

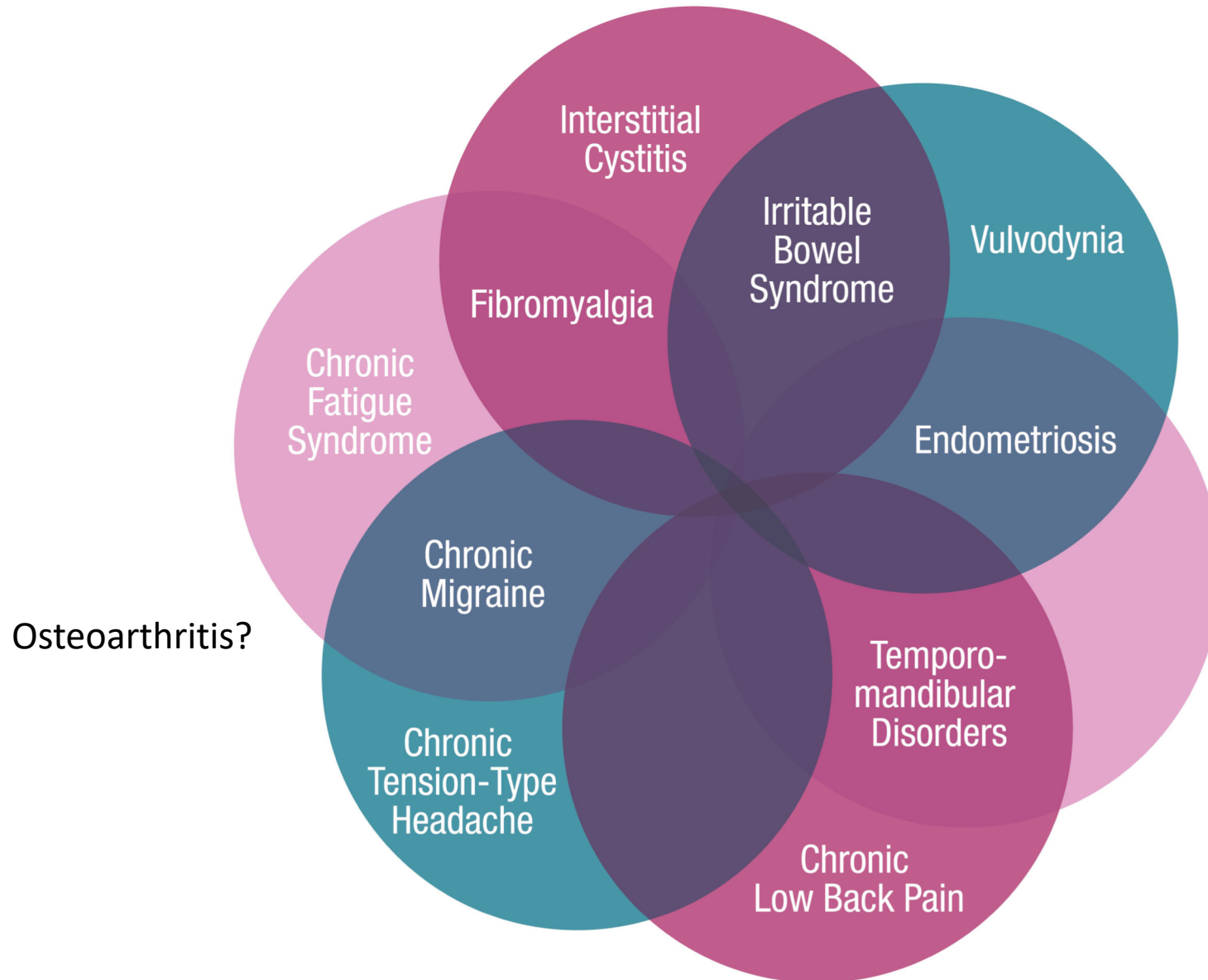


Central Sensitization and Chronic Overlapping Pain Conditions

Roger B. Fillingim, PhD
Distinguished Professor & Director
Pain Research & Intervention Center of Excellence
University of Florida, Gainesville, FL USA

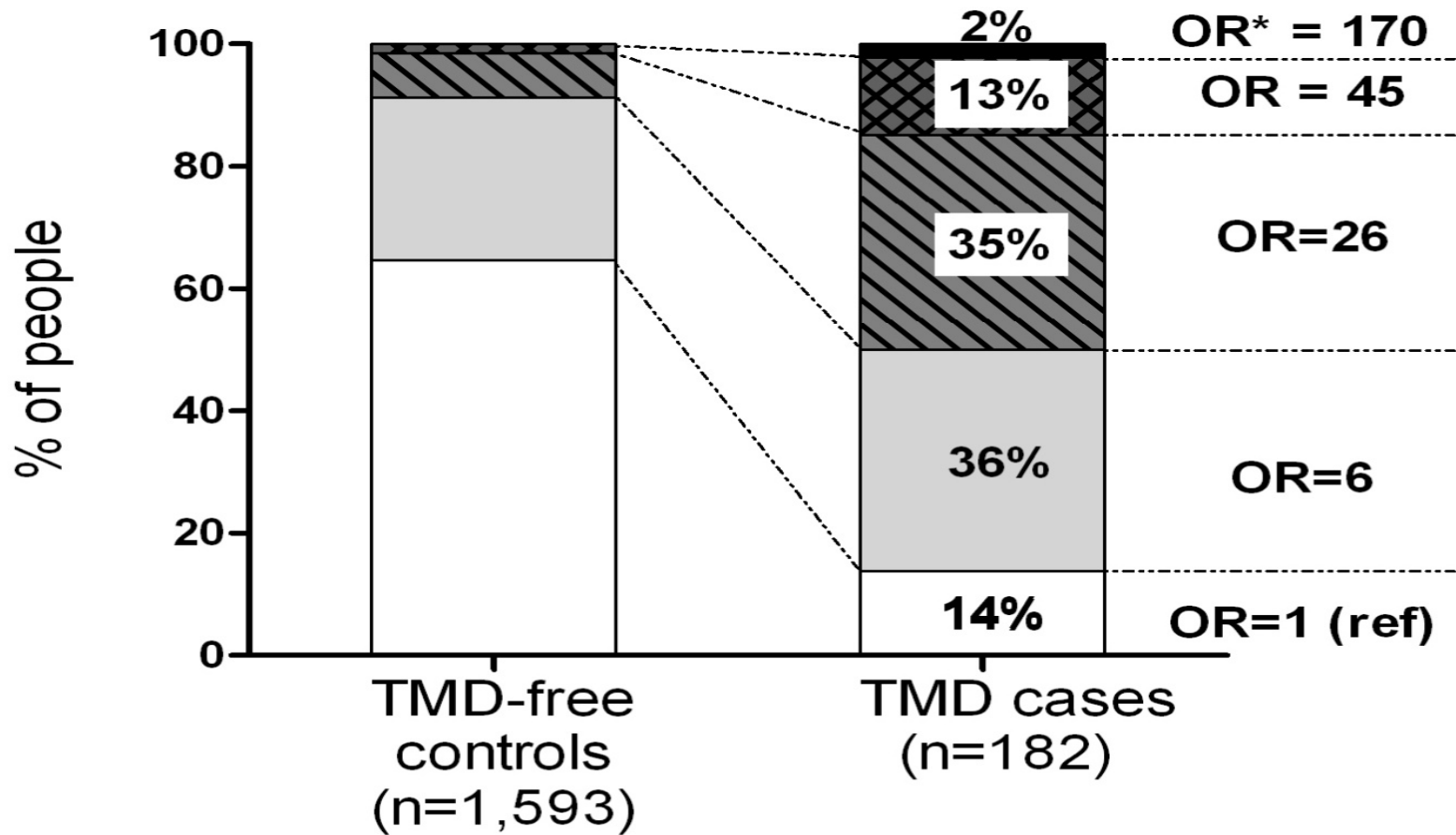
Pain Conditions Overlap

Chronic Overlapping Pain Conditions (COPCs)



Number of TMD-related, idiopathic pain conditions

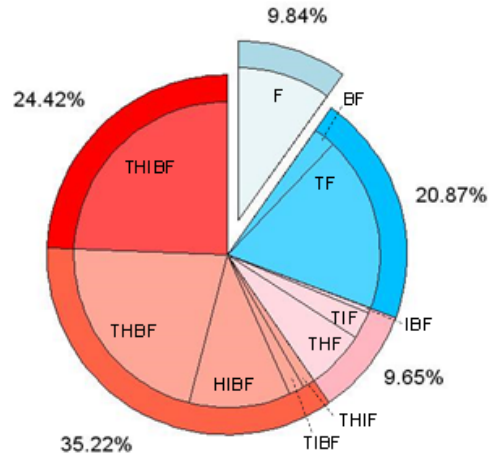
0
 1
 2
 3
 4



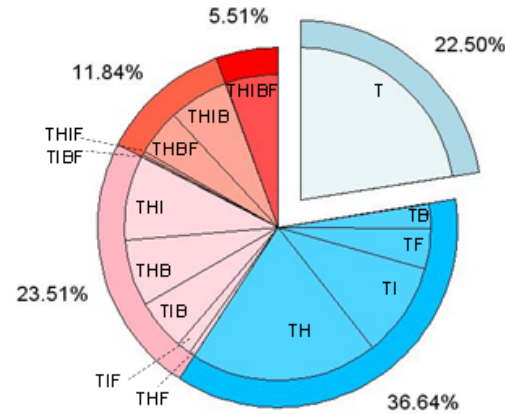
From the OPPERA Study. Idiopathic pain conditions (IPCs) related to TMD. The four related conditions were: headache, low back pain, widespread pain and IBS.

*OR = odds ratio for TMD in people with 1, 2, 3 or 4 IPCs relative to people with no IPCs

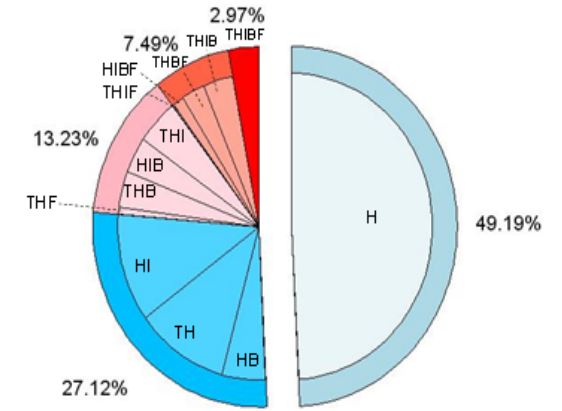
Fibromyalgia cases



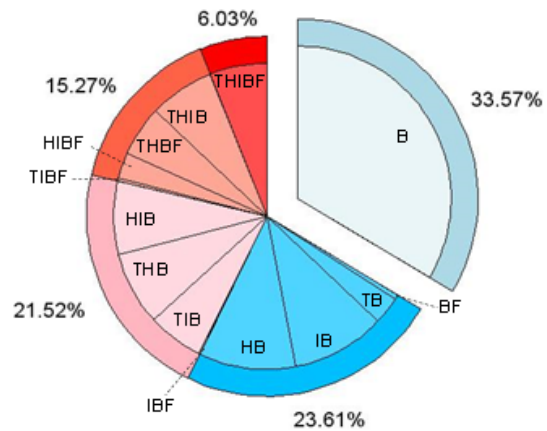
TMD cases



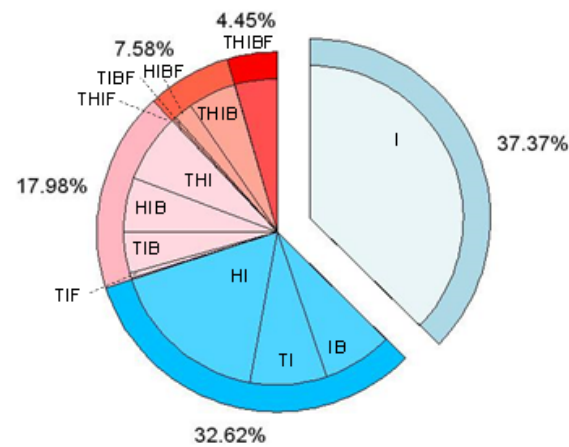
Headache cases



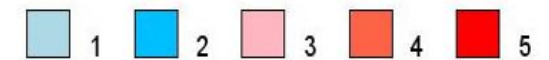
Low back pain cases



IBS cases



Number of overlapping conditions*



Percentages represent weighted percentage of subjects with permutations of five IPCs: T=TMD (unweighted n=182, [weighted n=108 cases]), H=Headache (270 [201] cases), I=Irritable Bowel Syndrome (158 [134] cases), B=Low Back Pain (139 [99] cases), F=Fibromyalgia (52 [24] cases). Weights adjust for sampling probabilities of TMD cases and controls when enrolled in the OPPERA-1 project and probability of cohort retention in this OPPERA-2 analysis.



Review

Central sensitization: Implications for the diagnosis and treatment of pain

Clifford J. Woolf

Program in Neurobiology and FM Kirby Neurobiology Center, Children's Hospital Boston, Department of Neurobiology, Harvard Medical School, Boston, MA, USA

Central Sensitization

...an amplification of neural signaling within the CNS that elicits pain hypersensitivity...

Clinical Signs of Central Sensitization

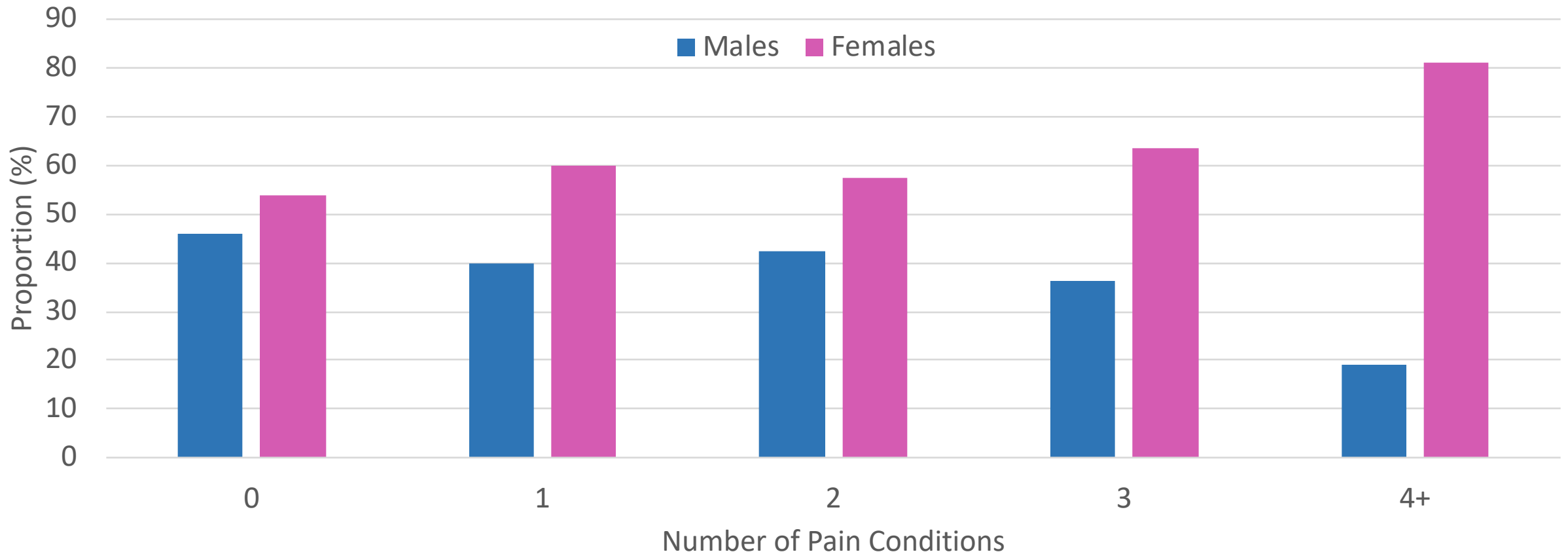
- Pain mediated by low threshold A β fibers
- Spread of pain sensitivity to areas with no demonstrable pathology
- Aftersensations
- Enhanced temporal summation
- Maintenance of pain by low frequency stimuli that normally do not evoke any ongoing pain

Risk Factors Common to Chronic Overlapping Pain Conditions

- Female Sex*
- **Widespread Pain Sensitivity**
- Psychological Factors*
- Somatic Symptom Burden*
- Familial/Genetic Factors*

* Previously associated with pain sensitivity

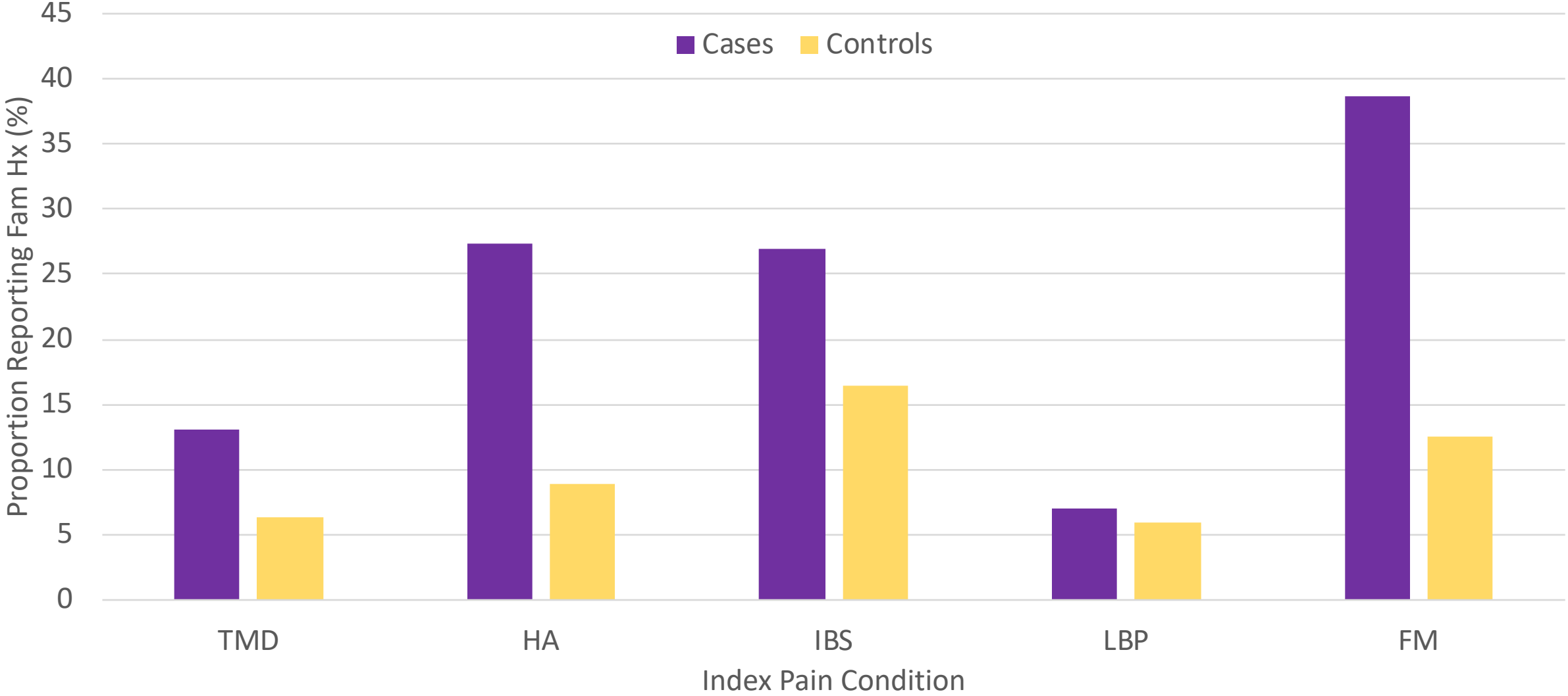
Proportion of Females and Males by Number of Pain Conditions



Pain Conditions included: temporomandibular disorder, irritable bowel syndrome, headache, low back pain, fibromyalgia

Unpublished data from OPPERA Study

Family History of COPCs in Cases and Controls

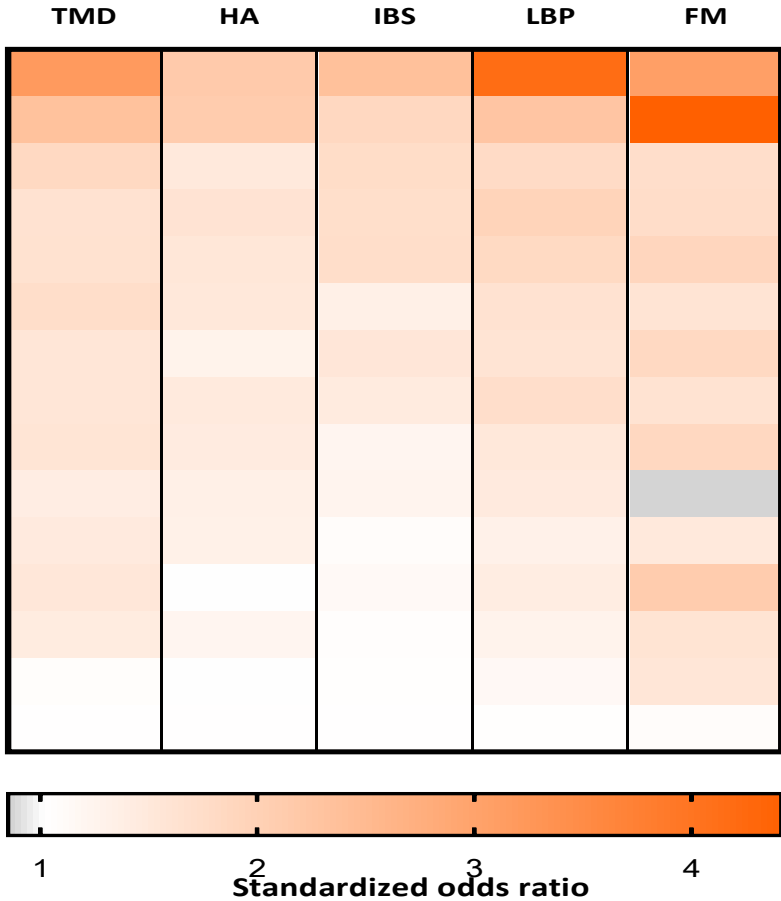


Psychological Factors Associated with Idiopathic Pain Conditions (IPCs)

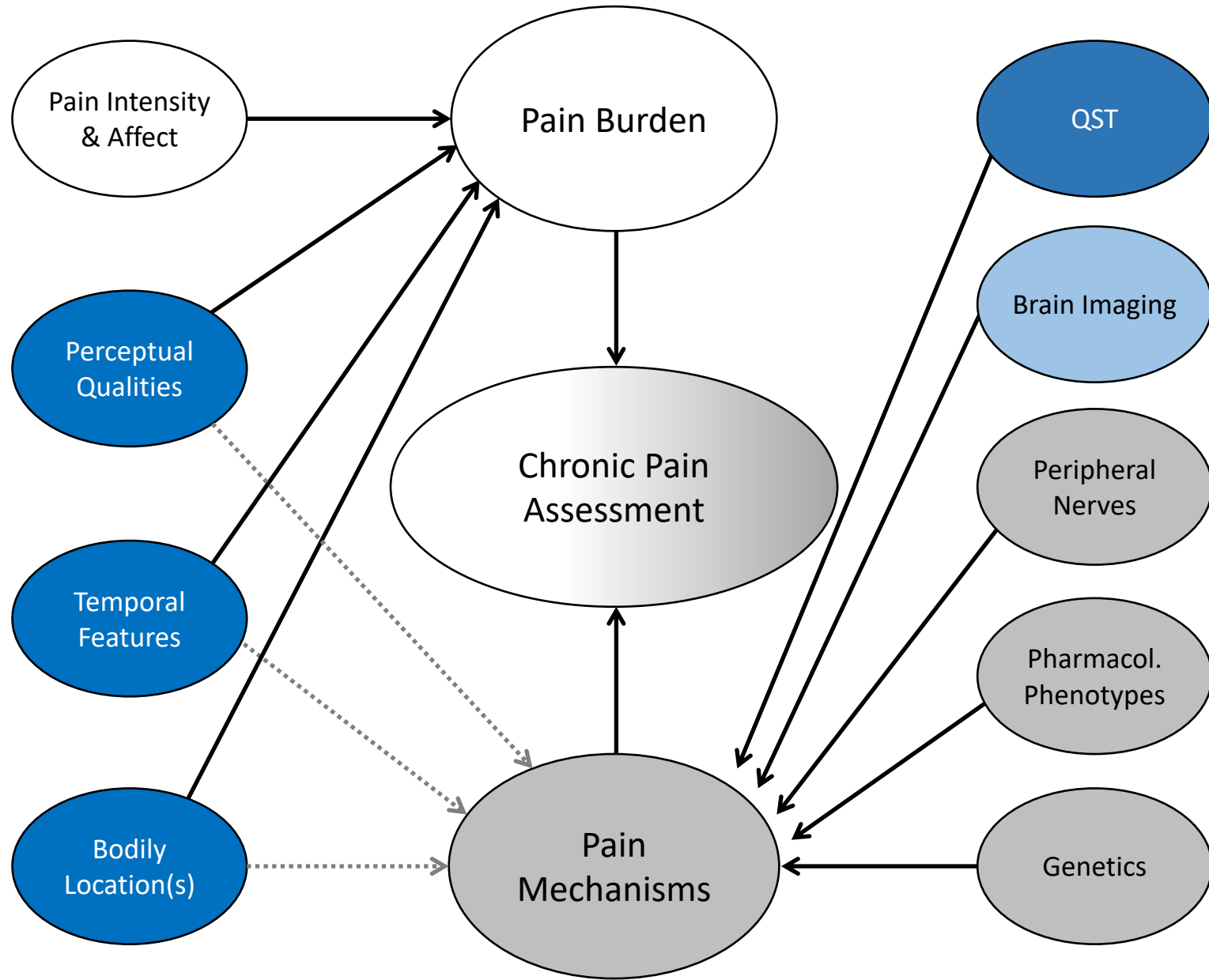
Psych measure

- SCL90R-Som
- PILL
- SCL90R-Dep
- PSS
- Trait Anxiety
- PTSD
- LES-Negative
- POMS-NA
- CSQ-Catastroph
- POMS-PA(r)
- CSQ-Distance
- CSQ-Distract
- CSQ-Praying
- CSQ-Coping
- CSQ-Ignore

Univariate association of psych. measure and IPC:



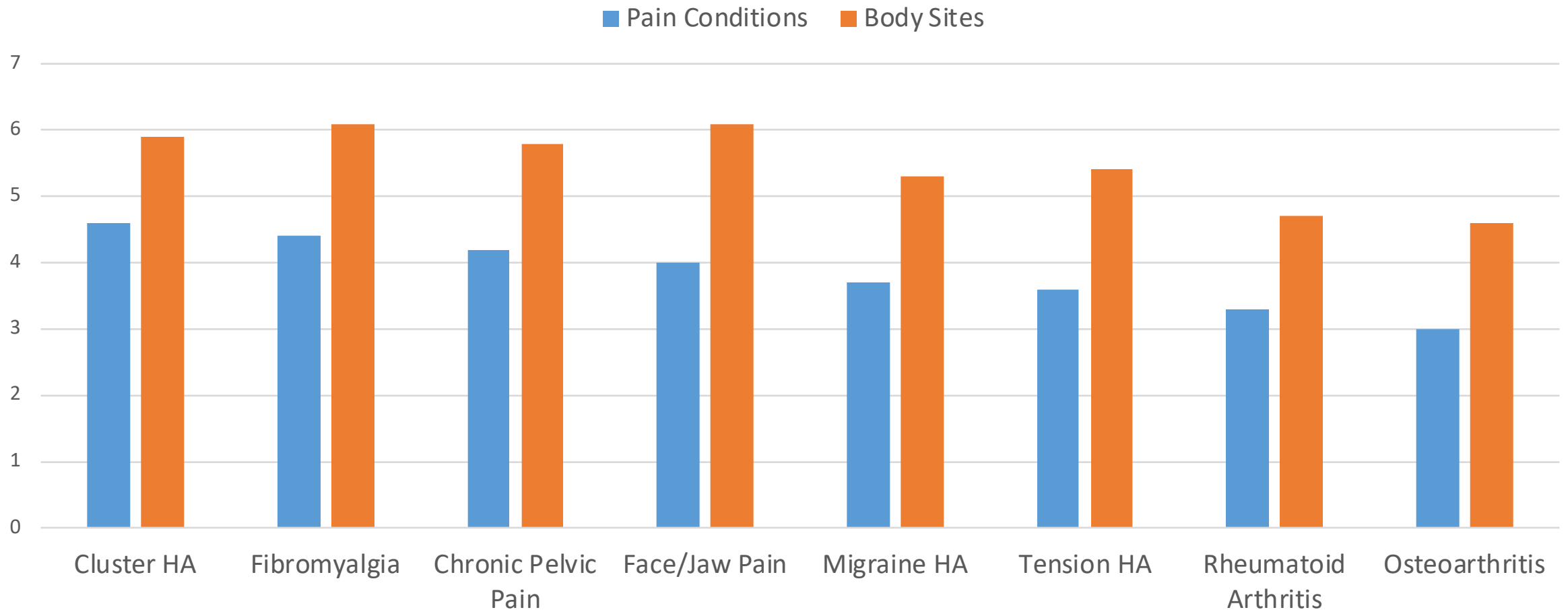
Approaches in Mechanism-Based Pain Assessment



Evidence for Central Sensitization in COPCs

- Pain distribution and qualities
- QST findings
- Neuroimaging

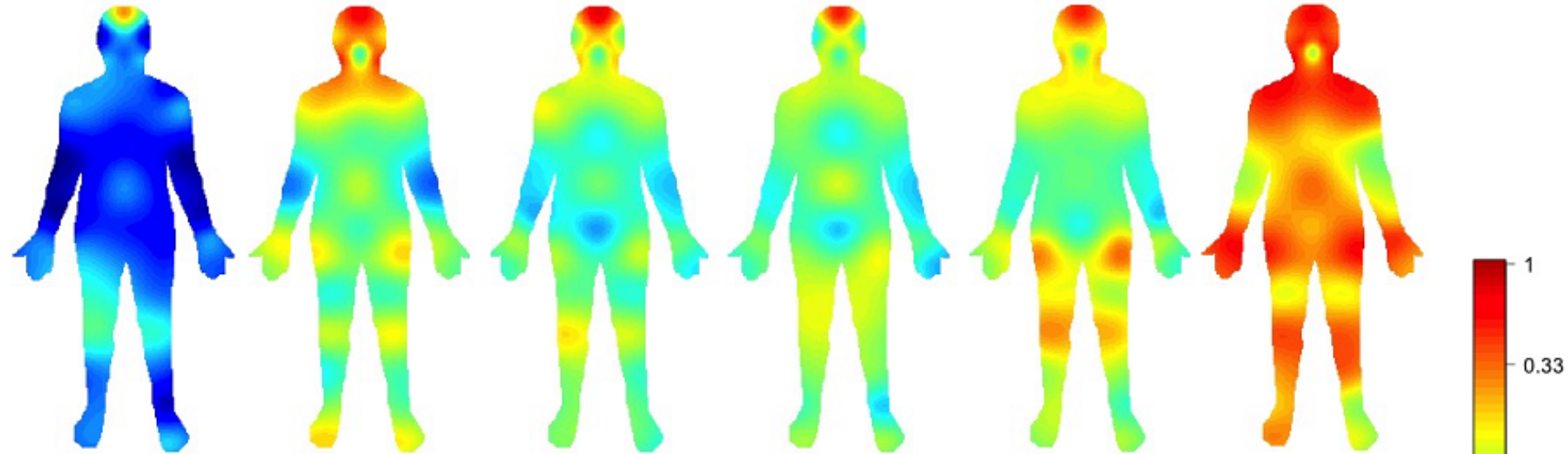
Number of Pain Conditions and Painful Body Sites for Different Index Pain Conditions



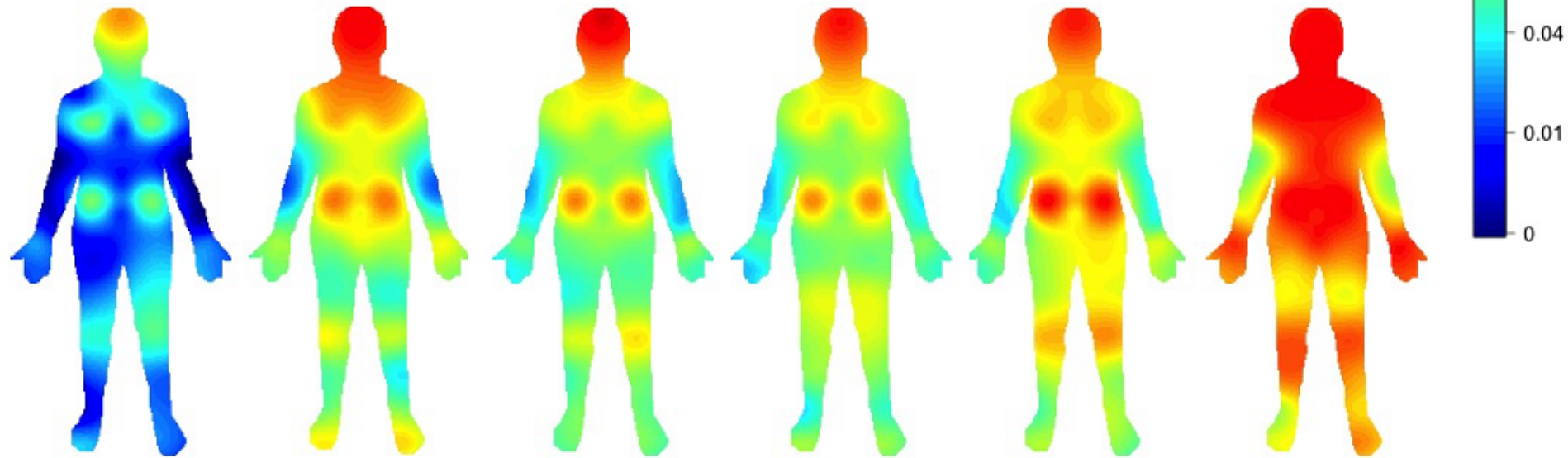
Pain Sites Endorsed by Individuals with Different Pain Conditions

Ohrbach, et al, under review

Anterior



Posterior



Non-IPC

TMD

Headache

IBS

LBP

Fibromyalgia

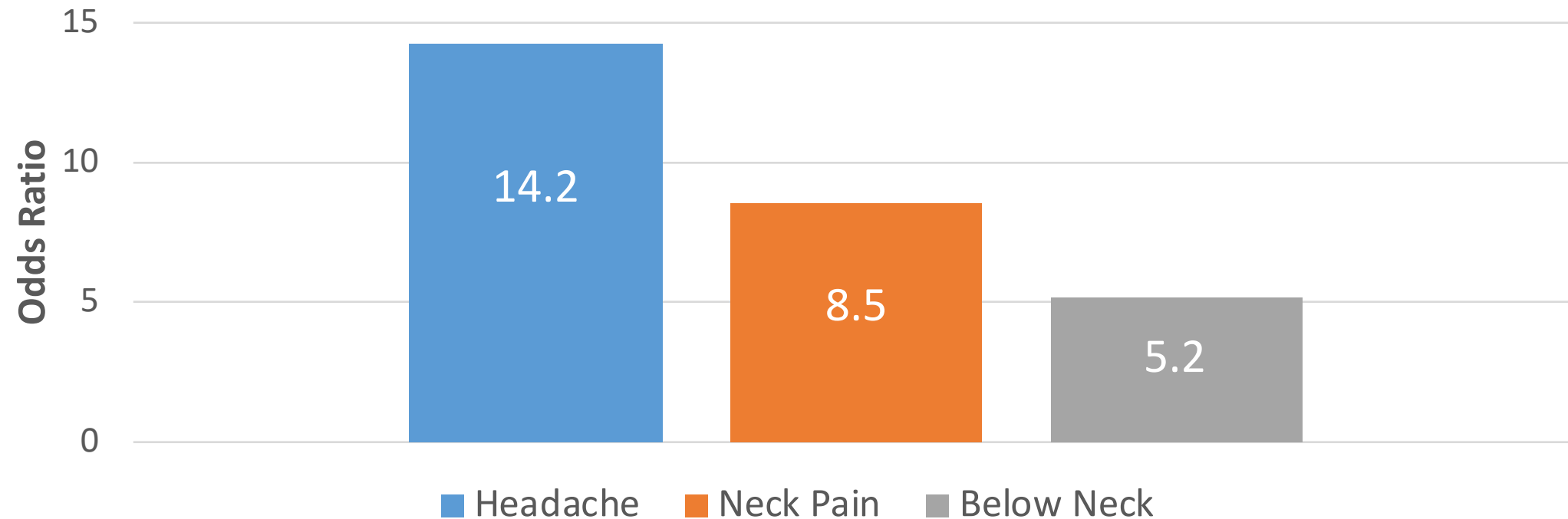


OPEN

Anatomical selectivity in overlap of chronic facial and bodily pain

Gary D. Slade^{a,b,c,*}, Jonathan D. Rosen^d, Richard Ohrbach^e, Joel D. Greenspan^{f,g}, Roger B. Fillingim^h, Marc Parisienⁱ, Samar Khoury^j, Luda Diatchenko^j, William Maixner^j, Eric Bair^{a,d,k}

Odds of TMD Based on Presence of Other Bodily Pains





Quantitative sensory testing in patients with migraine: a systematic review and meta-analysis

Hadas Nahman-Averbuch^{a,*}, Tom Shefi^b, Victor J. Schneider II^a, Dan Li^c, Lili Ding^c, Christopher D. King^a, Robert C. Coghill^a

Quantitative sensory testing and predicting outcomes for musculoskeletal pain, disability, and negative affect: a systematic review and meta-analysis

Vasileios Georgopoulos^{a,b,*}, Kehinde Akin-Akinyosoye^{a,b}, Weiya Zhang^{a,b,c}, Daniel F. McWilliams^{a,b,c}, Paul Hendrick^{b,c,d}, David A. Walsh^{a,b,c}

Quantitative assessment of nonpelvic pressure pain sensitivity in urologic chronic pelvic pain syndrome: a MAPP Research Network study

Steven E. Harte^{a,*}, Andrew Schrepf^a, Robert Gallop^{b,c}, Grant H. Kruger^{a,d}, Hing Hung Henry Lai^e, Siobhan Sutcliffe^f, Megan Halvorson^a, Eric Ichesco^a, Bruce D. Naliboff^g, Niloofar Afari^{h,i}, Richard E. Harris^a, John T. Farrar^c, Frank Tu^j, John Richard Landis^c, Daniel J. Clauw^a, for the MAPP Research Network



IASP

Central and peripheral hypersensitivity in the irritable bowel syndrome

QiQi Zhou^{a,d}, Roger B. Fillingim^{b,c}, Joseph L. Riley III^b, William B. Malarkey^{a,e}, G. Nicholas Verne^{a,d,*}

^a Department of Medicine, Ohio State University, Columbus, OH, USA

^b College of Dentistry, University of Florida, Gainesville, FL, USA

^c North Florida/South Georgia Veteran Health System, USA

^d Research Service, Cincinnati VAMC, Cincinnati, OH, USA

^e Institute of Behavioral Medicine Research, Columbus, OH, USA



IASP

Somatosensory profiles in subgroups of patients with myogenic temporomandibular disorders and fibromyalgia syndrome

Doreen B. Pfau^{a,*1}, Roman Rolke^{b,1}, Ralf Nickel^c, Rolf-Detlef Treede^a, Monika Daublaender^d

^a Department of Neurophysiology, Center of Biomedicine and Medical Technology Mannheim, Ruprecht-Karls-University Heidelberg, Mannheim, Germany

^b Department of Neurology, University Medical Center, Johannes Gutenberg-University, Mainz, Germany

^c Department of Psychosomatic Medicine and Psychotherapy, HSK Wiesbaden, Germany

^d Polyclinic of Oral Surgery, University Medical Center, Johannes Gutenberg-University Mainz, Mainz, Germany

Early changes in somatosensory function in spinal pain: a systematic review and meta-analysis

Anna Marcuzzi^{a,b,*}, Catherine M. Dean^{a,b}, Paul J. Wrigley^{c,d}, Julia M. Hush^{a,b}

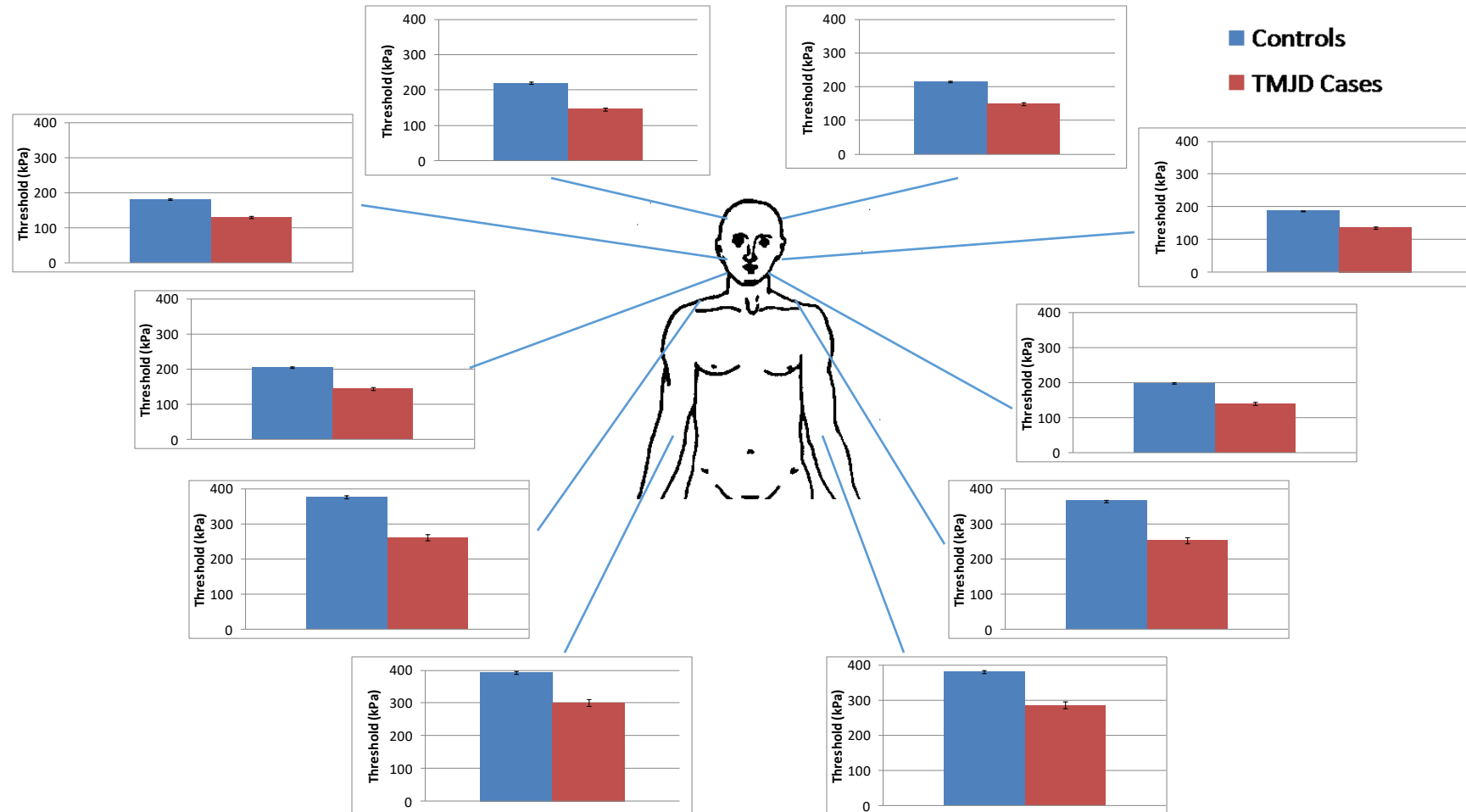


Endogenous pain modulation in chronic orofacial pain: a systematic review and meta-analysis

Estephan J. Moana-Filho^{a,*}, Alberto Herrero Babiloni^b, Nicole R. Theis-Mahon^c



Pressure Pain Thresholds (PPT) for TMD Cases vs. Controls



PPTs are significantly lower for chronic TMJD cases than pain-free controls in both cranial and extra-cranial body sites. (Mean +/- SEM; all $p < 0.001$)

Osteoarthritis and Cartilage



Experimental pain sensitivity differs as a function of clinical pain severity in symptomatic knee osteoarthritis

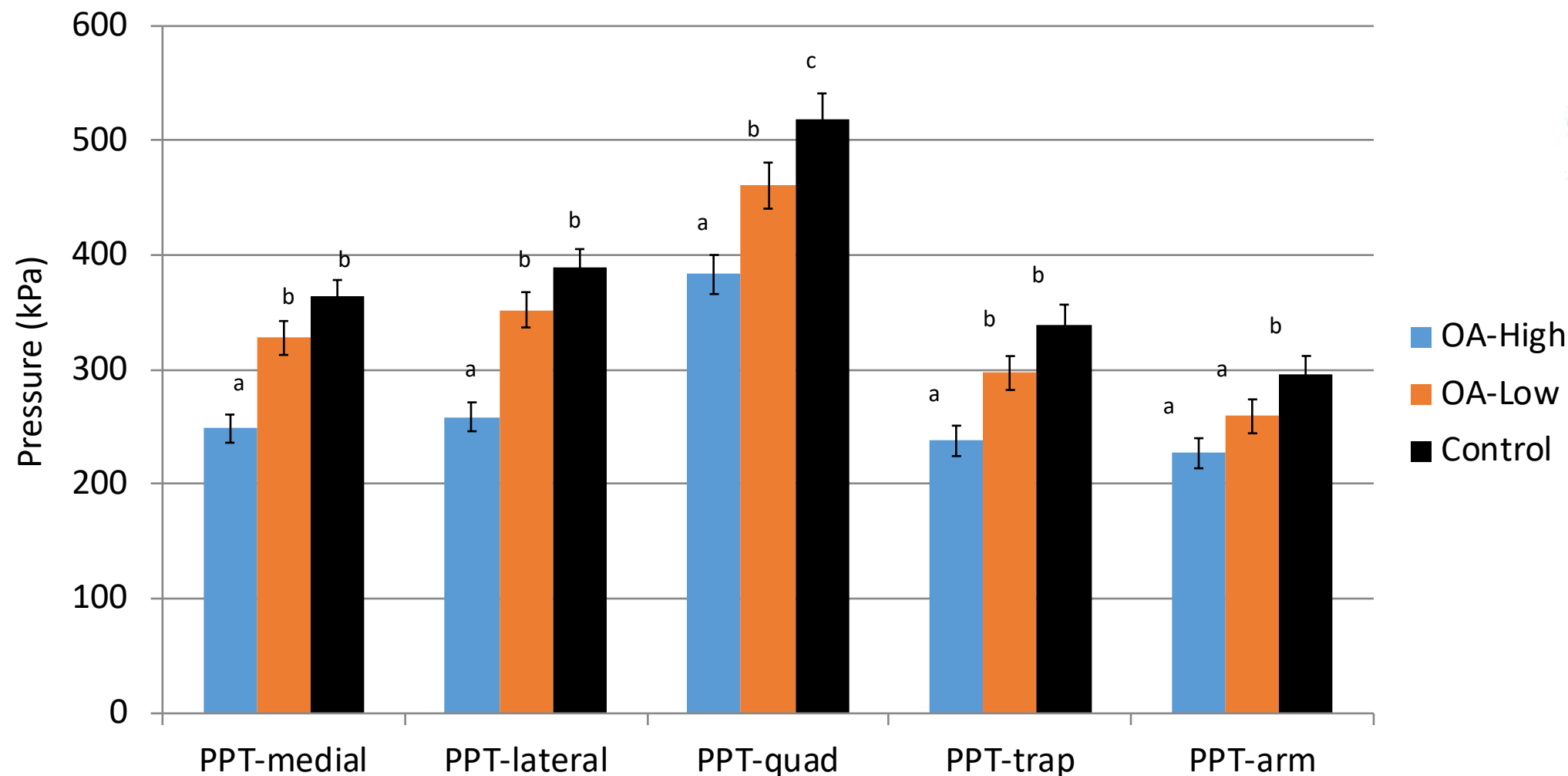


C.D. King †*, K.T. Sibille †, B.R. Goodin ‡, Y. Cruz-Almeida †, T.L. Glover †§, E. Bartley †, J.L. Riley †, M.S. Herbert ||, A. Sotolongo ||, J. Schmidt ||, B.J. Fessler ||, D.T. Redden ¶, R. Staud #, L.A. Bradley ||, R.B. Fillingim †

Variable	OA High Pain* (n=155)	OA Low Pain* (n=129)	Controls (n=119)
Demographic Variables			
Age (Years)	55.4 (7.1)	58.4 (7.9)	57.4 (8.0)
Sex (% Female)	65.3	64.8	63.9
Race (% White)†	27.3	39.2	70.6
Clinical Variables			
GCPS-Characteristic Pain (0-100)	67.7 (14.1)	30.6 (12.7)	10.2 (16.8)
GCPS-Disability (0-100)	59.7 (24.5)	24.6 (21.7)	2.1 (7.0)
WOMAC-Pain (0-20)	9.8 (4.1)	4.5 (2.8)	0.6 (1.7)
WOMAC-Physical Function (0-)	31.8 (13.7)	13.9 (10.2)	1.8 (4.8)
SPPB Total Score	9.2 (2.1)	10.5 (1.5)	10.9 (1.4)
CES-D Scores	11.8 (8.3)	7.6 (6.4)	6.5 (6.7)

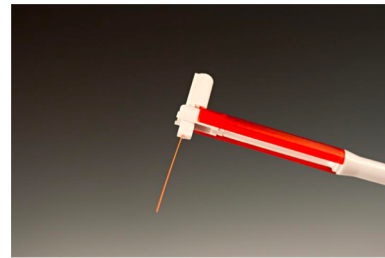
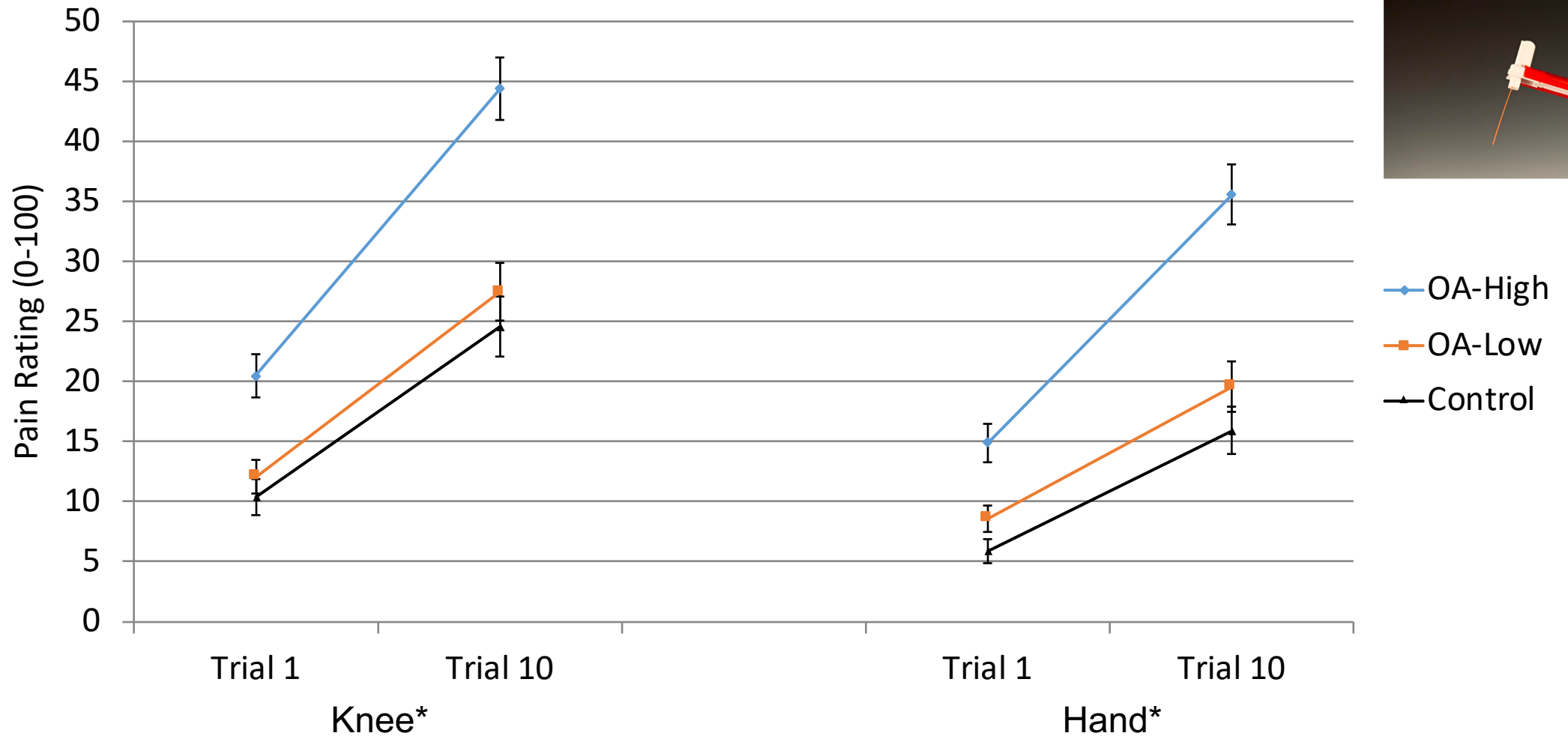
* High vs. low OA pain based on median split of GCPS-Characteristic Pain Score (median=50)

Pressure Pain Thresholds for OA Patients and Controls



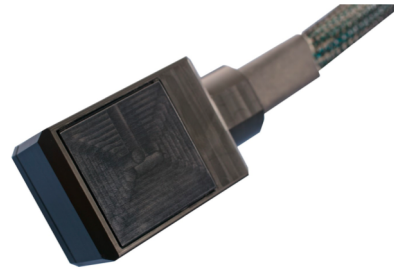
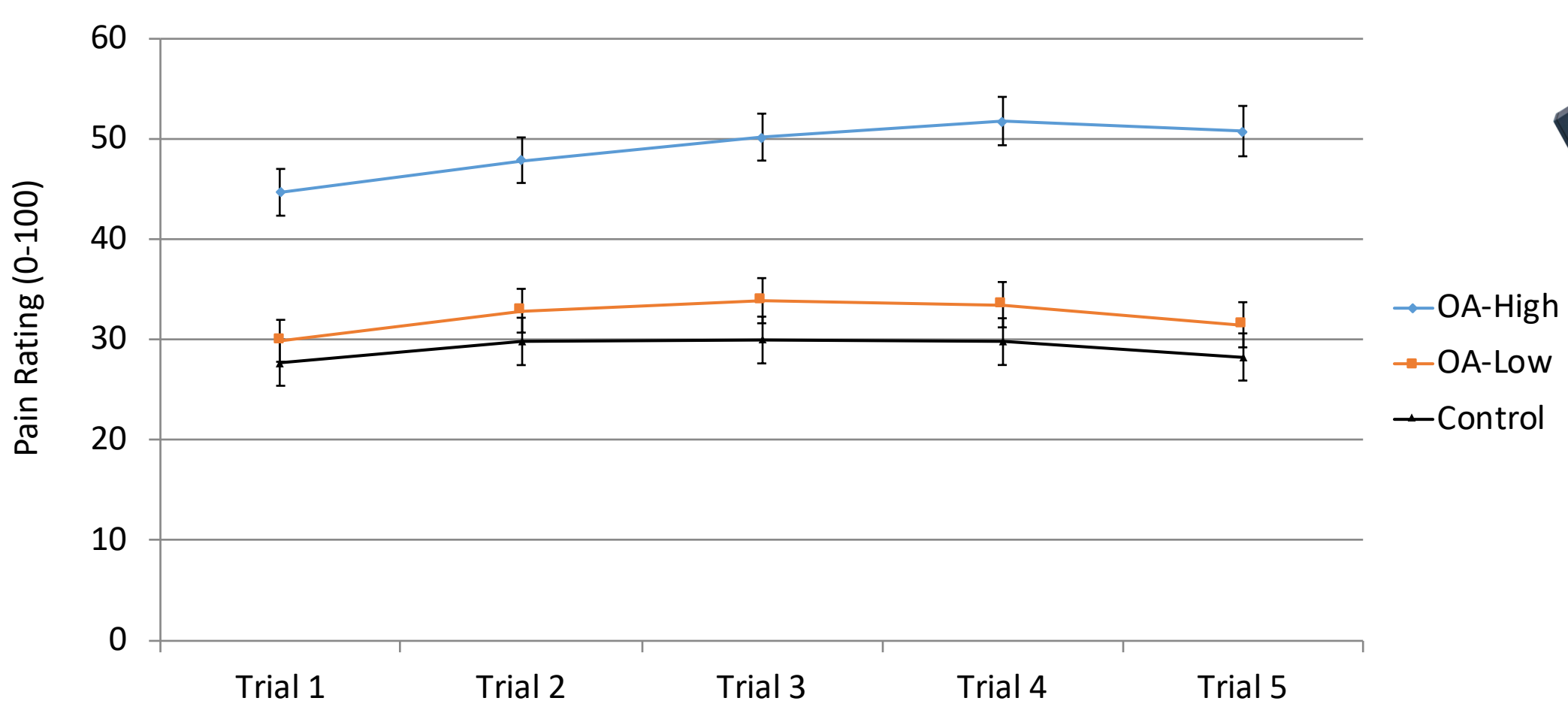
Groups with unlike letters differ from each other, $p < 0.05$

Punctate Mechanical Pain for OA Patients and Controls



***OA-High differs from the other two groups in both average rating and slope ($p < 0.05$)**

Temporal Summation of Heat Pain (Arm) for OA Patients and Controls



***OA-High differs from the other two groups in both average rating and slope ($p < 0.05$)**

Neuropathic-Like Pain Symptoms in a Community-Dwelling Sample with or at Risk for Knee Osteoarthritis

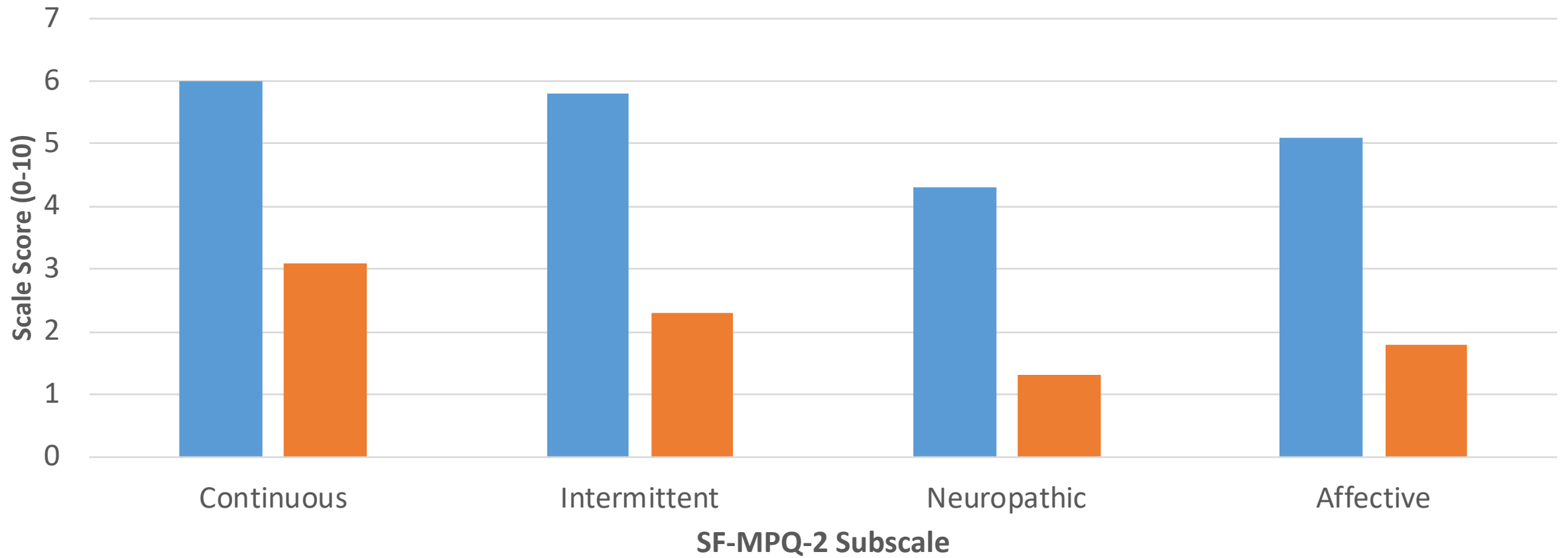
Ellen L. Terry, PhD,* Staja Q. Booker, PhD, RN,* Josue S. Cardoso,* Kimberly T. Sibille, PhD,* Emily J. Bartley, PhD,* Toni L. Glover, PhD, GNP-BC, ACHPN,[†] Ivana A. Vaughn, MPH,* Kathryn A. Thompson,[‡] Hailey W. Bulls, PhD,[§] Adriana S. Addison, MPH,[¶] Roland Staud, MD,* Laura B. Hughes, MD,[¶] Jeffrey C. Edberg, PhD,[¶] David T. Redden, PhD,^{||} Laurence A. Bradley, PhD,[¶] Burel R. Goodin, PhD,[‡] and Roger B. Fillingim, PhD*

Sample Characteristics

	NP (n=32)	non-NP (n=152)
Age*	54.6 (7.0)	58.6 (7.7)
Sex (%F)	62.5	63.8
Race (% white)*	31.3	51.3
BMI (% obese)*	63.3	55
# Pain Sites	4.7 (2.7)	3.9 (2.2)
Pain Duration		
≤ 3 Years	43.7	47.8
> 3 Years	56.3	62.2

Short Form McGill Pain Questionnaire-2

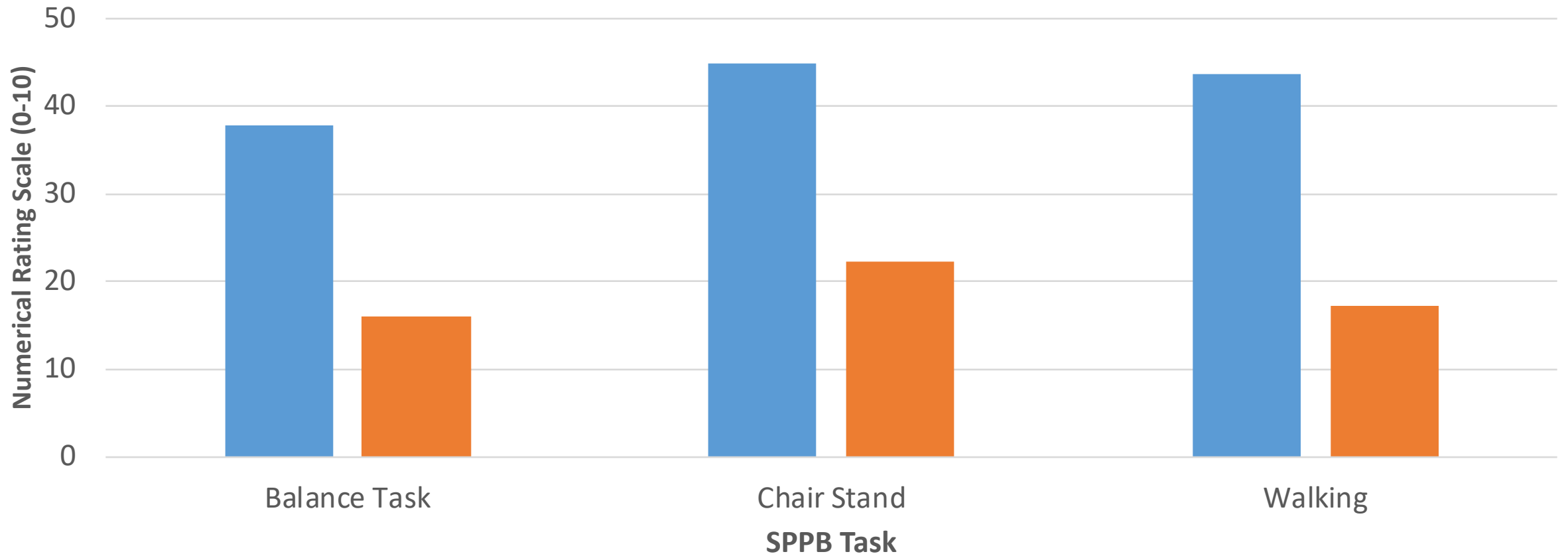
■ NP ■ non-NP



All p's < 0.01, adjusting for study site, age, race, education, and BMI

Movement Evoked Pain

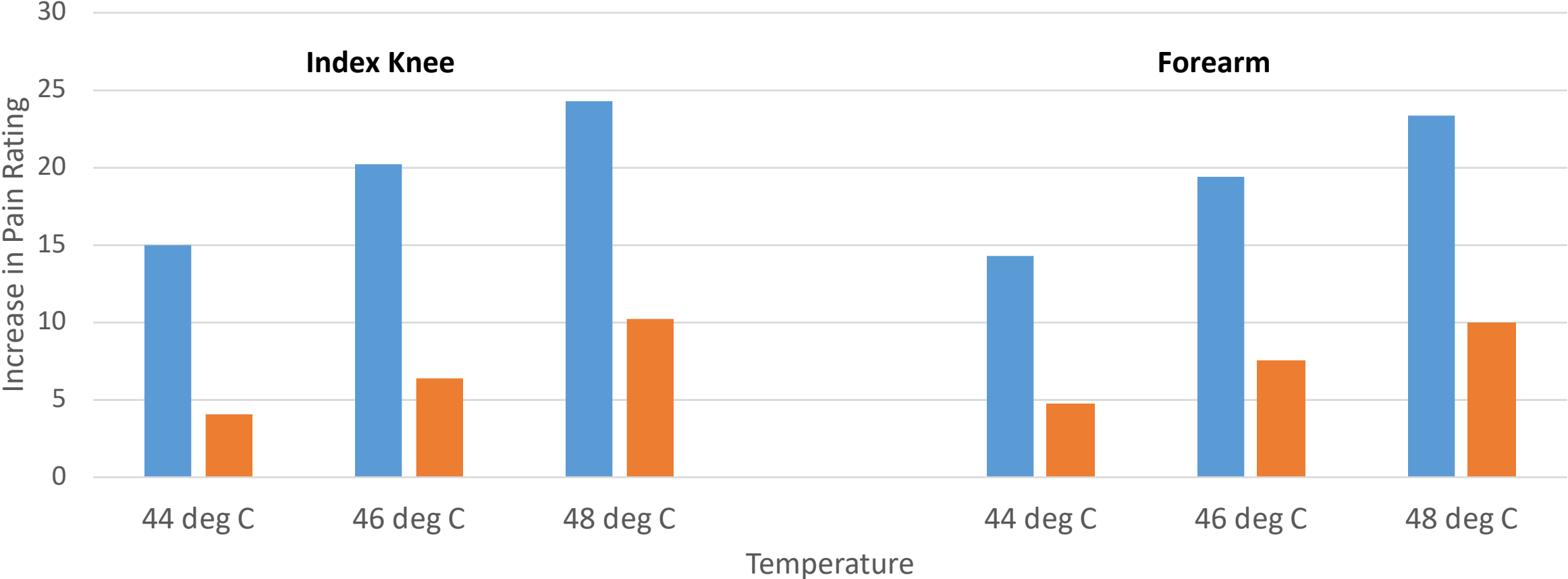
■ NP ■ non-NP



All p's < 0.01, adjusting for study site, age, race, education, and BMI. SPPB=Short Physical Performance Battery

Temporal Summation of Heat Pain

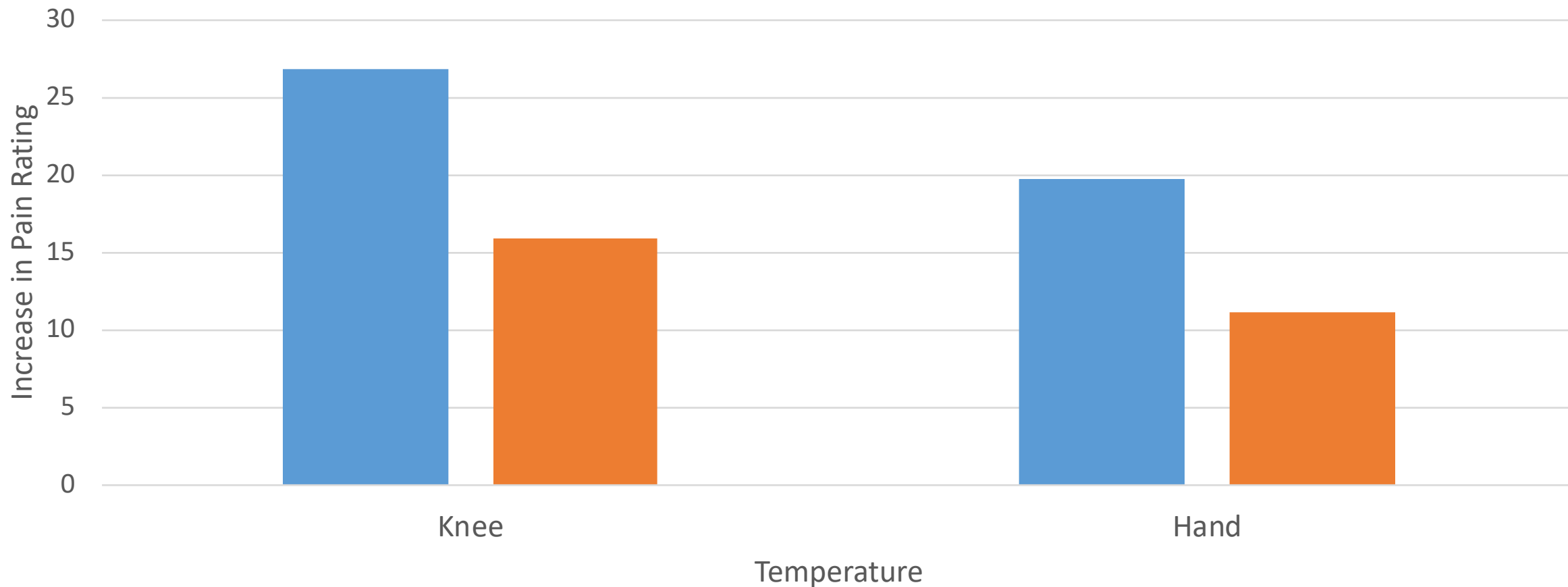
NP non-NP



All p's < 0.01, adjusting for study site, age, race, education, and BMI

Temporal Summation of Mechanical Pain

■ NP ■ non-NP



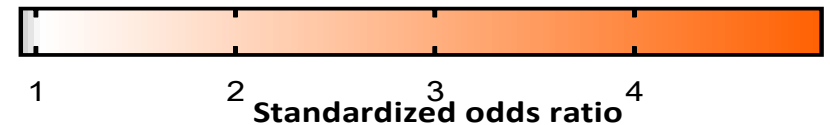
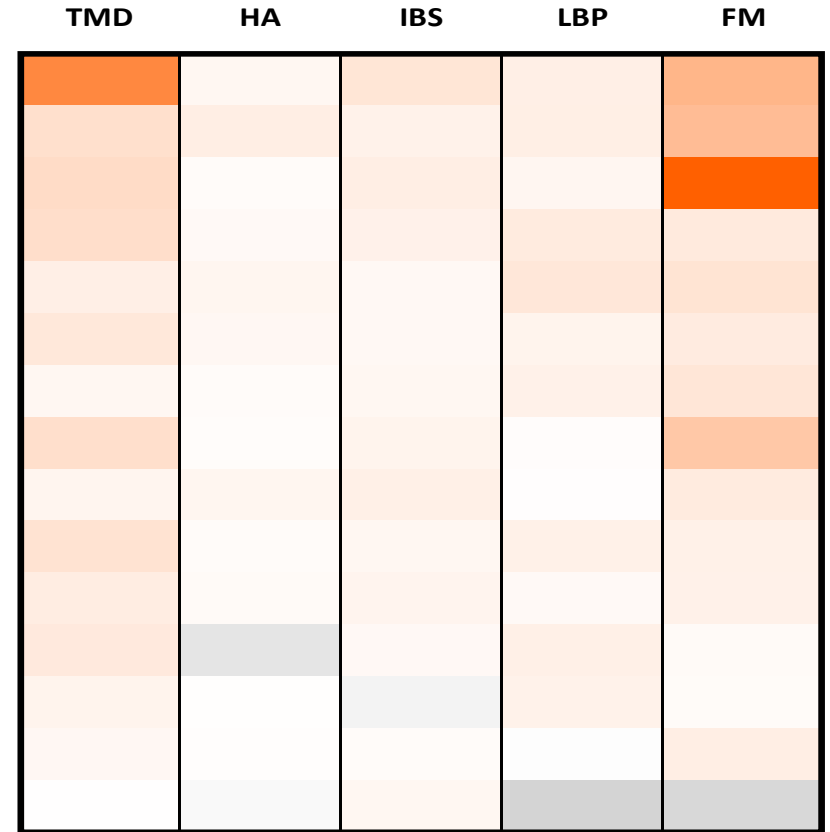
All p's < 0.01, adjusting for study site, age, race, education, and BMI

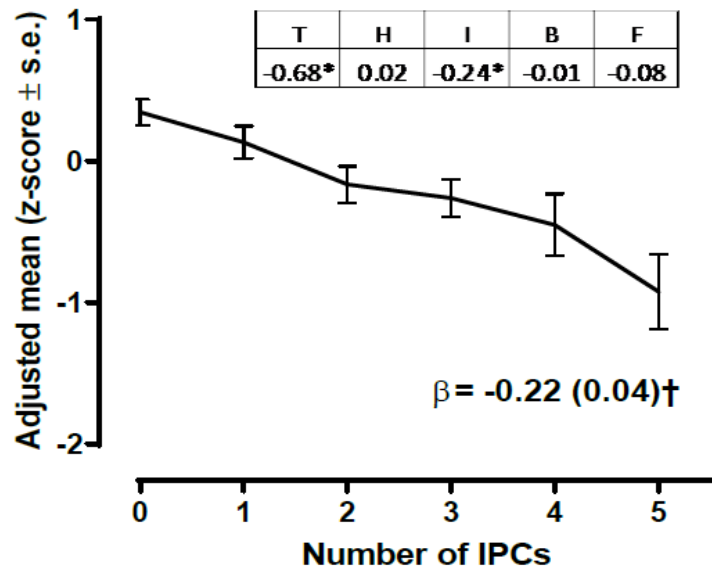
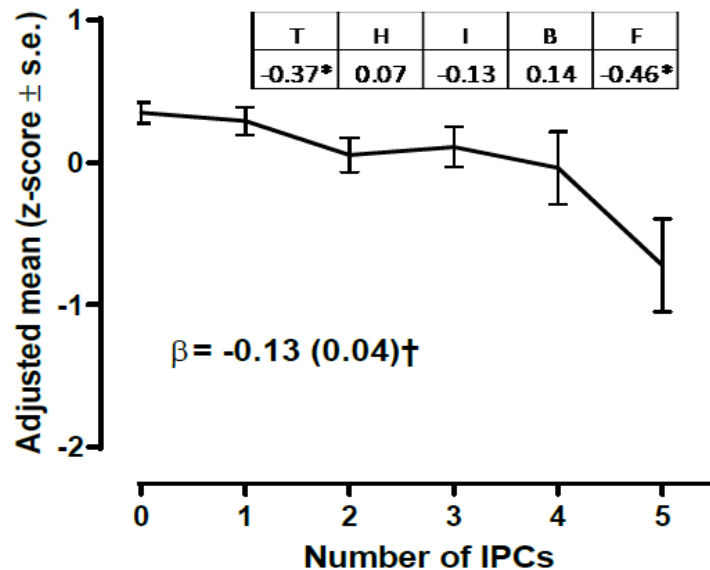
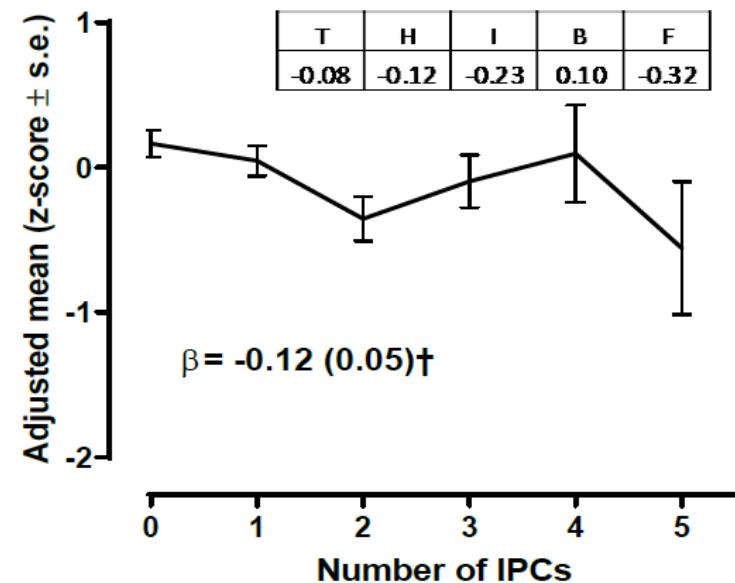
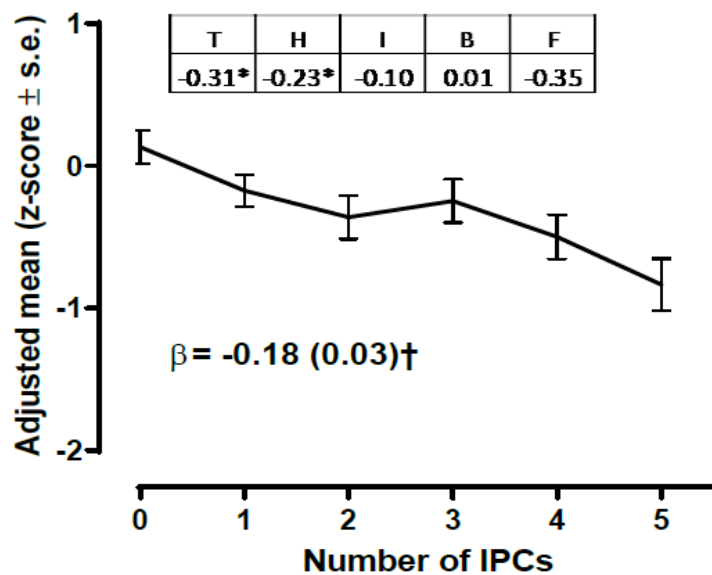
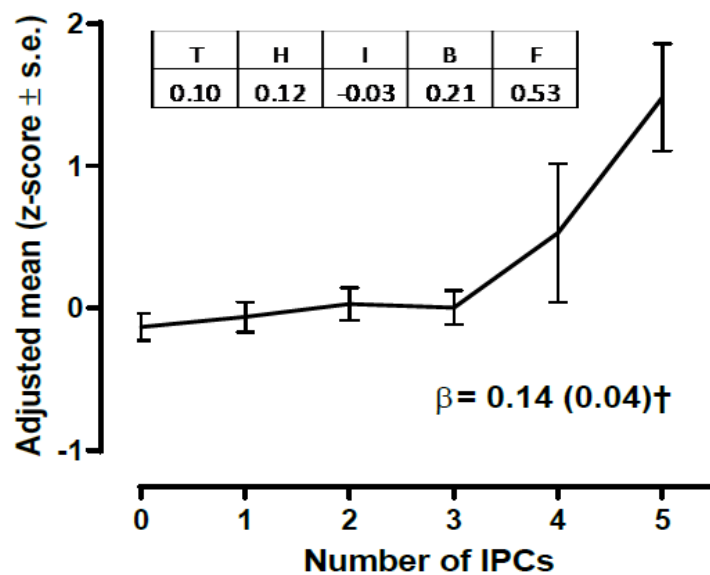
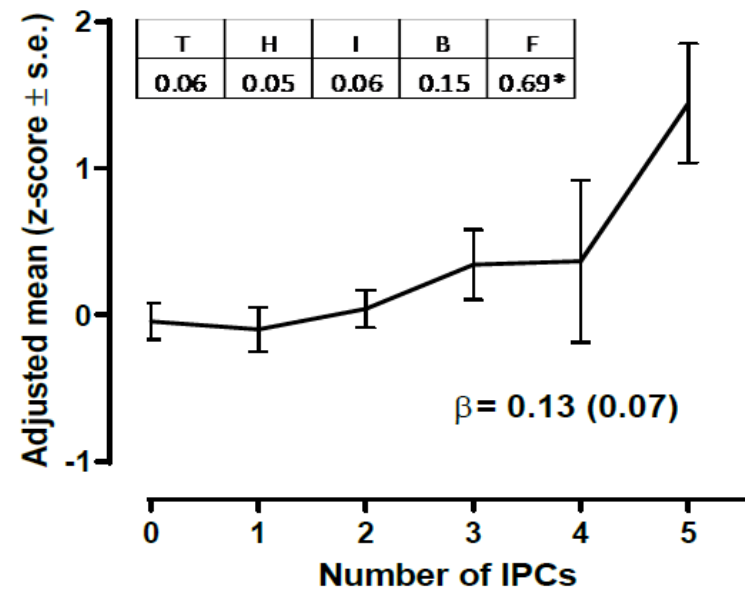
Laboratory Pain Measures Associated with Multiple Idiopathic Pain Conditions (IPCs)

QST

- PPT-Temp(r)
- MCP-Thresh(r)
- PPT-Trap(r)
- HP-Max48
- MCP-15After
- MCP-Single
- HP-15After48
- PPT-AntTib(r)
- HP-Thresh(r)
- HP-AUC48
- MCP-10stim
- HP-Single48
- HP-Tol(r)
- HP-TS48
- MCP-TS

Univariate association of health measure and IPC:



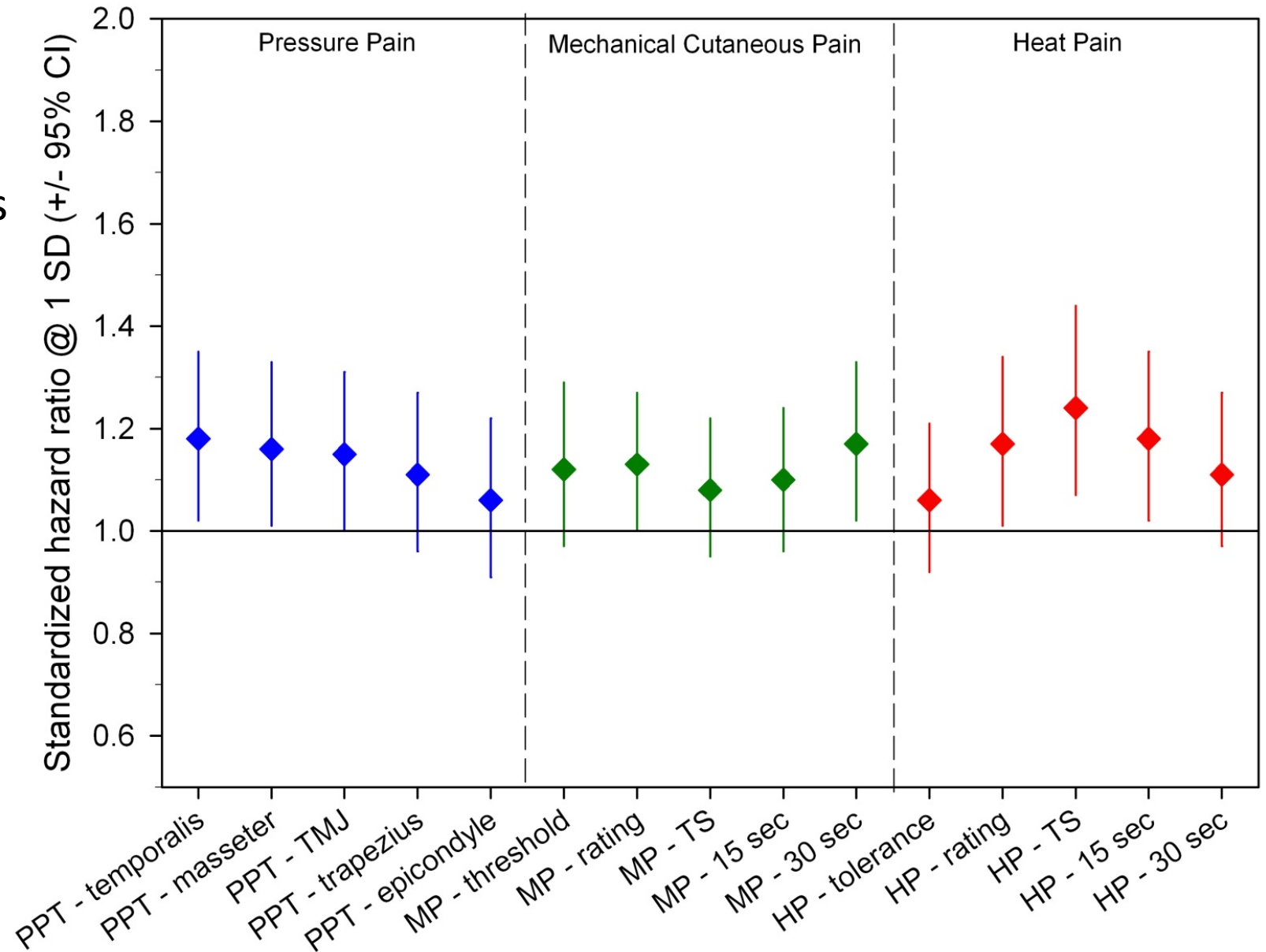
PPT temporalis**PPT anterior tibialis****HP threshold****MCP threshold****MCP 15s aftersensation****HP 48°C 15s aftersensation**

**Is “Central Sensitization” a Predictor or
Consequence of COPCs?**

Standardized Hazard Ratios for TMD Incidence Related to QST Measures

Significant (but weak) Predictors of TMD Onset include:

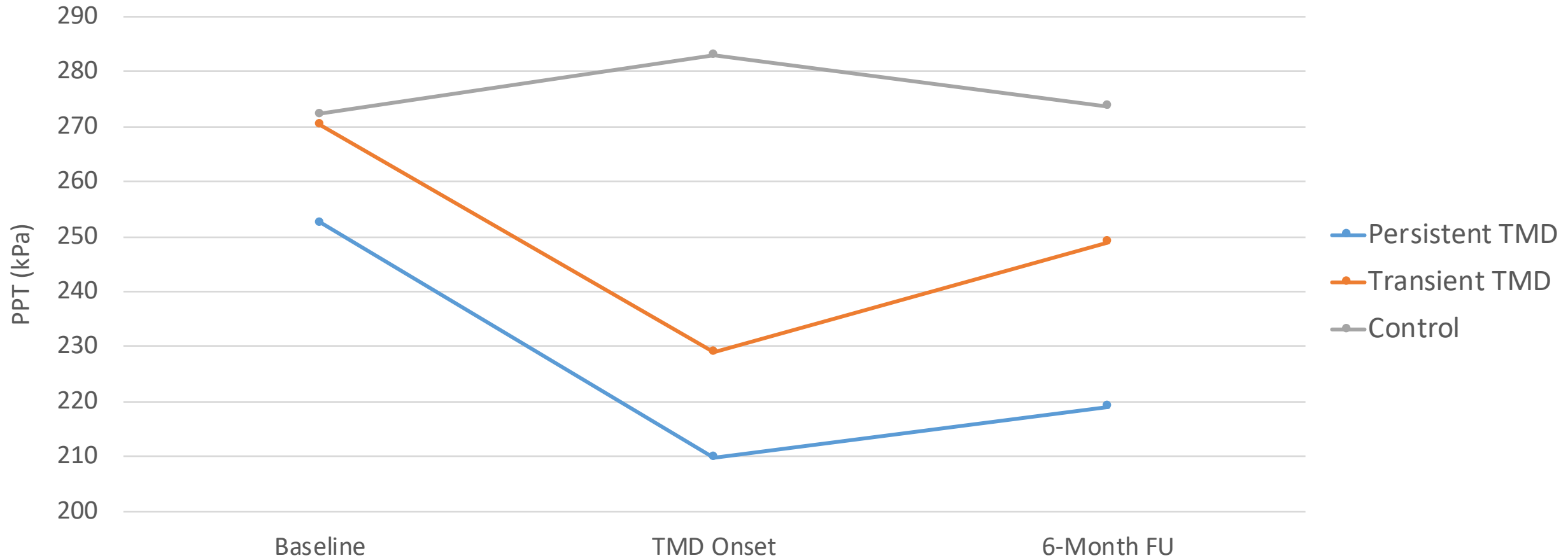
- Cranial PPTs
- Mechanical aftersensation
- Suprathreshold heat ratings
- Heat temporal summation & aftersensation




Pressure pain thresholds fluctuate with, but do not usefully predict, the clinical course of painful temporomandibular disorder



Gary D. Slade^{a,b,c,*}, Anne E. Sanders^{a,b}, Richard Ohrbach^d, Roger B. Fillingim^e, Ron Dubner^{f,g}, Richard H. Gracely^{a,h}, Eric Bair^{a,h,i}, William Maixner^{a,h}, Joel D. Greenspan^{f,g}



Pain Susceptibility Phenotypes in Those Free of Knee Pain With or at Risk of Knee Osteoarthritis: The Multicenter Osteoarthritis Study

Lisa C. Carlesso,¹ Neil A. Segal,²  Laura Frey-Law,³ Yuqing Zhang,⁴ Lu Na,⁴ Michael Nevitt,⁵ Core E. Lewis,⁶ and Tuhina Neogi⁴

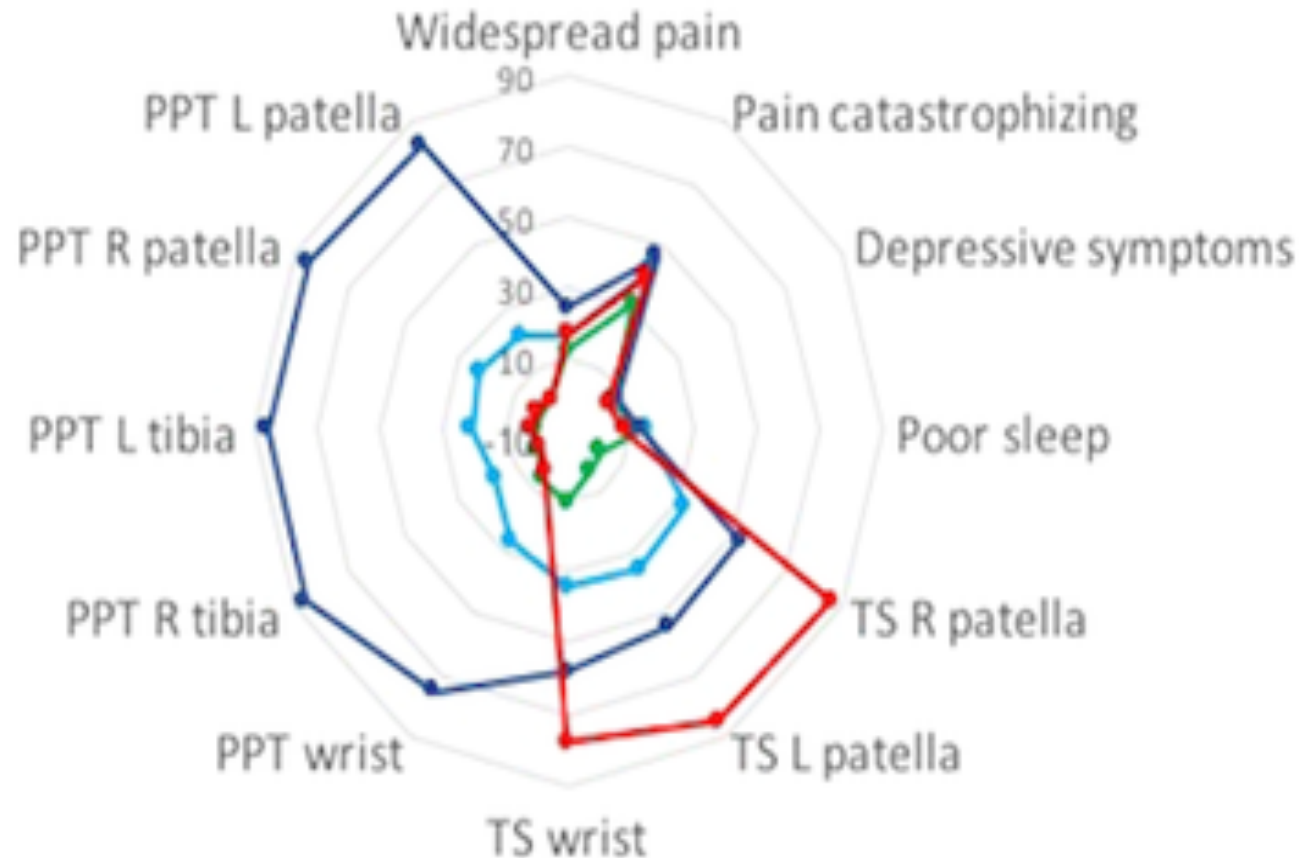
QST Profiles Predict Development of Persistent Knee Pain (PKP)

→ 1- Low-to-moderate proportion of PP sensitivity + facilitated TS n=285 (34)

→ 2- Low/Absent proportion of both PP sensitivity + facilitated TS n=265 (31)

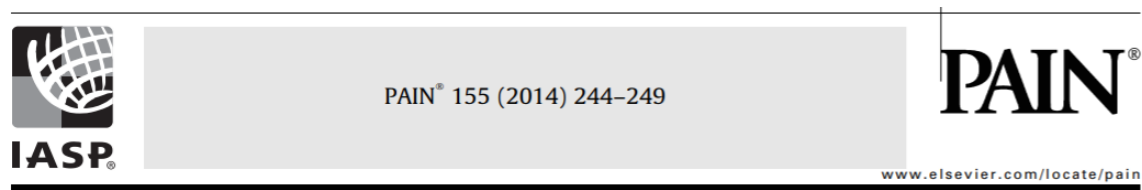
→ 3- High proportion of PP sensitivity + moderate proportion of facilitated TS n=199 (23)

→ 4- Low proportion of PP sensitivity + high proportion of facilitated TS n=103 (12)



Group 3 had greater risk of developing persistent knee pain over two-year follow-up. OR=1.98 (1.07-3.68)

Inconsistent Findings Regarding Brain Structure and Pain Sensitivity



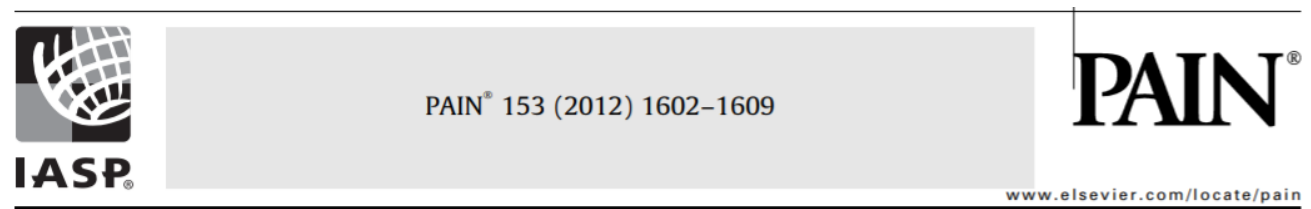
Visceral sensitivity correlates with decreased regional gray matter volume in healthy volunteers: A voxel-based morphometry study



Sigrid Elsenbruch^{a,*}, Julia Schmid^a, Jennifer S. Kullmann^{a,b}, Joswin Kattoor^a, Nina Theysohn^b, Michael Forsting^b, Vassilios Kotsis^a

^aInstitute of Medical Psychology and Behavioral Immunobiology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany

^bInstitute of Diagnostic and Interventional Radiology and Neuroradiology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany



Cortical thickness correlates of pain and temperature sensitivity

Nathalie Erpelding^a, Massieh Moayed^{a,b}, Karen D. Davis^{a,b,c,*}

^aDivision of Brain, Imaging and Behaviour—Systems Neuroscience, Toronto Western Research Institute, University Health Network, Toronto, Ontario, Canada

^bInstitute of Medical Science, University of Toronto, Toronto, Ontario, Canada

^cDepartment of Surgery, University of Toronto, Toronto, Ontario, Canada

Research Paper

PAIN[®]

Gray matter correlates of pressure pain thresholds and self-rated pain sensitivity: a voxel-based morphometry study

Ruth Ruscheweyh^{a,b,c,*}, Heike Wersching^d, Harald Kugel^e, Benedikt Sundermann^e, Anja Teuber^d

ORIGINAL ARTICLE

Brain structural changes in patients with chronic myofascial pain

D.M. Niddam^{1,2}, S.-H. Lee^{3,4}, Y.-T. Su⁵, R.-C. Chan^{3,4}

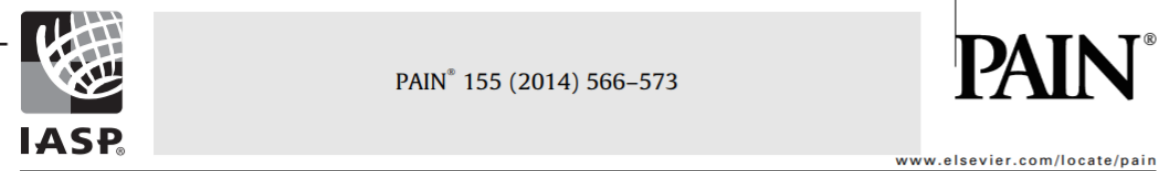
1 Brain Research Center, National Yang-Ming University, Taipei, Taiwan

2 Institute of Brain Science, School of Medicine, National Yang-Ming University, Taipei, Taiwan

3 Department of Physical Medicine and Rehabilitation, National Yang-Ming University, Taipei, Taiwan

4 Department of Physical Medicine and Rehabilitation, Taipei Veterans General Hospital, Taipei, Taiwan

5 Department of Physical Medicine and Rehabilitation, Far Eastern Memorial Hospital, New Taipei City, Taiwan



Pain sensitivity is inversely related to regional grey matter density in the brain



Nichole M. Emerson^a, Fadel Zeidan^a, Oleg V. Lobanov^a, Morten S. Hadsel^a, Katherine T. Martucci^a, Alexandre S. Quevedo^a, Christopher J. Starr^a, Hadas Nahman-Averbuch^b, Irit Weissman-Fogel^c, Yelena Granovsky^{b,d}, David Yarnitsky^{b,d}, Robert C. Coghill^{a,*}

Pain Medicine, 0(0), 2018, 1–11

doi: 10.1093/pm/pny108

Original Research Article

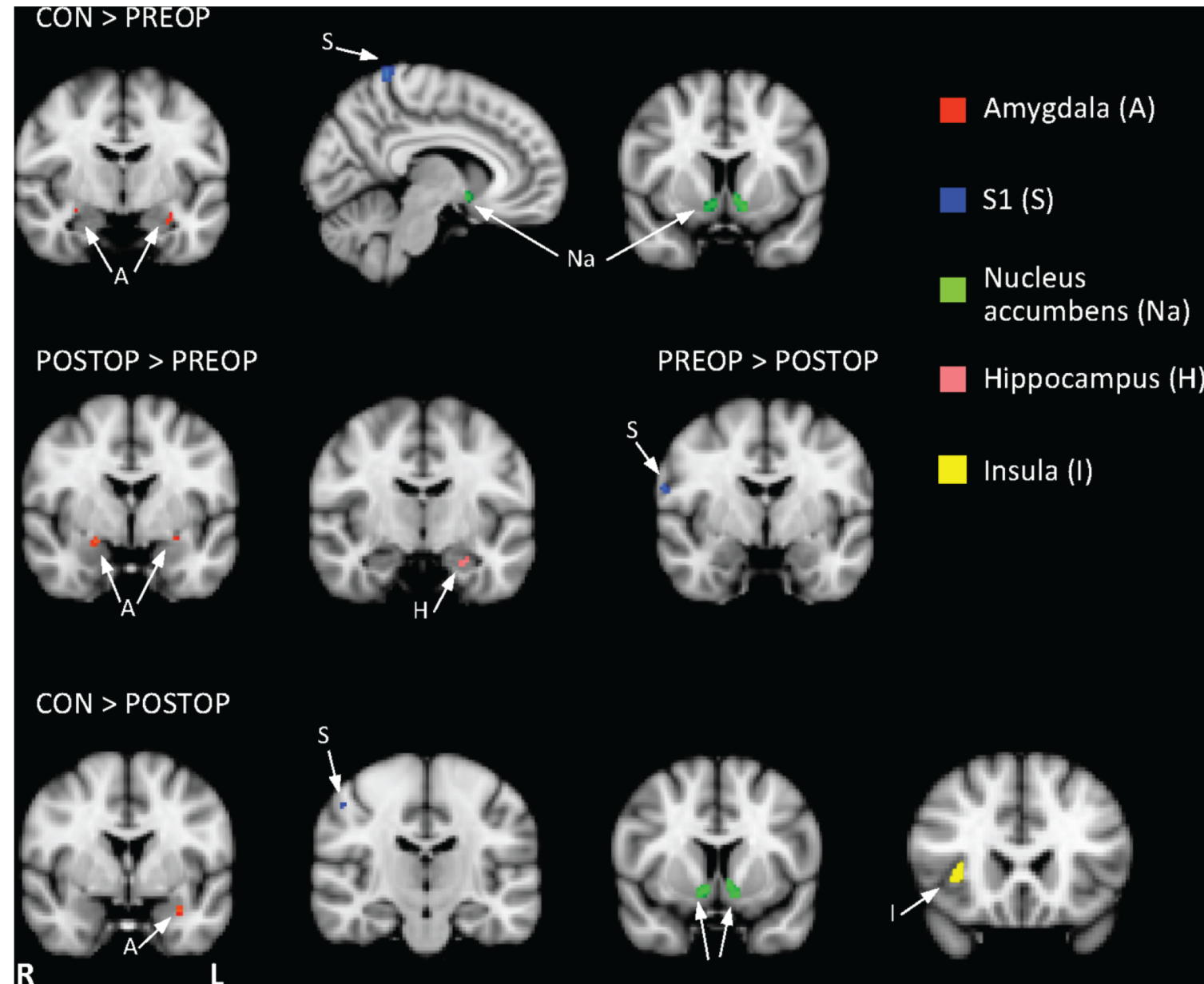
OXFORD

Structural Brain Alterations Before and After Total Knee Arthroplasty: A Longitudinal Assessment

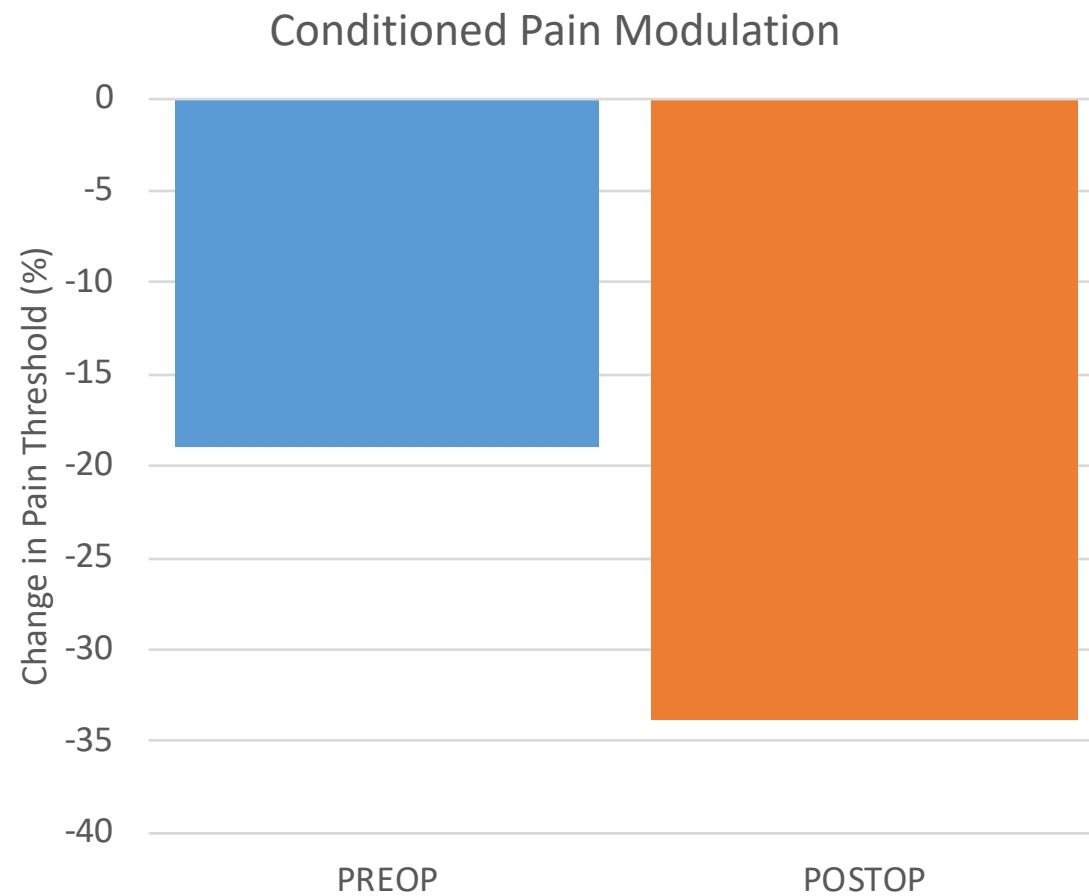
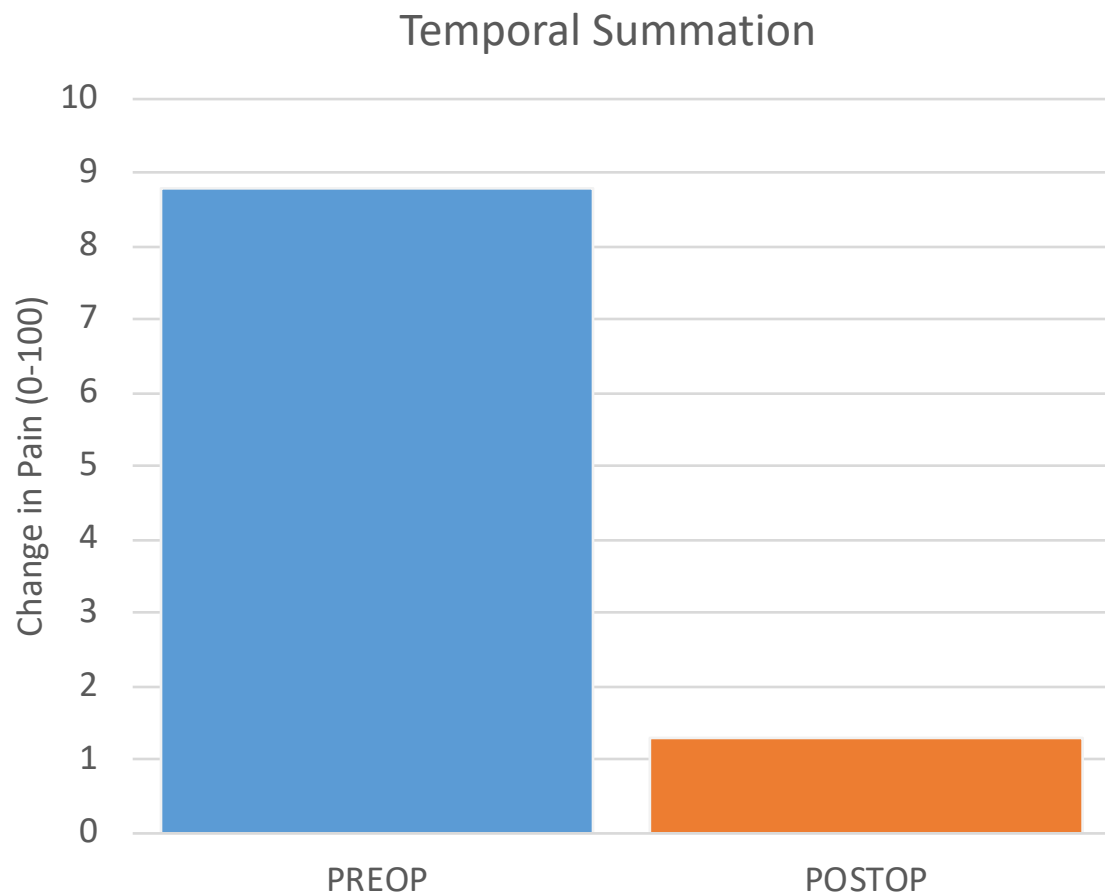
Gwyn N. Lewis, PhD,* Rosalind S. Parker, MPhil,* Sheena Sharma, PhD,* David A. Rice, PhD,*[†] and Peter J. McNair, PhD*

Significant increases in gray matter volume were observed after TKA in: bilateral amygdala, contralateral hippocampus, and contralateral PAG.

In contrast, gray matter volume was significantly smaller in bilateral S1 at POSTOP compared with PREOP.

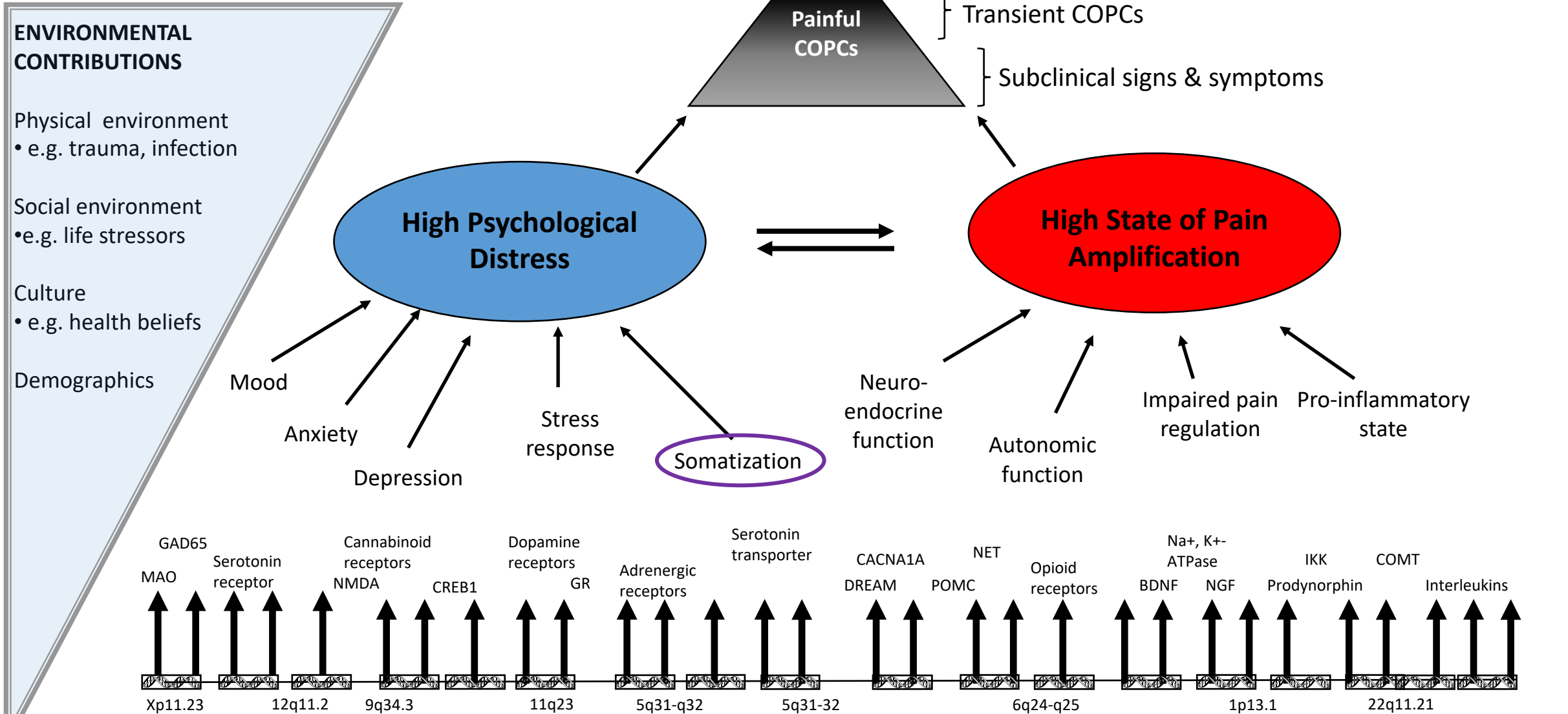


Changes in QST Responses Pre to Post-Op



All changes significant $p < 0.05$

Etiology of Chronic Overlapping Pain Conditions (COPCs)



Conclusions

- COPCs exhibit multiple signs of central sensitization
- Increased # pain conditions associated with greater sensitization
- Sensitization may represent both risk factor and consequence
- Overlapping measures related to sensitization need to be reconciled

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