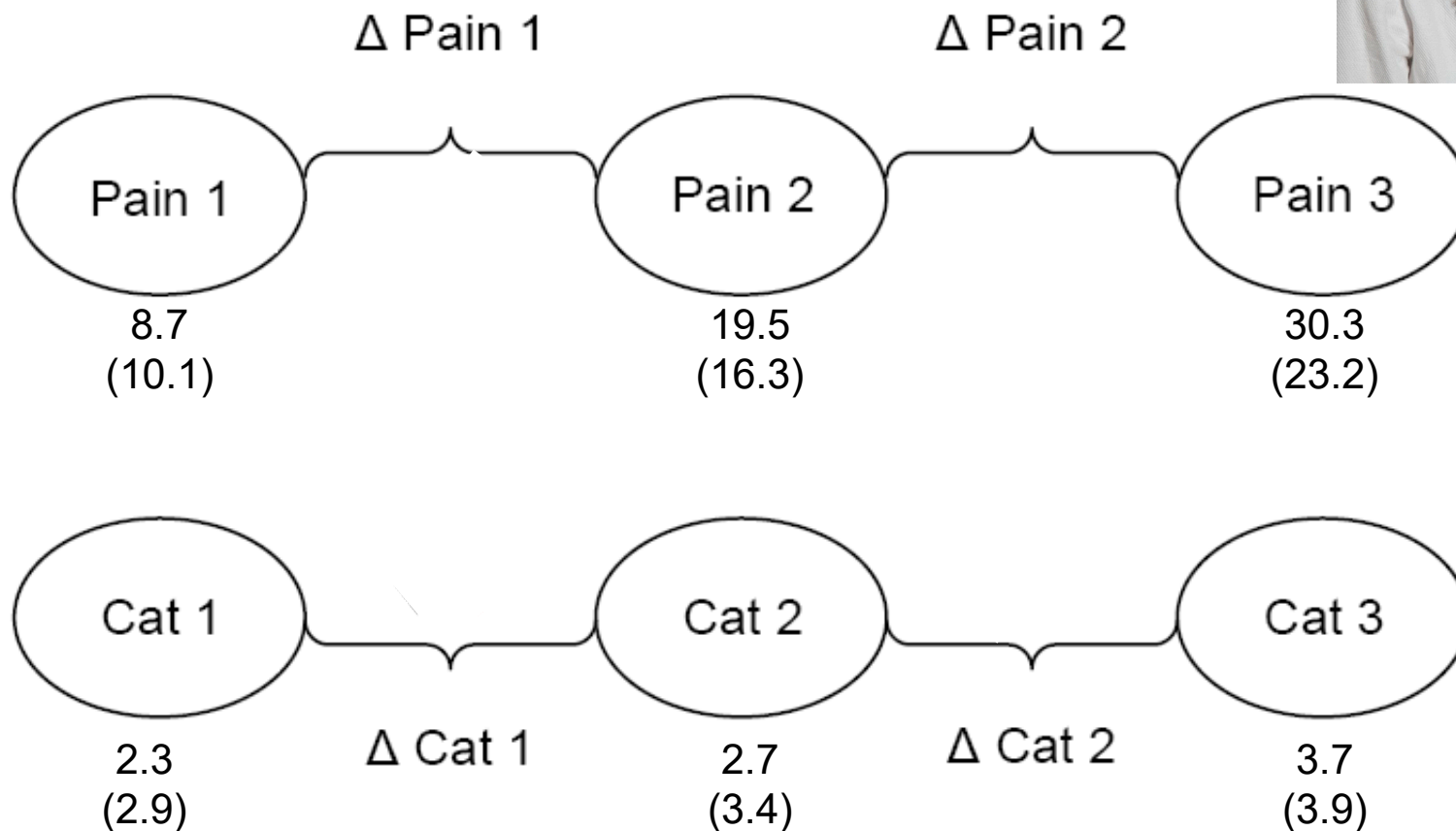
**In healthy subjects, does situational CAT predict outcomes?**



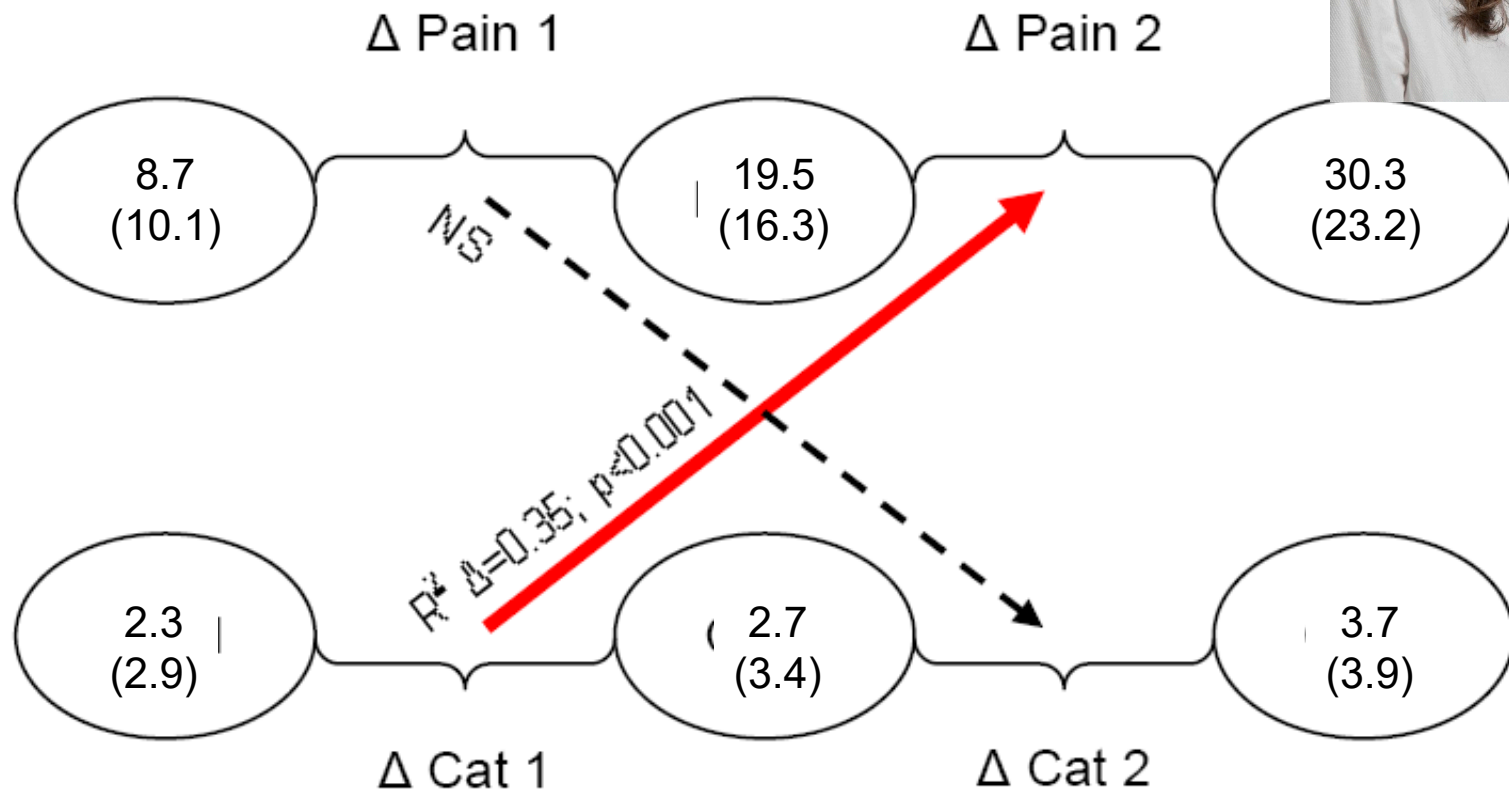
# Situational CAT $\rightarrow$ $\rightarrow$ Pain



N=38 healthy adults



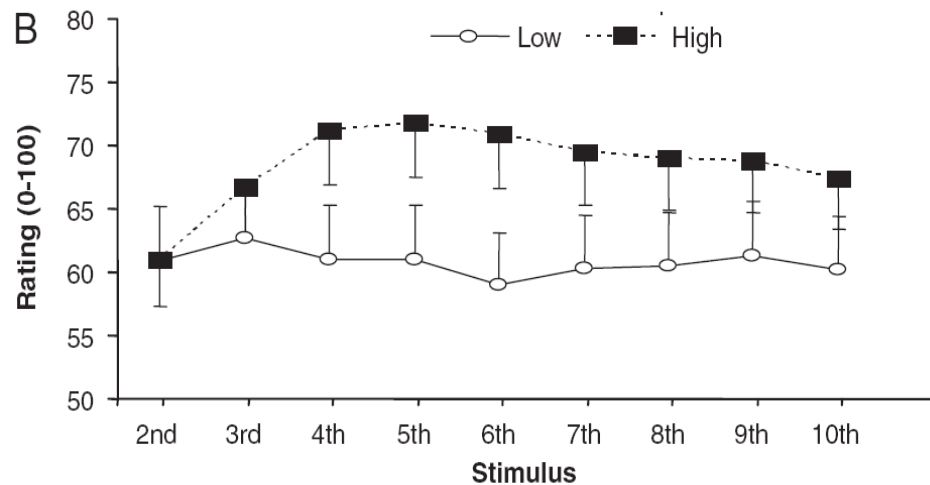
# Situational CAT → → Pain





# Situational CAT and pain modulation

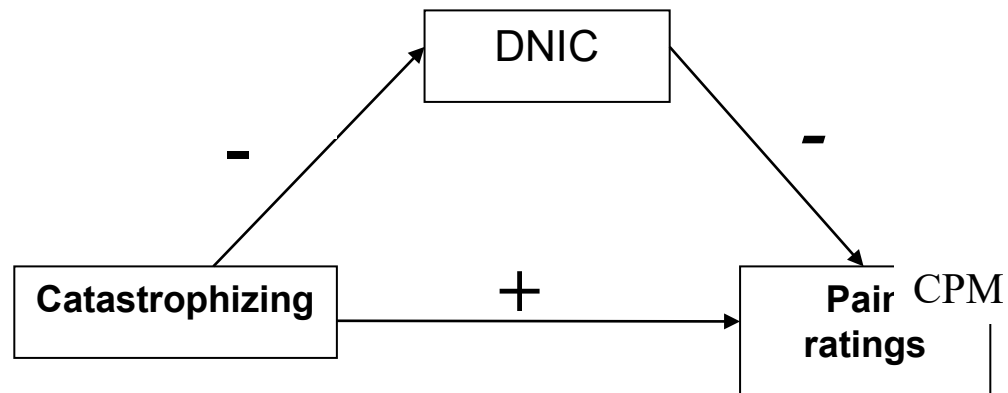
↑ Temporal summation



N=38 healthy women, 49° C stimulus

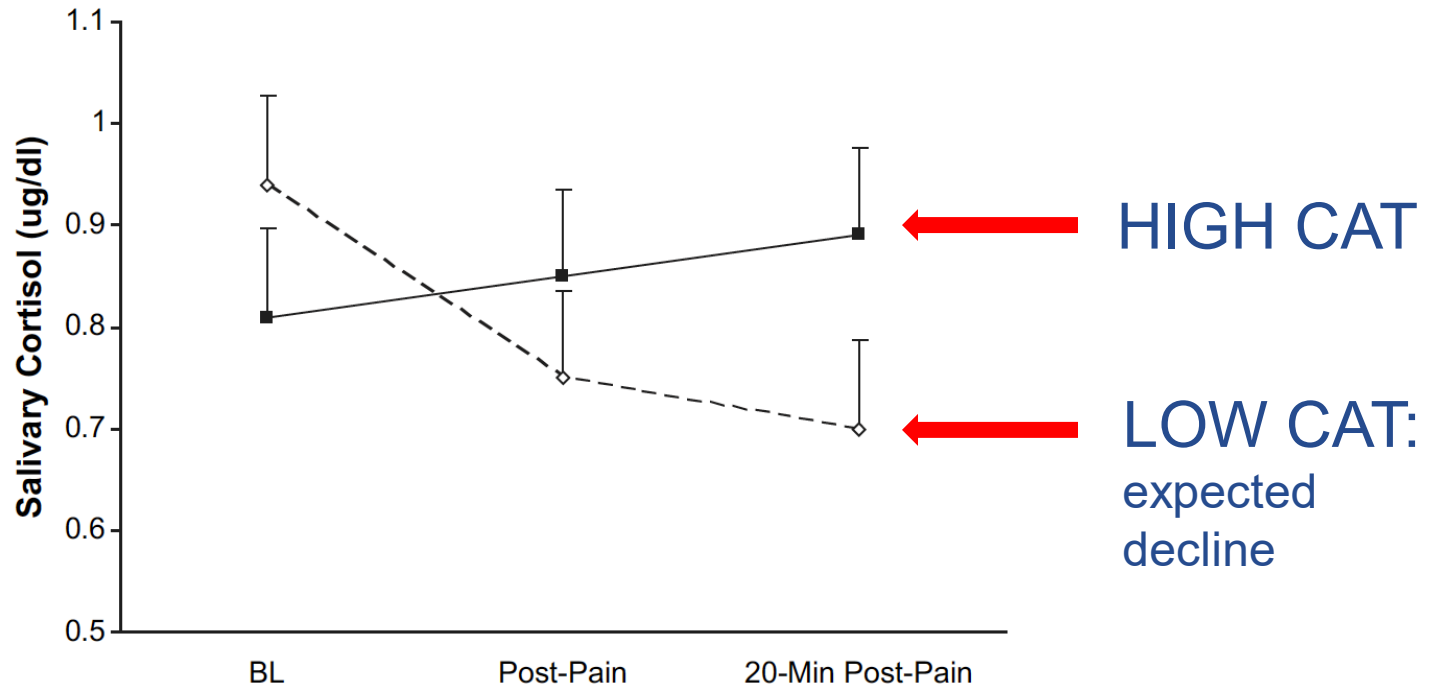
# Situational CAT and pain modulation

↓ Conditioned Pain Modulation



N= 35 healthy men and women

# Situational CAT



**Figure 1.** Marginal means (SE) of salivary cortisol values ( $\mu\text{g/dL}$ ) at hypothetical values of high (+1 SD) and low (-1 SD) Pain Catastrophizing Scale (PCS) scores.

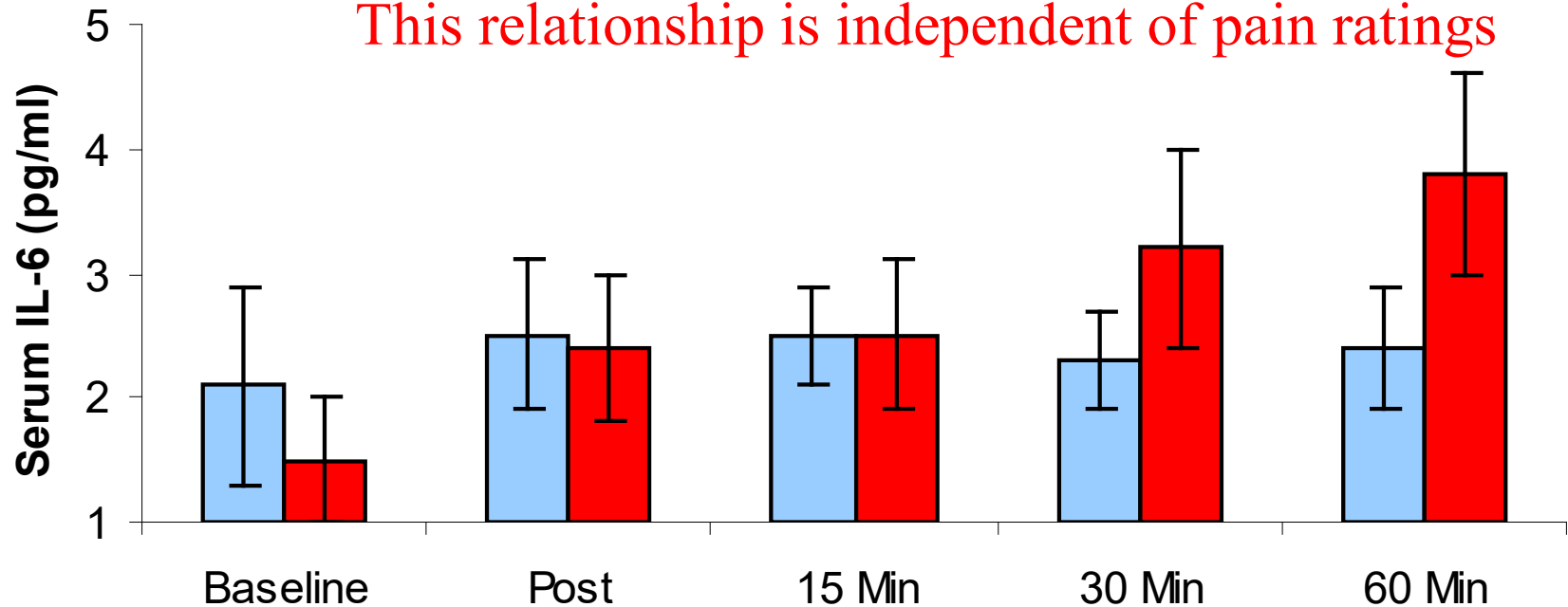
Healthy (n= 22) and TMD (n=39) subjects  
45 minutes after final awakening – morning peak

# Situational CAT

## Serum IL-6 For Low and High Catastrophizers

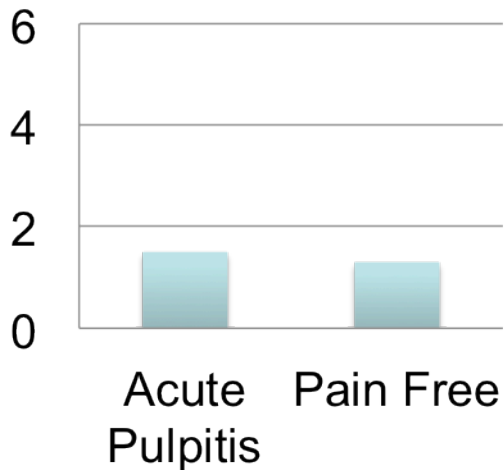
Low Cat High Cat

This relationship is independent of pain ratings

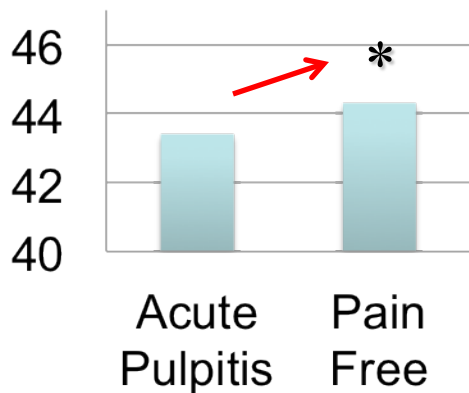




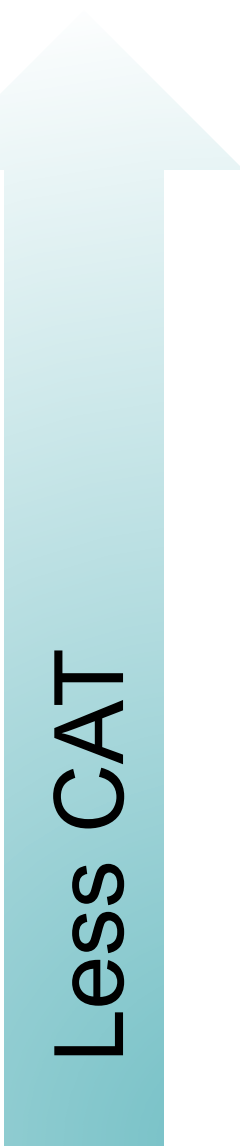
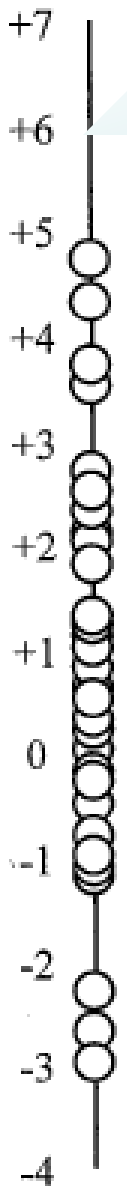
### Pain CAT



### Heat Pain Th



### $\Delta$ HPTH

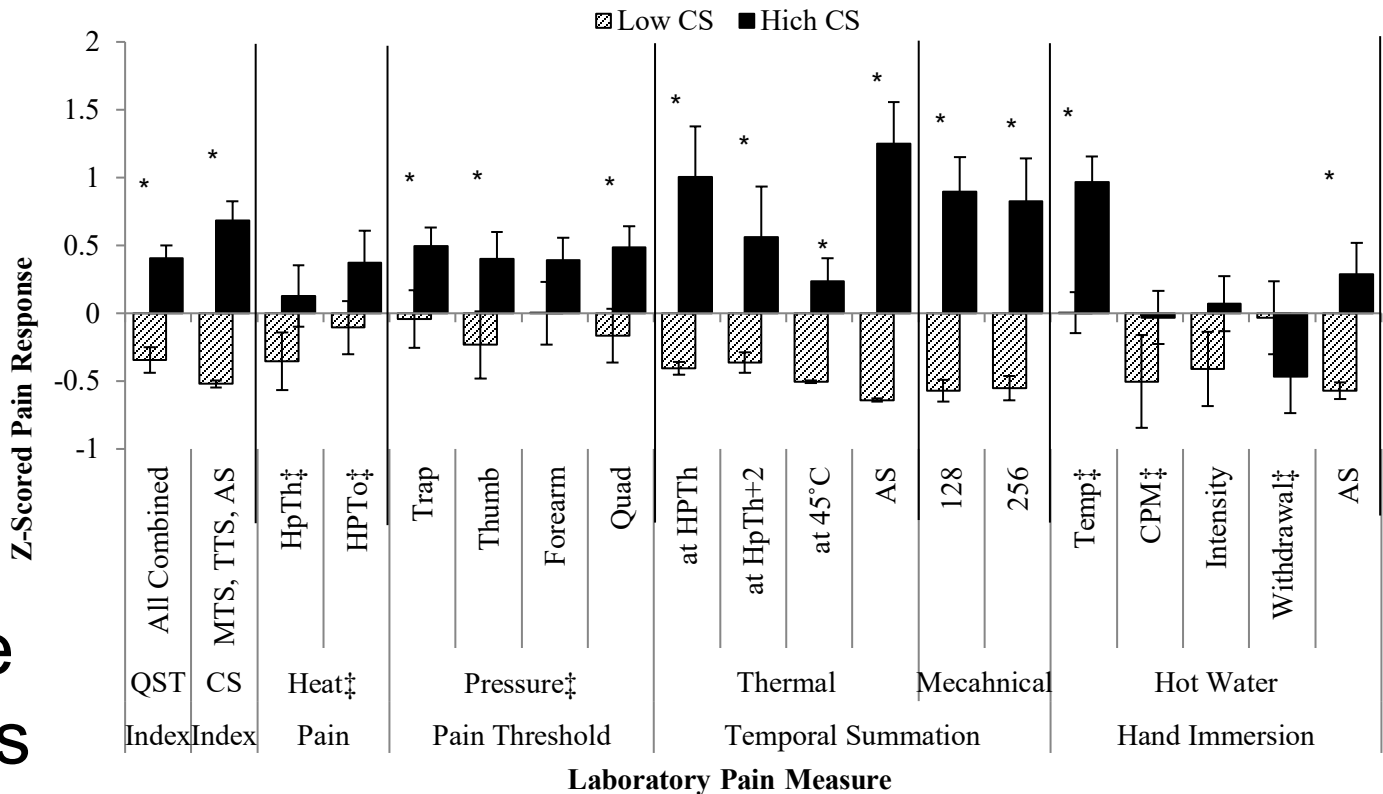


? Is CAT associated with PROLONGED sensitization following acute pain?





# Adult sickle cell patients



| Measure         | Low CS (N=17) | High CS (N=21) | p value |
|-----------------|---------------|----------------|---------|
| Trait CAT       | 24.6 (15.4)   | 26.4 (11.7)    | 0.7     |
| Situational CAT | 0.4 (0.3)     | 1.4 (0.9)      | <.001   |
| Daily Diary CAT | 5.0 (8.2)     | 22.1 (20.2)    | 0.003   |

# Trait AND Situational CAT

- Situational Catastrophizing
  - Inconsistently correlates with dispositional catastrophizing (healthy vs. arthritis vs. TMD) and depressive symptoms





# PAIN<sup>®</sup>

Z. Trost et al. • 156 (2015) 514–520

## **Heritability of pain catastrophizing and associations with experimental pain outcomes: a twin study**

Zina Trost<sup>a</sup>, Eric Strachan<sup>b</sup>, Michael Sullivan<sup>c</sup>, Tine Vervoort<sup>d</sup>, Ally R. Avery<sup>e</sup>, Niloofar Afari<sup>f,\*</sup>

Heritability of CAT is estimated to be 37%

...environmental contribution is estimated to be 63%

Genes

# Pain Catastrophizing Develops Early

- Data suggest that CAT develops early in healthy people
  - We see CAT in children and adolescents





# Polymorphism in Serotonin Receptor 3B Is Associated with Pain Catastrophizing

**Emilia Horjales-Araujo<sup>1,2\*</sup>, Ditte Demontis<sup>3</sup>, Ellen Kielland Lund<sup>1</sup>, Nanna Brix Finnerup<sup>1</sup>, Anders D. Børglum<sup>3</sup>, Troels Staehelin Jensen<sup>1,5</sup>, Peter Svensson<sup>2,6</sup>, Lene Vase<sup>1,4</sup>**

**1** Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark, **2** Center for Functionally Integrative Neuroscience (CFIN), MindLab, Aarhus University Hospital, Aarhus, Denmark, **3** Department of Biomedicine and Center for Integrative Sequencing (iSEQ), Aarhus University, Aarhus, Denmark, **4** Department of Psychology and Behavioral Sciences, Aarhus University, Aarhus, Denmark, **5** Department of Neurology, Aarhus University Hospital, Aarhus, Denmark, **6** Section of Clinical Oral Physiology, Department of Dentistry, Aarhus University, Aarhus, Denmark

PLOS ONE

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Genes

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PLOS ONE

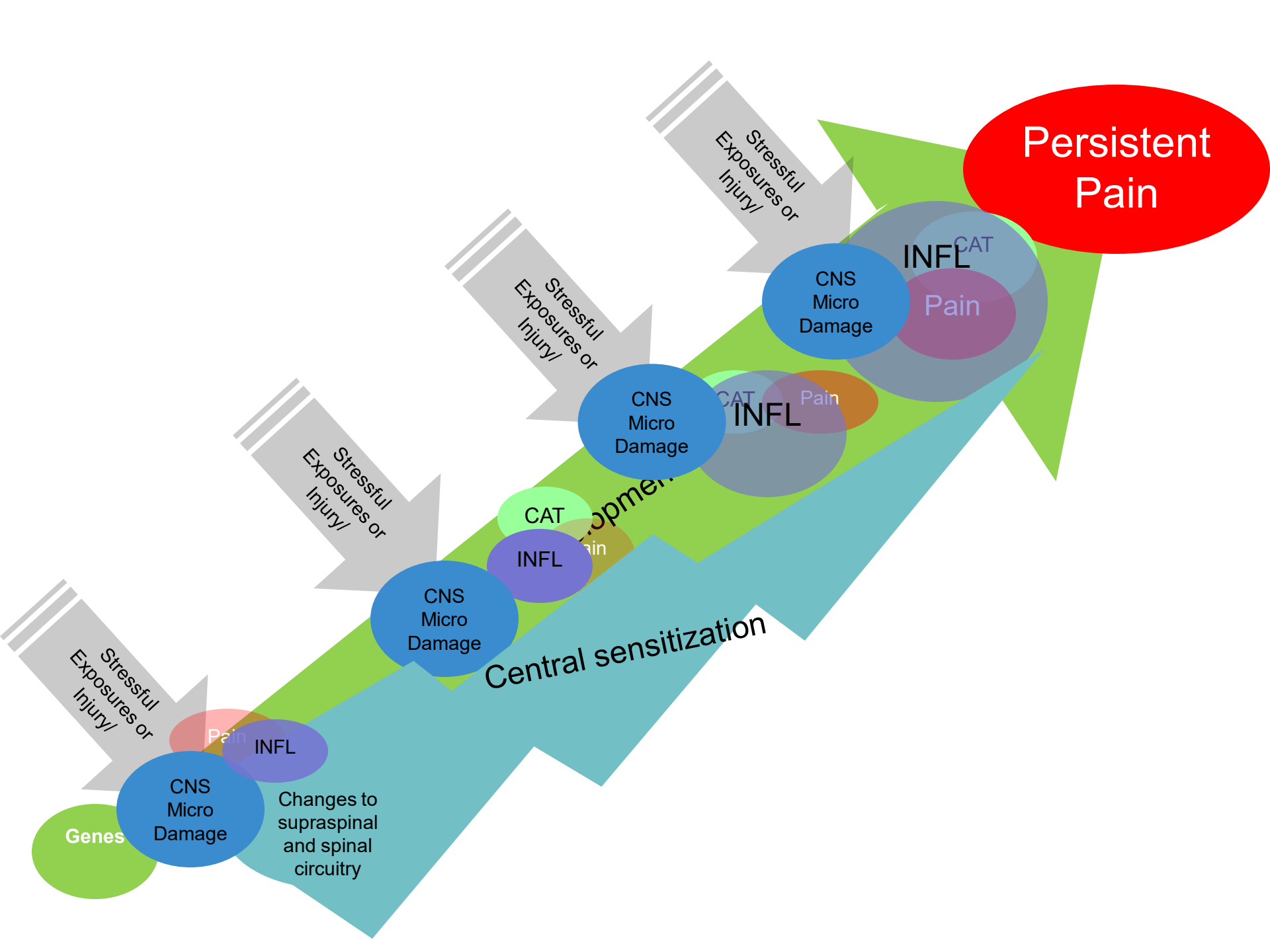
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Arthritis Care & Research  
Vol. 68, No. 11, November 2016, pp 1671–1680  
DOI 10.1002/acr.22876  
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ORIGINAL ARTICLE

## Biopsychosocial Influence on Shoulder Pain: Influence of Genetic and Psychological Combinations on Twelve-Month Postoperative Pain and Disability Outcomes

STEVEN Z. GEORGE,<sup>1</sup> SAMUEL S. WU,<sup>1</sup> MARGARET R. WALLACE,<sup>2</sup> MICHAEL W. MOSER,<sup>1</sup> THOMAS W. WRIGHT,<sup>1</sup> KEVIN W. FARMER,<sup>1</sup> WARREN H. GREENFIELD III,<sup>1</sup> YUNFENG DAI,<sup>1</sup> HUA LI,<sup>2</sup> AND ROGER B. FILLINGIM<sup>1</sup>



Persistent Pain

Stressful Exposures or Injury/

Stressful Exposures or Injury/

Stressful Exposures or Injury/

Stressful Exposures or Injury/

Central sensitization

Neuroplasticity

Changes to supraspinal and spinal circuitry

CNS Micro Damage

INFL

Pain

CAT

CNS Micro Damage

INFL

Pain

CAT

CNS Micro Damage

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INFL

Pain

Genes

# Objectives: Pain-related suffering

- Review findings on the effects of pain catastrophizing on various pain outcomes
- Identify pathophysiological mechanisms linking pain catastrophizing to clinical outcomes
- Discuss recent controversies and misconceptions about pain catastrophizing



# What are the pressing issues?

- CAT is a robust predictor of the individual's experience of pain.
  - Yet there are **inconsistencies** that need to be understood
- There is a reasonable signal that CAT is associated with (even provokes?) mechanisms that contribute to pain and its perpetuation....it places people at risk for chronification

# What are the pressing issues?

- We know very little about the **developmental and environmental factors** that influence CAT over time

# Words of caution

- Patients and their advocates express concern that health care providers use CAT to:
  - Be dismissive about their suffering
  - Blame them for their suffering
  - Question the authenticity of their pain complaints

# In Closing

- I hope I have convinced you that CAT is a very important dimension of the experience of a subgroup of individuals experiencing pain that puts them at risk to experience more pain and disability, continue experiencing pain over time, develop central sensitization, leading to more pain and suffering.
- These patients need your respect, understanding, and care

# Thank you to the NIH



National Institute of  
Neurological Disorders  
and Stroke



National Institute of Dental  
and Craniofacial Research



National Institute of  
Arthritis and Musculoskeletal  
and Skin Diseases



National Center for  
Complementary and  
Integrative Health



National Heart, Lung,  
and Blood Institute

And my many collaborators, particularly Claudia  
Campbell and Rob Edwards, among others:

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M. Smith, PhD

L. Buenaver, PhD

Pat Carroll, M.D.

C. Haywood, Ph.D. (deceased)

S. Lanzkron, M.D.

P. Quartana, Ph.D.

B. Goodin, Ph.D.

G. Page, RN, PhD

Numerous post-docs and the expert staff who run our studies