Somatosensory Amplification and the Development and Maintenance of Chronic Pain

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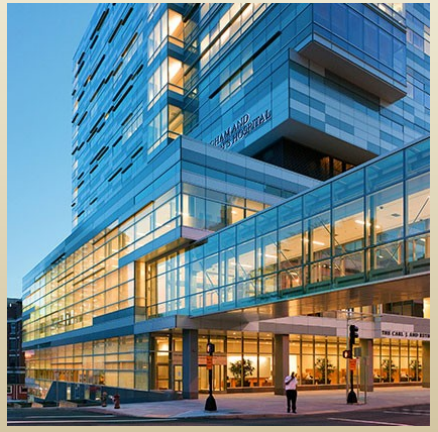

Somatosensory Amplification

On June 19 (which was- highly uncharacteristically- more than a month before this presentation), I searched "Somatosensory Amplification" & "Pain" on PubMed.

The search returned exactly 41 results, half of which were only marginally relevant. I had assumed (apparently incorrectly) that "Somatosensory Amplification" was a fairly commonly-used term in our field. In comparison, a search for "Pain Modulation" returned over 2,000 results, and "Central Sensitization" & "Pain" got almost 2,500.

History

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Review article

Somatosensory amplification – An old construct from a new perspective☆

Ferenc Köteles[a,*], Michael Witthöft[b]

In the late 1970's, Art Barsky and others (many of them in Psychiatry), began writing regularly about "amplification", somatization, and hypochondriasis. For example: "*Patients who amplify bodily sensations*." Barsky AJ. Ann Intern Med, 1979. Later, the term somatosensory amplification was introduced and defined as: "the tendency to experience somatic sensations as intense, noxious, and disturbing". Amplification included both lower-level (sensory) and higher-level (cognitive-emotional) processes. In the '80s and '90s a Somatosensory Amplification Scale was developed and validated:

Table 1
Items of the Somatosensory Amplification Scale and their associations with intero- and exteroception (i.e. perception of stimuli from within the body or from the environment, respectively).

Items	Interoception	Exteroception
1. When someone else coughs, it makes me cough too	Yes (secondary)	Yes
2. I can't stand smoke, smog, or pollutants in the air	Yes (secondary)	Yes
3. I find I'm often aware of various things happening in my body	Yes	
4. When I bruise myself, it stays noticeable for a long time	Yes (secondary)	Yes
5. Sudden loud noises really disturb me		Yes
6. I can sometimes hear my pulse or my heartbeat throbbing in my ear	Yes	
7. I hate to be too hot or too cold	Yes	
8. I'm quick to sense the hunger contractions in my stomach	Yes	
9. Even something minor, like an insect bite or a splinter, really bothers me	Yes (secondary)	yes
10. I have a low tolerance for pain	Yes	

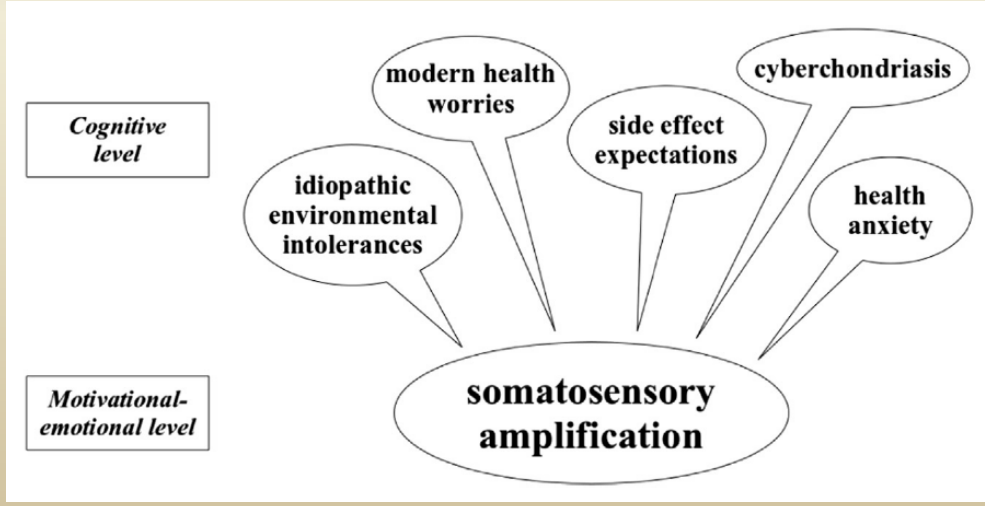
Conceptualization

Table 2
Empirical studies investigating the association between SSA and various characteristics of pathological conditions.

Clinical condition	Association with SSA	References
1. Pain related		
Myo-fascial pain (diagnosis and acute presence of symptoms)	Positive	[78]
Rheumatoid arthritis (severity of symptoms and medication side effects)	Positive	[79]
Aspects of chronic pain (diagnosis and location)	Positive	[80–82]
Pain with sexual intercourse in women (presence of pain)	Positive	[83]
Non cardiac chest pain (diagnosis)	Positive	[37,84,85]
Aspects of headache (frequency) and migraine	Positive	[86,87]
Migraine (diagnosis, disability, frequency)	Positive	[88]
Back pain (incidence in children)	Positive	[86]
Chronic low back pain (disability)	Positive	[89]
Fibromyalgia (diagnosis)	Positive	[90]
Aspects of laboratory induced pain (quality, intensity)	Positive	[29,91,92]
Non cardiac chest pain (diagnosis)	Null	[93]
Headache (incidence in boys)	Null	[86]
Visceral sensitivity in patients with IBS (intensity of rectal pain)	Null	[38]
Vulvodynia (diagnosis)	Null	[94]
Laboratory induced pain in chronic pain patients (threshold, tolerance)	Null	[19]
Chronic pain (diagnosis)	Negative	[61]
2. Not pain related		
Functional dyspepsia (diagnosis)	Positive	[95,96]
Infections of the upper respiratory tract (perceived severity symptoms)	Positive	[11,97]
Asthma and dispnoe (accuracy of symptom reporting, perceived severity of symptoms)	Positive	[76,77,98]
Joint hypermobility syndrome (diagnosis)	Positive	[99,100]
Visual discomfort (severity)	Positive	[101]
Chronic fatigue (severity - longitudinal)	Null	[102]
Dyspnea after asthma therapy (severity)	Null	[103]
Chemotherapy induced nausea (severity)	Null	[104,105]

Conceptualized as: "Strongly related to but distinct from: (1) Catastrophizing, (2) Central Sensitization, (3) Hypervigilance."

However, I don't actually find the distinction convincingly made: "As decreased pain threshold/tolerance are the most often reported concomitants of SSA (Table 2), the differences between the 2 phenomena need to be explained. Sensitization basically represents an acquired characteristic *(SSA does not)*, SSA also encompasses non-pain-related sensations (*CS does not*), and the CS concept assumes the presence of sensory input, thus it cannot explain the association between SSA and expectations/worries (*CS is not related to cognitive & emotional factors*)".



Differentiation of Components of SA?

Is it even possible?

Somatic focus?

Sensitization?

Pain Facilitation?

Failure of Inhibition?

Hypervigilance? Anxiety? Catastrophizing?

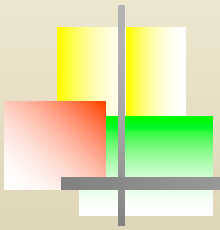
Comprehensive Review

PAIN®

Patient phenotyping in clinical trials of chronic pain treatments: IMMPACT recommendations

Robert R. Edwards[a,*], Robert H. Dworkin[b], Dennis C. Turk[c], Martin S. Angst[d], Raymond Dionne[e], Roy Freeman[a], Per Hansson[f], Simon Haroutounian[g], Lars Arendt-Nielsen[h], Nadine Attal[i], Ralf Baron[j], Joanna Brell[k], Shay Bujanover[l], Laurie B. Burke[m,n], Daniel Carr[o], Amy S. Chappell[p], Penney Cowan[q], Mila Etropolski[r], Roger B. Fillingim[s], Jennifer S. Gewandter[b], Nathaniel P. Katz[o,t], Ernest A. Kopecky[u], John D. Markman[b], George Nomikos[v], Linda Porter[w], Bob A. Rappaport[x], Andrew S.C. Rice[y], Joseph M. Scavone[z], Joachim Scholz[aa], Lee S. Simon[bb], Shannon M. Smith[b], Jeffrey Tobias[cc], Tina Tockarshewsky[dd], Christine Veasley[ee], Mark Versavel[ff], Ajay D. Wasan[gg], Warren Wen[hh], David Yarnitsky[ii]

In order to give you the option of not even listening to the rest of the talk but still absorbing the take-home message, my answer is going to be that we can measure these components separately, but they all inter-relate with one another and share neurobiological substrates.



Importance: Top Predictive Psychosocial Factor in OPPERA

American Pain Society RESEARCH EDUCATION TREATMENT ADVOCACY

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Available online at www.jpain.org and www.sciencedirect.com

Multivariable Modeling of Phenotypic Risk Factors for First-Onset TMD: The OPPERA Prospective Cohort Study

Eric Bair,*,†,‡ Richard Ohrbach,§ Roger B. Fillingim,‖ Joel D. Greenspan,¶ Ronald Dubner,¶ Luda Diatchenko,*,†,**,†† Erika Helgeson,‡ Charles Knott,‡‡ William Maixner,*,†,§§ and Gary D. Slade*,‖‖,¶¶

Table 1. Lasso Regression Coefficients

Variable	Standardized HR	HR
Somatization (SCL 90R)	1.180	
Count of 20 comorbid conditions	1.123	
Count of 6 nonspecific orofacial symptoms	1.071	
Global sleep score (PSQI)	1.069	
Study site (Florida)	1.035	1.057
No. of palpation sites with pain (right temporalis)	1.029	
Bodily pain (SF-12v2)	.975	
Smoking history (never)	.984	.991
Lifetime U.S. residence (less than all my life)	.985	.967
Average diastolic BP (orthostatic challenge)	1.013	
No. of painful anatomic locations during protrusion	1.009	
No. of palpation sites with pain (left temporalis)	1.008	
Negative impact of life events (LES)	1.005	
General health (SF-12v2)	.996	
Count of 10 IBS symptoms	1.003	
No. of palpation sites with pain (left TM joint)	1.003	

OPPERA is widely considered one of the premier (e.g., thousands of subjects, detailed phenotyping, careful long-term follow-up) prospective cohort studies of risk factors for the development of a chronic pain condition

Table 3. Putative TMD Risk Factors With the Largest Importance Scores

Variable	Importance Score
Count of 20 comorbid conditions	100.0
Count of 6 nonspecific orofacial symptoms	92.9
Study site	90.7
Bodily pain (SF-12v2)	80.6
Oral parafunction sum score (OBC)	66.0
Could not open mouth wide in the last month	54.1
Age	51.6
No. of palpation sites with pain (right masseter)	50.0
Marital status	44.7
Somatic symptom reporting (PILL)	42.4
General health (SF-12v2)	31.8
Ever had orthodontic procedures	29.3
Race	25.1
No. of palpation sites with pain (left masseter)	23.0
HRV: total power (color-word Stroop)	19.1
No. of painful anatomic locations during protrusion	16.3
Average mean arterial pressure (pain-affect Stroop)	16.2
No. of different types of headaches in the last year	16.1
Average mean arterial pressure (color-word Stroop)	15.8
Pain with TMJ noises in the past month	15.4
Sleep latency (PSQI)	12.7
Average heart rate—ECG (pain-affect Stroop)	12.6
Lifetime U.S. residence	12.4
Count of 10 IBS symptoms	11.9
Functional limitation in jaw opening (JFLS)	11.5
Self-rated general health	11.1
Could not open mouth wide prior to 1 month ago	10.8
HRV: total power (pain-affect Stroop)	10.8
No. of painful anatomic locations during right lateral excursion	10.6
Catastrophizing—magnification (PCS)	10.4

PILL

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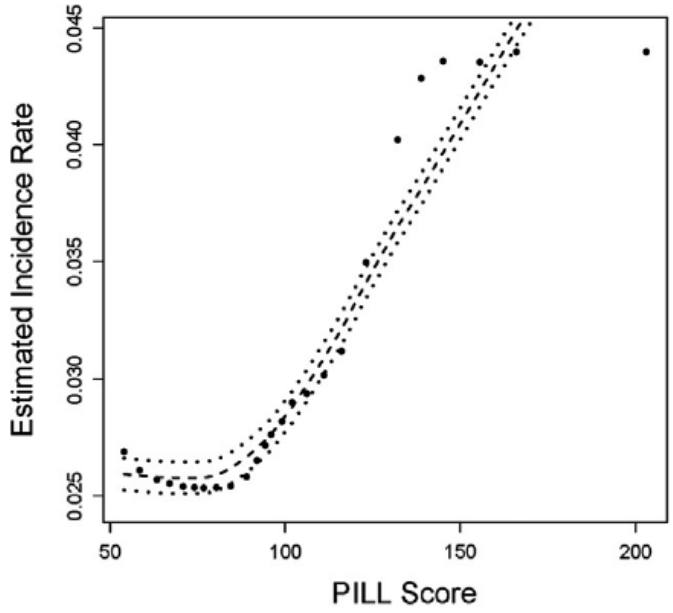
Psychological Factors Associated With Development of TMD: The OPPERA Prospective Cohort Study

Roger B. Fillingim,* Richard Ohrbach,† Joel D. Greenspan,‡ Charles Knott,§ Luda Diatchenko,||,¶,**,†† Ronald Dubner,‡ Eric Bair,||,¶,‡‡ Cristina Baraian,‡‡ Nicole Mack,‡‡ Gary D. Slade,||,§§,¶¶ and William Maixner||,¶,†††

"Two of the most important risk factors for elevated TMD incidence were greater numbers of comorbid pain conditions and greater extent of nonspecific orofacial symptoms. Other important baseline risk factors were preexisting bodily pain, **heightened somatic awareness**, and greater extent of pain in response to examiners' palpation of the head, neck, and body."

"The PILL assesses the frequency with which individuals experience 54 common physical symptoms and sensations on a 5-category scale ("never or almost never" to "more than once every week")."

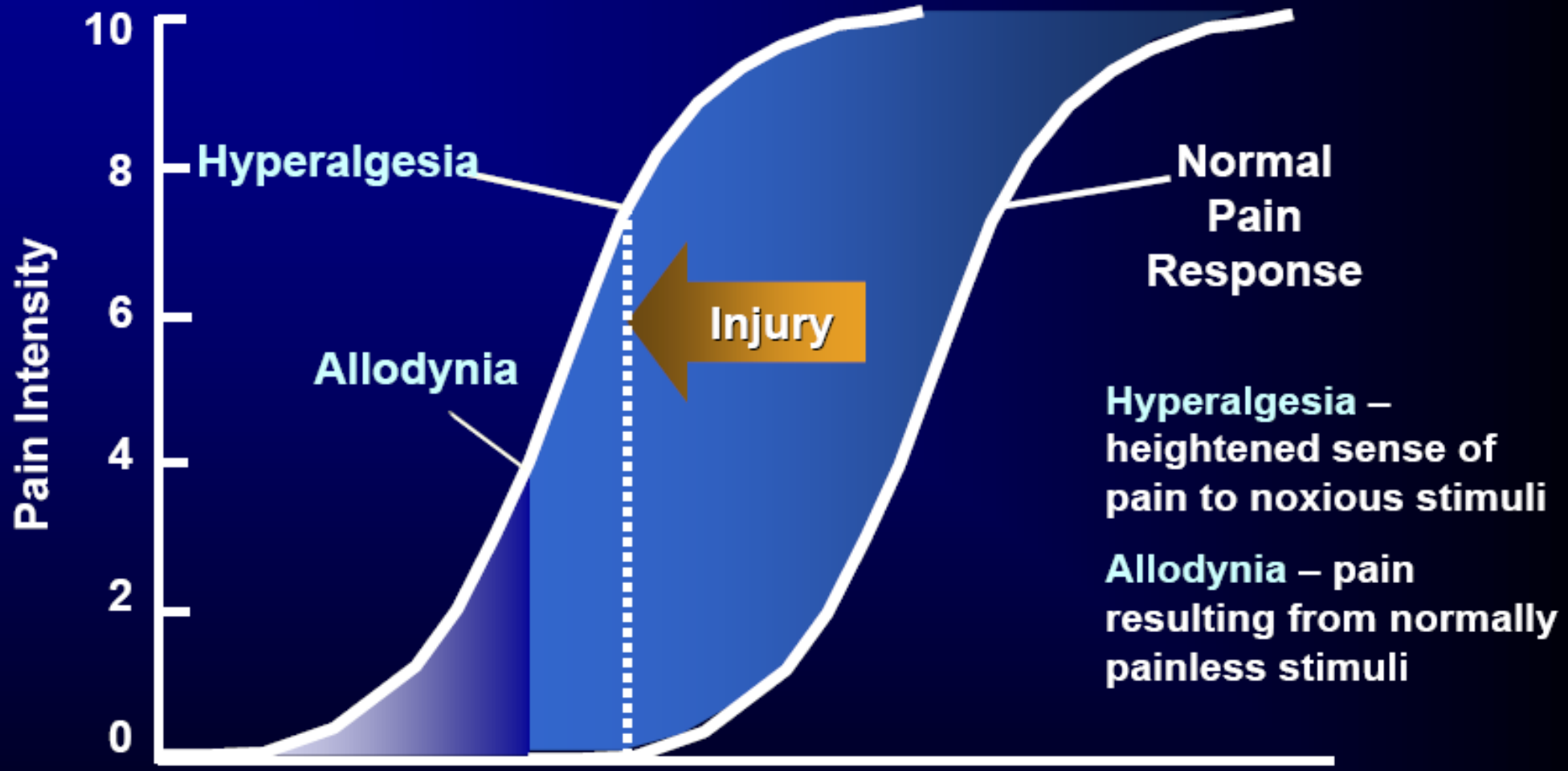


"Partial dependence plots for the PILL, etc. The plots depict the estimated TMD incidence rate that would be observed at several values of the variable after averaging over the values of all other variables in the model."

Variable	N	Percentage endorsed (%)
1. Acne or pimples on the face	590	70.7
2. Headaches	572	68.6
3. Upset stomach	501	60.1
4. Eyes watering	487	60.6
5. Itchy eyes or skin	484	58
6. Back pain	458	54.9
7. Heartburn or gas	454	54.4
8. Sore muscles	447	53.6
9. Insomnia or difficulty sleeping	438	52.4
9. Stiff or sore muscles	438	52.4
10. Running nose	433	51.9

Note. The PILL was scored as a total sum of complaints endorsed as present. Shown in the Table are the frequencies for common complaints endorsed as present.

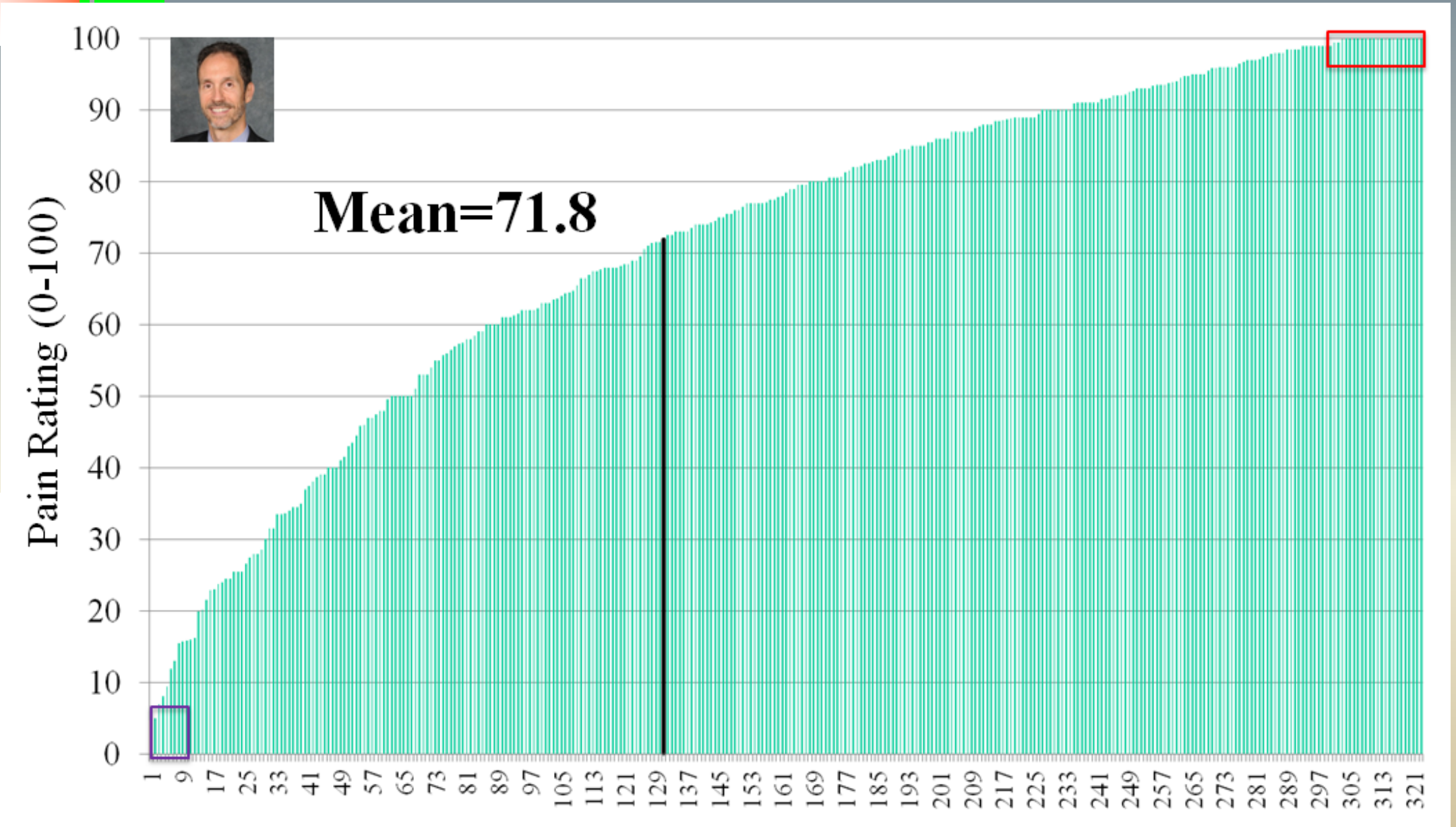
Sensitization



Hyperalgesia – heightened sense of pain to noxious stimuli

Allodynia – pain resulting from normally painless stimuli

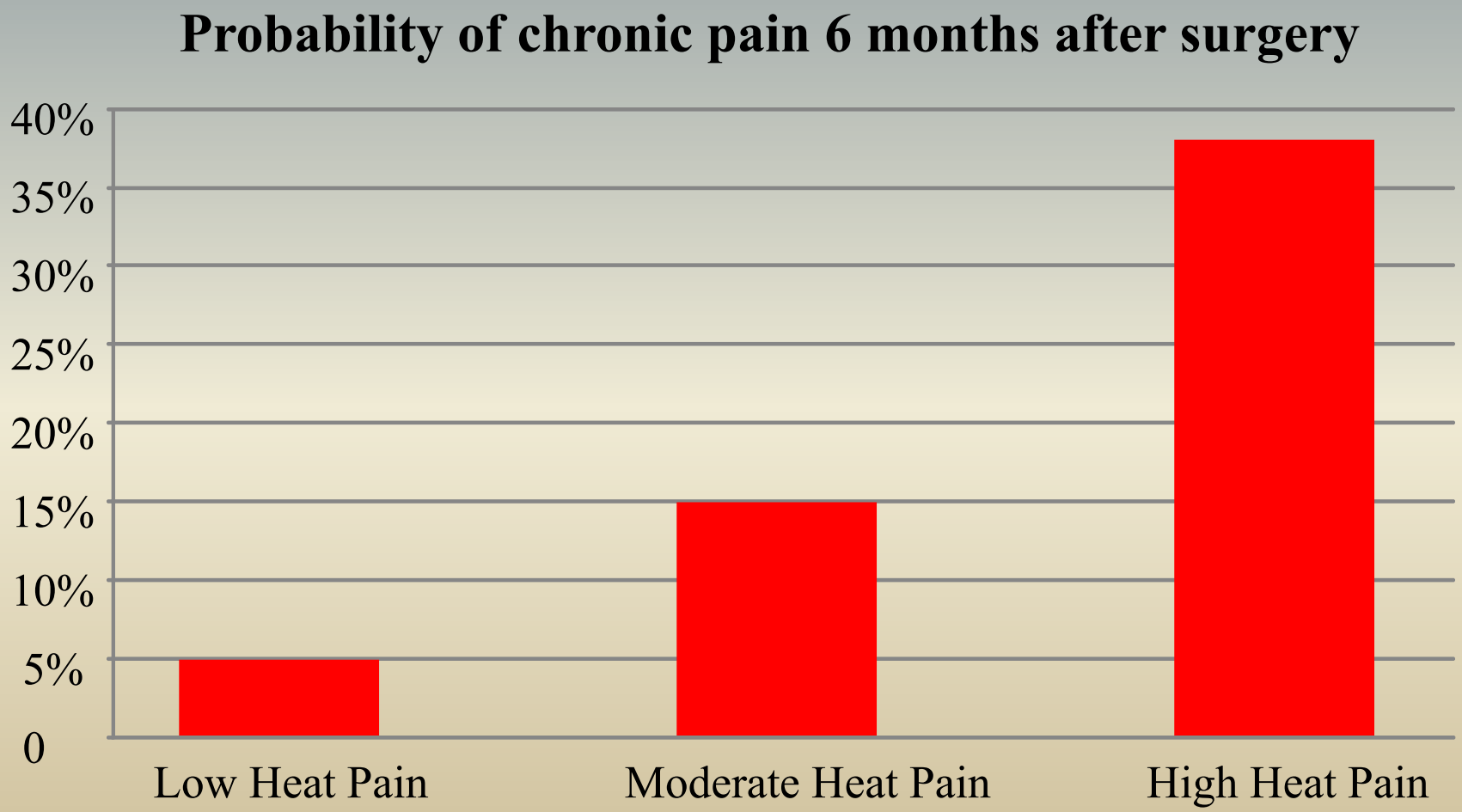
Quantitative Sensory Testing (QST)



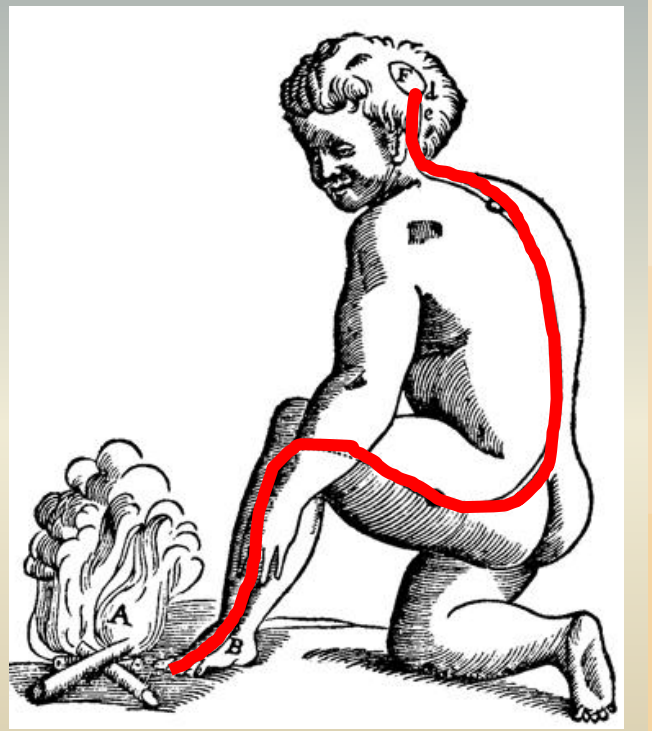
Predictive Relevance of Enhanced Pain Sensitivity

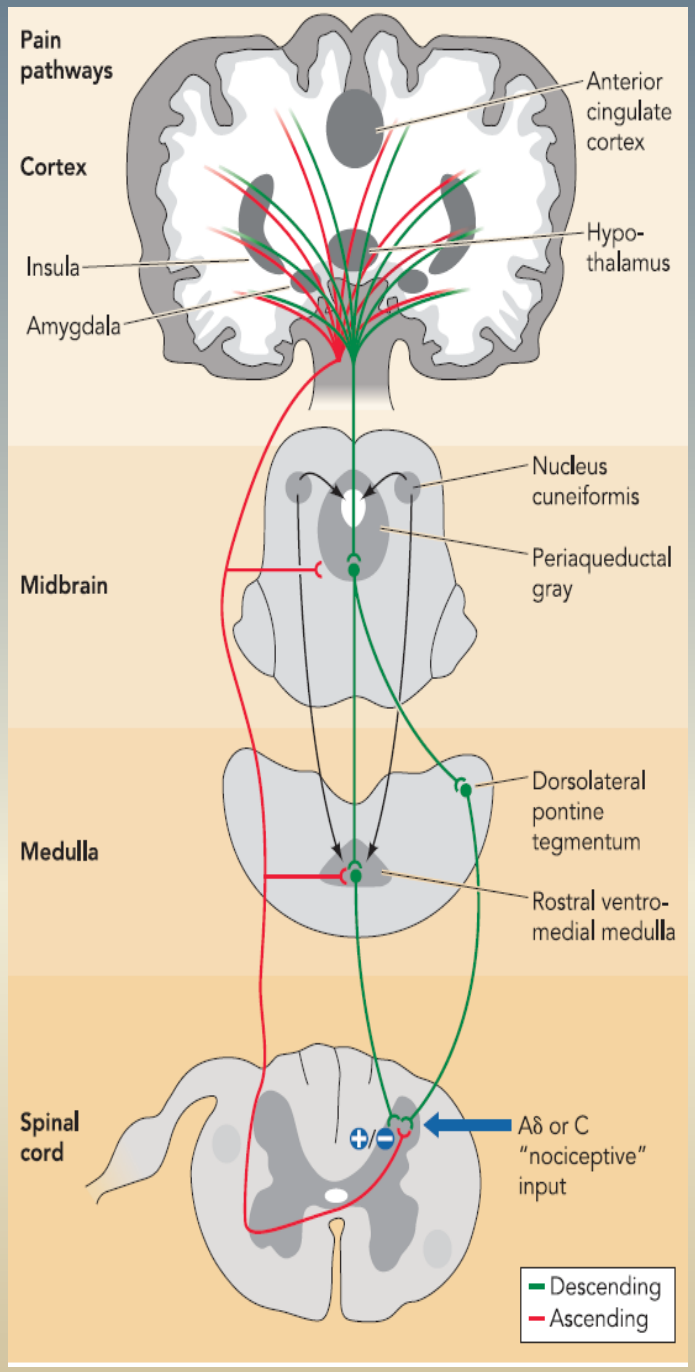
Nearly 500 patients followed for 6 months after hernia repair. Pre-surgical heat pain responses predict persistent pain symptoms.

Aasvang et al., 2010, Anesthesiology



*** Pain is <u>no longer viewed</u> in terms of a straight-through process of neurotransmission from the periphery to the brain**





Nociceptive signals within the CNS may be *<u>modulated</u>* by a number of endogenous
-pain-facilitatory processes
-pain-inhibitory processes

These endogenous pain modulation processes are known to operate at various levels of the CNS
-Brain
-Spinal cord

Play a determinant role in shaping the subjective experience of pain
-Experimental pain
-Clinical pain

*** In humans, the most common methods for assessing endogenous pain modulation are:**

Conditioned pain modulation (CPM) /DNIC paradigms	Temporal summation (TS) of pain paradigms
Pain-inhibition	**Pain-facilitation**
* CPM represents one form of endogenous pain inhibition * Process by which one noxious stimulus inhibits or reduces the perception of a 2nd noxious stimulus	* TS refers to the increased perception of pain with repetitive noxious stimuli * Temporal summation of pain suggests the involvement of central sensitization

Pain-inhibition (CPM) & Pain-facilitation (TS)

*** Assessed using two distinct psychophysical procedures**
*** Subserved by distinct neurophysiologic/biologic mechanisms**
*** Potentially out of balance in many chronic pain conditions**

CPM Variability

PAIN

Pain facilitation and pain inhibition during conditioned pain modulation in fibromyalgia and in healthy controls

Stéphane Potvin[a,b], Serge Marchand[c,d,*]

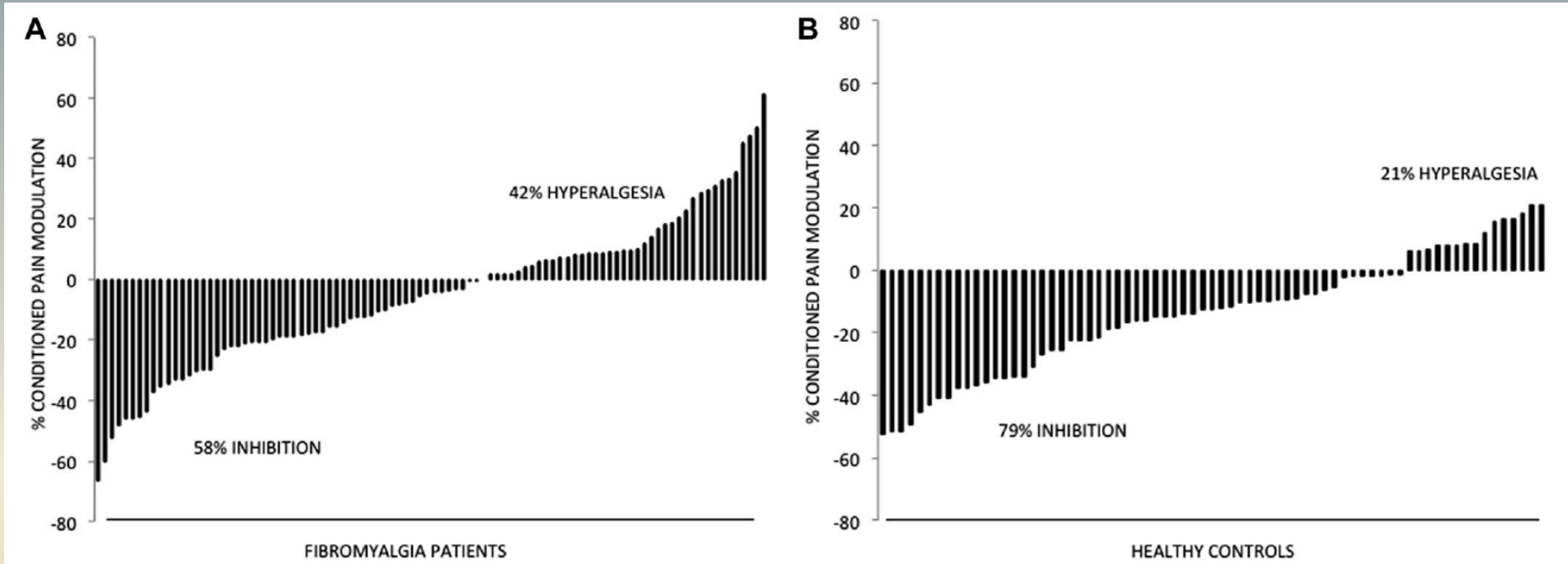


Figure 1. Individual pain inhibition or pain facilitation occurring during the condition pain modulation paradigm in healthy controls (A) and patients with fibromyalgia (B).

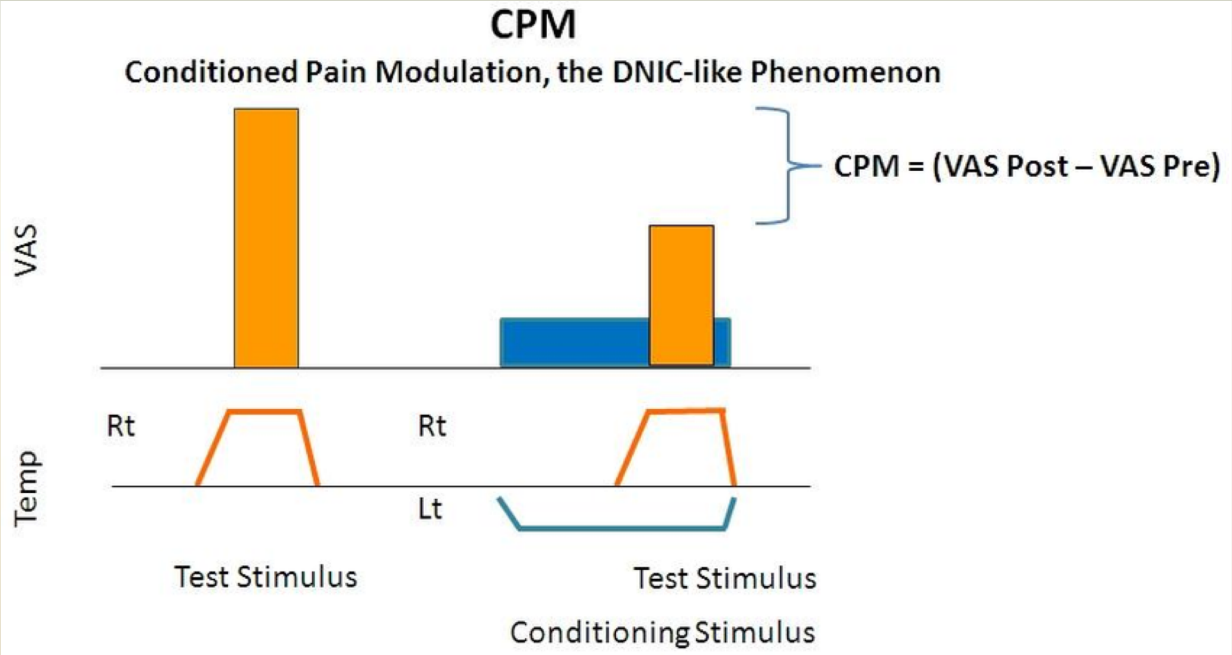
CPM is studied as a pathophysiologic contributor to chronic pain, as a trait-like predictor of outcomes, as an outcome of treatment, as a mechanism that underpins treatment effects, and more . . .

CPM

CPM is reduced or absent in many chronic pain conditions.

Variability in CPM has been shown to predict:

- *Daily pain severity*
- *Reduced physical function*
- *Post-operative pain*
- *Analgesic responses*
- *Exercise-induced analgesia*



FM: Imbalanced Pain Modulation and a Pro-Nociceptive Phenotype

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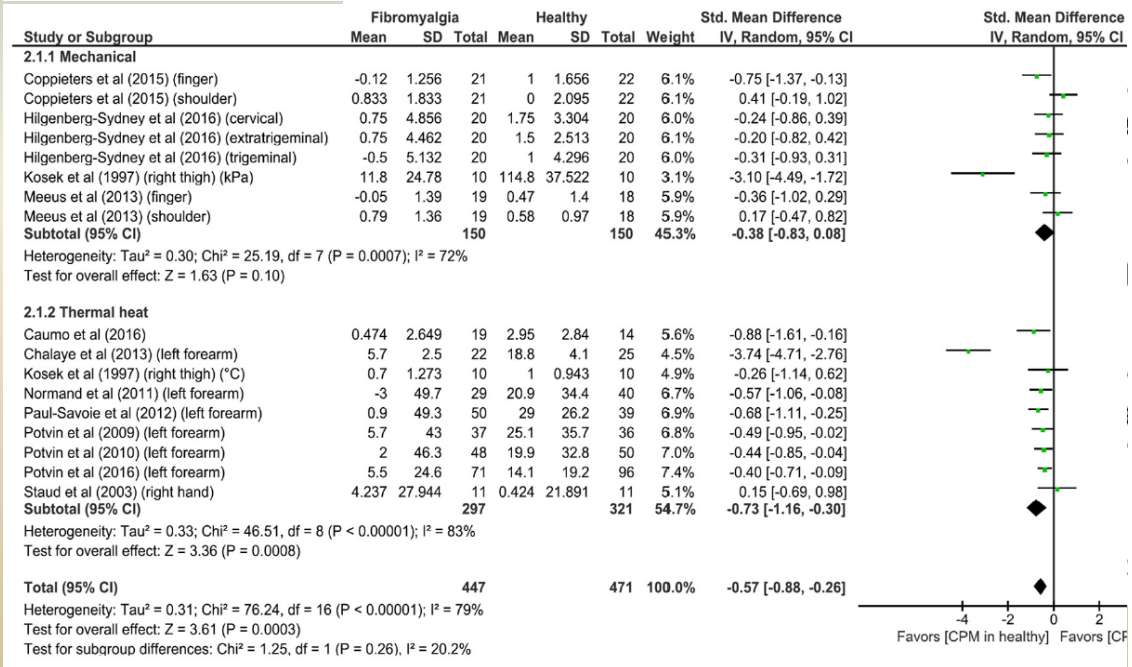
Critical Review

Defective Endogenous Pain Modulation in Fibromyalgia: A Meta-Analysis of Temporal Summation and Conditioned Pain Modulation Paradigms

Anthony Terrence O'Brien,* Alicia Deitos,*,†,‡ Yolanda Triñanes Pego,§ Felipe Fregni,* and Maria Teresa Carrillo-de-la-Peña*,§



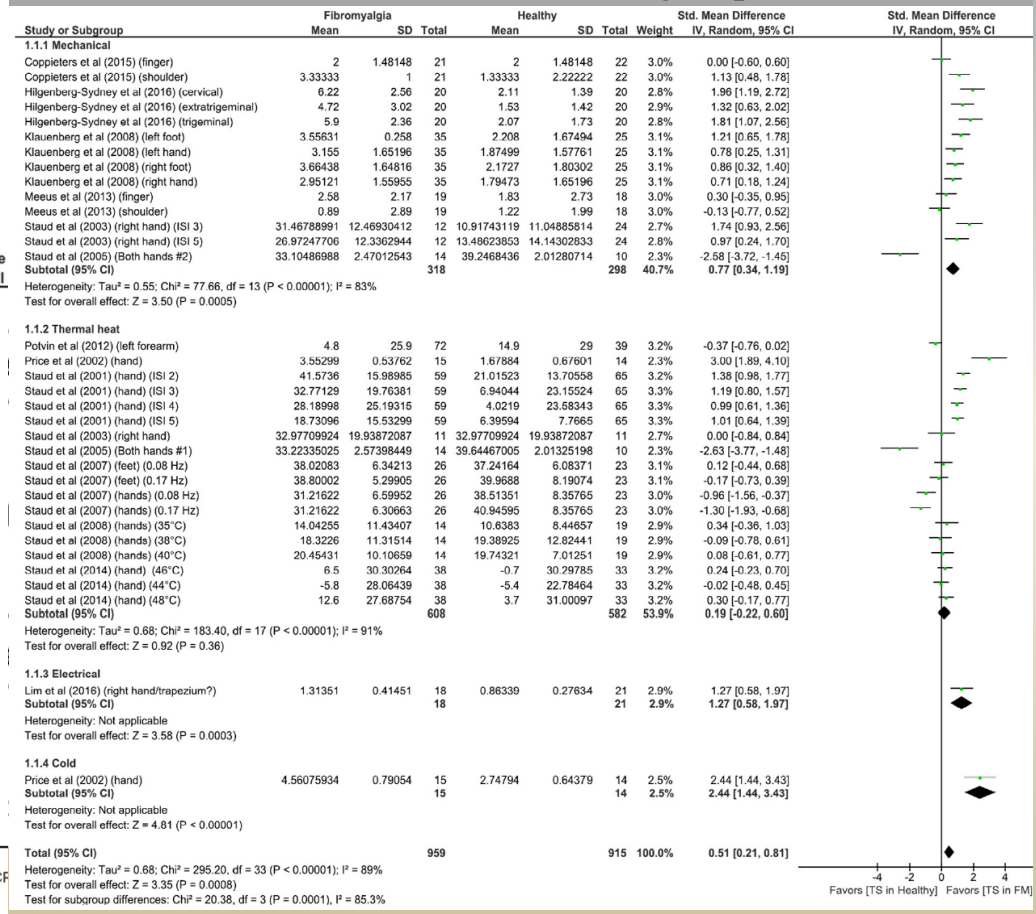
Study or Subgroup	Fibromyalgia Mean	SD	Total	Healthy Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 Mechanical								
Coppieters et al (2015) (finger)	-0.12	1.256	21	1	1.656	22	6.1%	-0.75 [-1.37, -0.13]
Coppieters et al (2015) (shoulder)	0.833	1.833	21	0	2.095	22	6.1%	0.41 [-0.19, 1.02]
Hilgenberg-Sydney et al (2016) (cervical)	0.75	4.856	20	1.75	3.304	20	6.0%	-0.24 [-0.86, 0.39]
Hilgenberg-Sydney et al (2016) (extratrigeminal)	0.75	4.462	20	1.5	2.513	20	6.1%	-0.20 [-0.82, 0.42]
Hilgenberg-Sydney et al (2016) (trigeminal)	-0.5	5.132	20	1	4.296	20	6.0%	-0.31 [-0.93, 0.31]
Kosek et al (1997) (right thigh) (kPa)	11.8	24.78	10	114.8	37.522	10	3.1%	-3.10 [-4.49, -1.72]
Meeus et al (2013) (finger)	-0.05	1.39	19	0.47	1.4	18	5.9%	-0.36 [-1.02, 0.29]
Meeus et al (2013) (shoulder)	0.79	1.36	19	0.58	0.97	18	5.9%	0.17 [-0.47, 0.82]
Subtotal (95% CI)			**150**			**150**	**45.3%**	**-0.38 [-0.83, 0.08]**
Heterogeneity: Tau² = 0.30; Chi² = 25.19, df = 7 (P = 0.0007); I² = 72%								
Test for overall effect: Z = 1.63 (P = 0.10)								
2.1.2 Thermal heat								
Caumo et al (2016)	0.474	2.649	19	2.95	2.84	14	5.6%	-0.88 [-1.61, -0.16]
Chalaye et al (2013) (left forearm)	5.7	2.5	22	18.8	4.1	25	4.5%	-3.74 [-4.71, -2.76]
Kosek et al (1997) (right thigh) (°C)	0.7	1.273	10	1	0.943	10	4.9%	-0.26 [-1.14, 0.62]
Normand et al (2011) (left forearm)	-3	49.7	29	20.9	34.4	40	6.7%	-0.57 [-1.06, -0.08]
Paul-Savoie et al (2012) (left forearm)	0.9	49.3	50	29	26.2	39	6.9%	-0.68 [-1.11, -0.25]
Potvin et al (2009) (left forearm)	5.7	43	37	25.1	35.7	36	6.8%	-0.49 [-0.95, -0.02]
Potvin et al (2010) (left forearm)	2	46.3	48	19.9	32.8	50	7.0%	-0.44 [-0.85, -0.04]
Potvin et al (2016) (left forearm)	5.5	24.6	71	14.1	19.2	96	7.4%	-0.40 [-0.71, -0.09]
Staud et al (2003) (right hand)	4.237	27.944	11	0.424	21.891	11	5.1%	0.15 [-0.69, 0.98]
Subtotal (95% CI)			**297**			**321**	**54.7%**	**-0.73 [-1.16, -0.30]**
Heterogeneity: Tau² = 0.33; Chi² = 46.51, df = 8 (P < 0.00001); I² = 83%								
Test for overall effect: Z = 3.36 (P = 0.0008)								
Total (95% CI)			**447**			**471**	**100.0%**	**-0.57 [-0.88, -0.26]**
Heterogeneity: Tau² = 0.31; Chi² = 76.24, df = 16 (P < 0.00001); I² = 79%								
Test for overall effect: Z = 3.61 (P = 0.0003)								
Test for subgroup differences: Chi² = 1.25, df = 1 (P = 0.26), I² = 20.2%								

Std. Mean Difference IV, Random, 95% CI

-4 -2 0 2

Favors [CPM in healthy] Favors [CP

23 studies showed an effect size of .53 for TS ($P < .001$), which is a 68% relative difference between patients and controls, and of .57 for CPM ($P < .001$), representing a 65% relative difference between the groups.



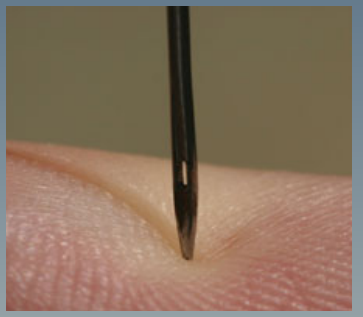
Study or Subgroup	Fibromyalgia Mean	SD	Total	Healthy Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Mechanical								
Coppieters et al (2015) (finger)	2	1.48148	21	2	1.48148	22	3.0%	0.00 [-0.60, 0.60]
Coppieters et al (2015) (shoulder)	3.33333	1	21	1.33333	2.22222	22	3.0%	1.13 [0.48, 1.78]
Hilgenberg-Sydney et al (2016) (cervical)	6.22	2.56	20	2.11	1.39	20	2.8%	1.96 [1.19, 2.72]
Hilgenberg-Sydney et al (2016) (extratrigeminal)	4.72	3.02	20	1.53	1.42	20	2.9%	1.32 [0.63, 2.02]
Hilgenberg-Sydney et al (2016) (trigeminal)	5.9	2.36	20	2.07	1.73	20	2.8%	1.81 [1.07, 2.56]
Klauenberg et al (2008) (left foot)	3.55831	0.258	35	2.208	1.67494	25	3.1%	1.21 [0.65, 1.78]
Klauenberg et al (2008) (left hand)	3.155	1.65196	35	1.87499	1.57761	25	3.1%	0.78 [0.25, 1.31]
Klauenberg et al (2008) (right foot)	3.66438	1.64816	35	2.1727	1.80302	25	3.1%	0.86 [0.32, 1.40]
Klauenberg et al (2008) (right hand)	2.95121	1.55955	35	1.79473	1.65196	25	3.1%	0.71 [0.18, 1.24]
Meeus et al (2013) (finger)	2.58	2.17	19	1.83	2.73	18	3.0%	0.30 [-0.35, 0.95]
Meeus et al (2013) (shoulder)	0.89	2.89	19	1.22	1.99	18	3.0%	-0.13 [-0.77, 0.52]
Staud et al (2003) (right hand) (ISI 3)	31.46788991	12.46930412	12	10.91743119	11.04885814	24	2.7%	1.74 [0.93, 2.56]
Staud et al (2003) (right hand) (ISI 5)	26.97247706	12.3362944	12	13.48623853	14.14302833	24	2.8%	0.97 [0.24, 1.70]
Staud et al (2005) (Both hands #2)	33.10486988	2.47012543	14	39.2468436	2.01280714	10	2.3%	-2.58 [-3.72, -1.45]
Subtotal (95% CI)			**318**			**298**	**40.7%**	**0.77 [0.34, 1.19]**
Heterogeneity: Tau² = 0.55; Chi² = 77.66, df = 13 (P < 0.00001); I² = 83%								
Test for overall effect: Z = 3.50 (P = 0.0005)								
1.1.2 Thermal heat								
Potvin et al (2012) (left forearm)	4.8	25.9	72	14.9	29	39	3.2%	-0.37 [-0.76, 0.02]
Price et al (2002) (hand)	3.55299	0.53762	15	1.67884	0.67601	14	2.3%	3.00 [1.89, 4.10]
Staud et al (2001) (hand) (ISI 2)	41.5736	15.98985	59	21.01523	13.70558	65	3.2%	1.38 [0.98, 1.77]
Staud et al (2001) (hand) (ISI 3)	32.77129	19.76381	59	6.94044	23.15524	65	3.3%	1.19 [0.80, 1.57]
Staud et al (2001) (hand) (ISI 4)	28.18998	25.19315	59	4.0219	23.58343	65	3.3%	0.99 [0.61, 1.36]
Staud et al (2001) (hand) (ISI 5)	18.73096	15.53299	59	6.39594	7.7665	65	3.3%	1.01 [0.64, 1.39]
Staud et al (2003) (right hand)	32.97709924	19.93872087	11	32.97709924	19.93872087	11	2.7%	0.00 [-0.84, 0.84]
Staud et al (2005) (Both hands #1)	33.22335025	2.57398449	14	39.64467005	2.01325198	10	2.3%	-2.63 [-3.77, -1.48]
Staud et al (2007) (feet) (0.08 Hz)	38.02083	6.34213	26	37.24164	6.08371	23	3.1%	0.12 [-0.44, 0.68]
Staud et al (2007) (feet) (0.17 Hz)	38.80002	5.29905	26	39.9688	8.19074	23	3.1%	-0.17 [-0.73, 0.39]
Staud et al (2007) (hands) (0.08 Hz)	31.21622	6.59952	26	38.51351	8.35765	23	3.0%	-0.96 [-1.56, -0.37]
Staud et al (2007) (hands) (0.17 Hz)	31.21622	6.30663	26	40.94595	8.35765	23	3.0%	-1.30 [-1.93, -0.68]
Staud et al (2008) (hands) (35°C)	14.04255	11.43407	14	10.6383	8.44657	19	2.9%	0.34 [-0.36, 1.03]
Staud et al (2008) (hands) (38°C)	18.3226	11.31514	14	19.38925	12.82441	19	2.9%	-0.09 [-0.78, 0.61]
Staud et al (2008) (hands) (40°C)	20.45431	10.10659	14	19.74321	7.01251	19	2.9%	0.08 [-0.61, 0.77]
Staud et al (2014) (hand) (46°C)	6.5	30.30264	38	-0.7	30.29785	33	3.2%	0.24 [-0.23, 0.70]
Staud et al (2014) (hand) (44°C)	-5.8	28.06439	38	-5.4	22.78464	33	3.2%	-0.02 [-0.48, 0.45]
Staud et al (2014) (hand) (48°C)	12.6	27.68754	38	3.7	31.00097	33	3.2%	0.30 [-0.17, 0.77]
Subtotal (95% CI)			**608**			**582**	**53.9%**	**0.19 [-0.22, 0.60]**
Heterogeneity: Tau² = 0.68; Chi² = 183.40, df = 17 (P < 0.00001); I² = 91%								
Test for overall effect: Z = 0.92 (P = 0.36)								
1.1.3 Electrical								
Lim et al (2016) (right hand/trapezium?)	1.31351	0.41451	18	0.86339	0.27634	21	2.9%	1.27 [0.58, 1.97]
Subtotal (95% CI)			**18**			**21**	**2.9%**	**1.27 [0.58, 1.97]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.58 (P = 0.0003)								
1.1.4 Cold								
Price et al (2002) (hand)	4.56075934	0.79054	15	2.74794	0.64379	14	2.5%	2.44 [1.44, 3.43]
Subtotal (95% CI)			**15**			**14**	**2.5%**	**2.44 [1.44, 3.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.81 (P < 0.00001)								
Total (95% CI)			**959**			**915**	**100.0%**	**0.51 [0.21, 0.81]**
Heterogeneity: Tau² = 0.68; Chi² = 295.20, df = 33 (P < 0.00001); I² = 89%								
Test for overall effect: Z = 3.35 (P = 0.0008)								
Test for subgroup differences: Chi² = 20.38, df = 3 (P = 0.0001), I² = 85.3%								

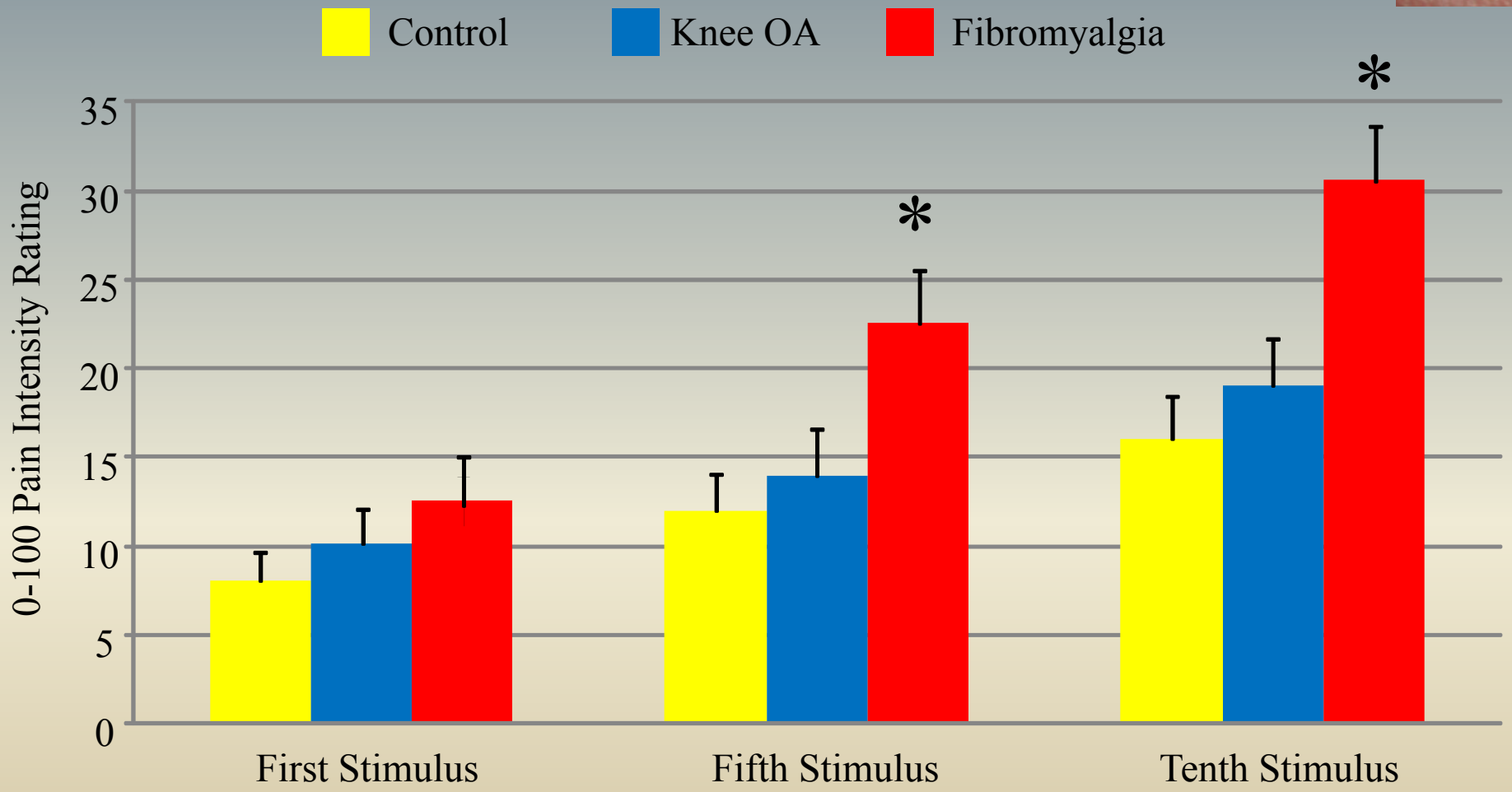
Std. Mean Difference IV, Random, 95% CI

-4 -2 0 2 4

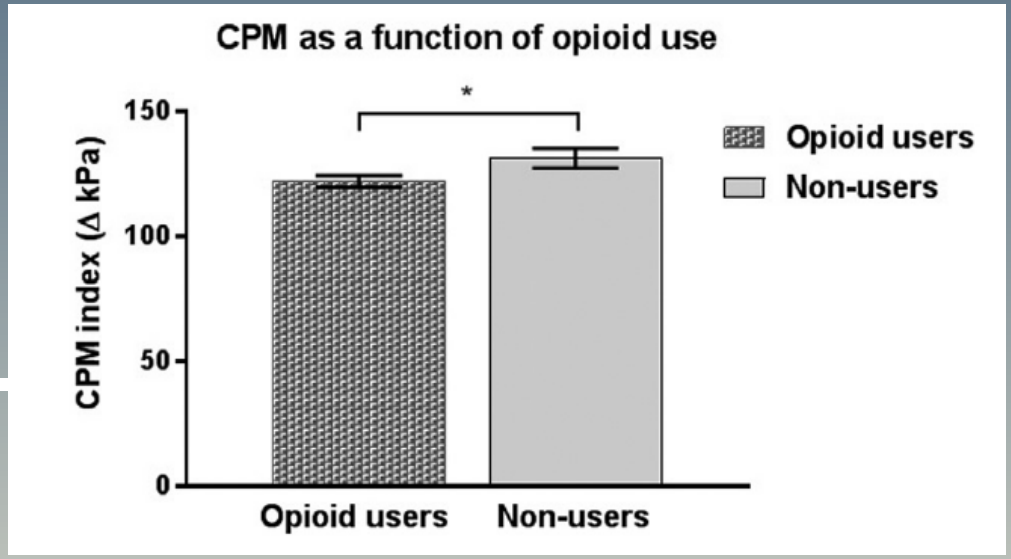
Favors [TS in Healthy] Favors [TS in FM]

Temporal Summation





Relationship Between TS & CPM



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The Journal of Pain, Vol 20, No 4 (April), 2019: pp 462–471
Available online at www.jpain.org and www.sciencedirect.com

Endogenous Pain Modulation Profiles Among Individuals With Chronic Pain: Relation to Opioid Use

Marc O. Martel,*† Kristian Petersen,‡ Marise Cornelius,‡ Lars Arendt-Nielsen,§ and Robert Edwards‡

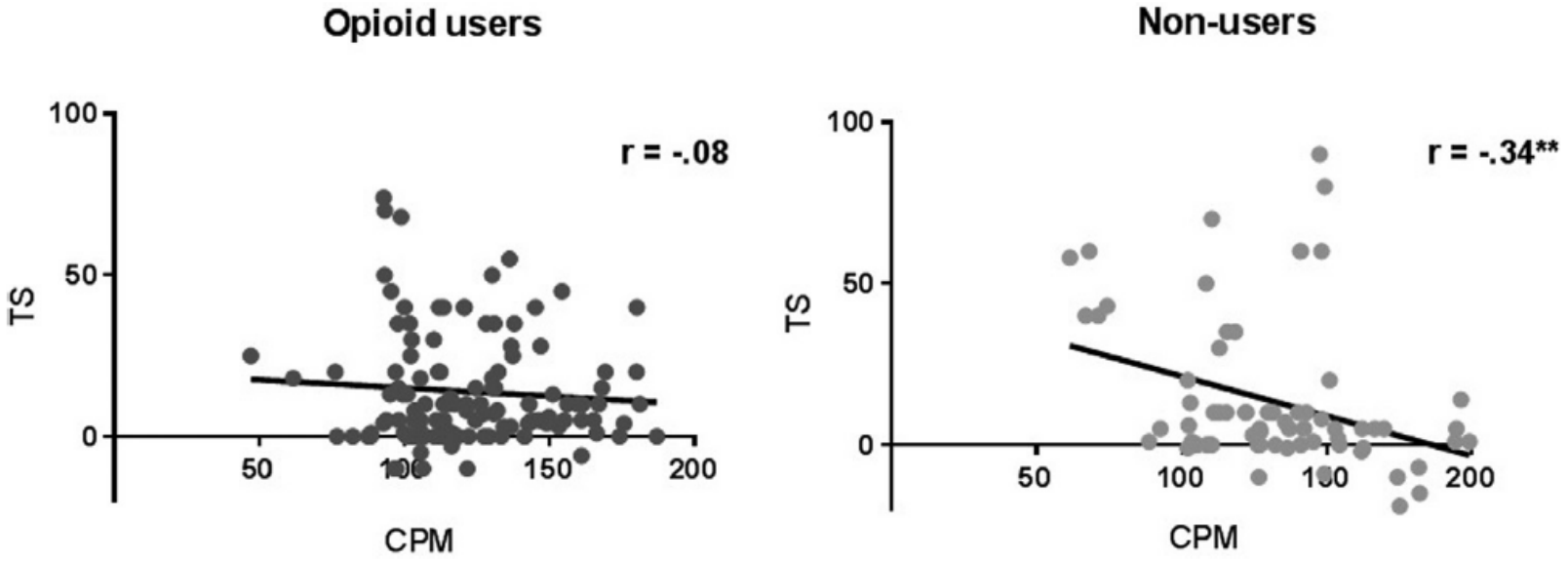
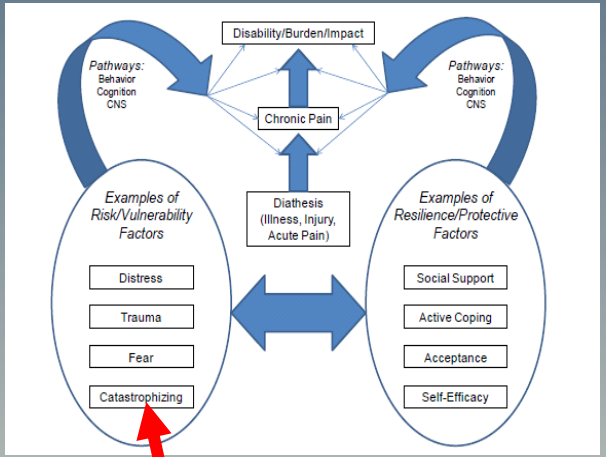
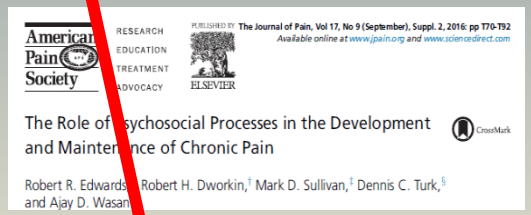
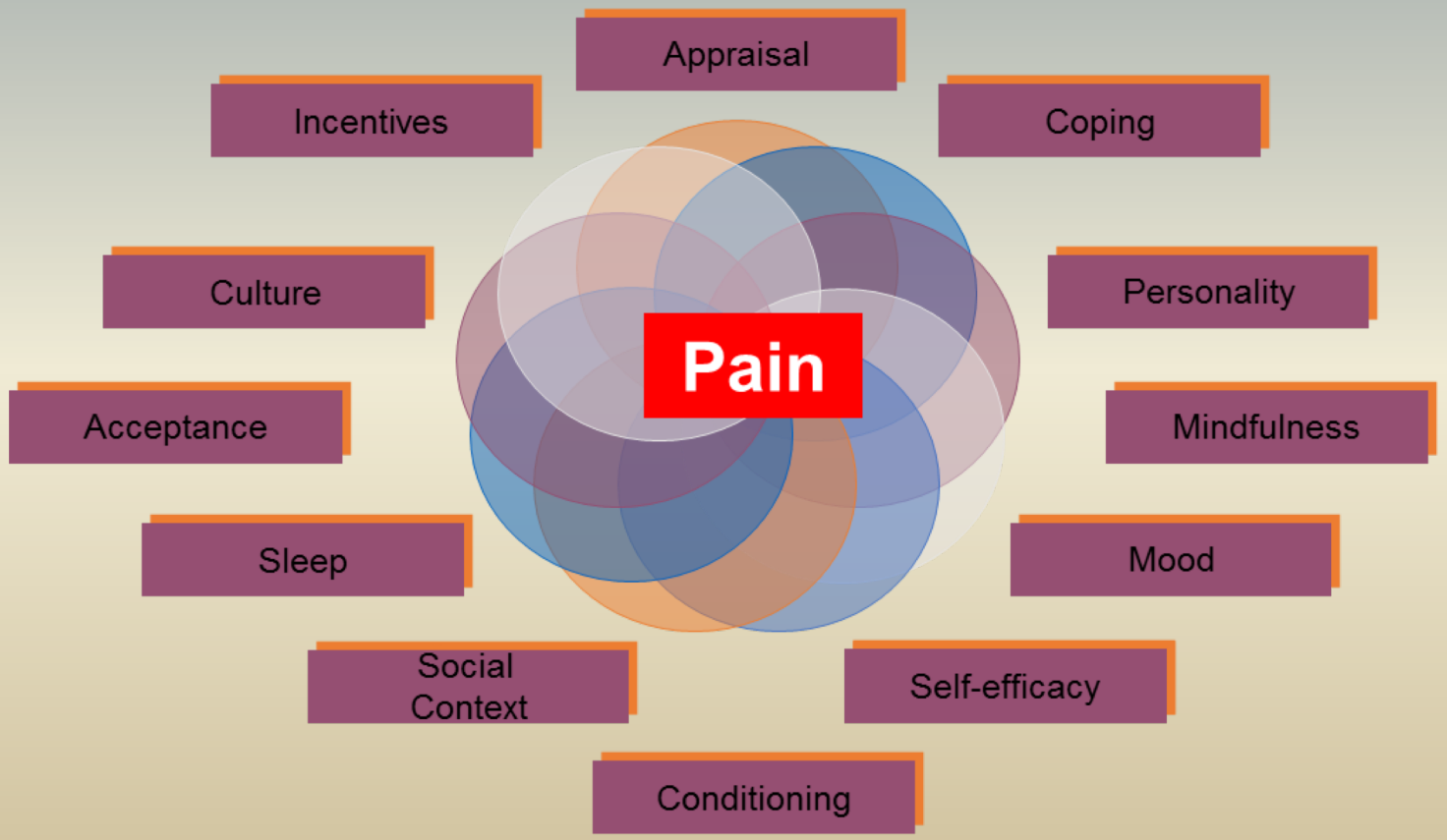


Figure 3. Association between conditioned pain modulation and temporal summation as a function of individuals' opioid status.

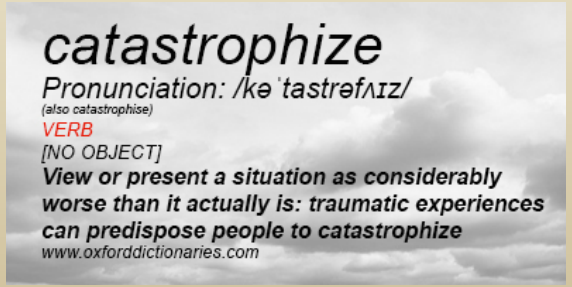
Depicting the Biopsychosocial Model of Pain







A critical risk/ vulnerability factor



Higher-Order Constructs Such as "Negative Affect" Contain Many Inter-Correlated Variables

Patients often exhibit symptom combinations/clusters

Catastrophizing Predicts the Future Onset of Chronic Back Pain

American Journal of Epidemiology
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Vol. 156, No. 11
Printed in U.S.A.
DOI: 10.1093/aje/kwf136

Pain Catastrophizing and Kinesiophobia: Predictors of Chronic Low Back Pain

H. Susan J. Picavet[1], Johan W. S. Vlaeyen[2], and Jan S. A. G. Schouten[1,3]

		Current low back pain (*n* = 132)		Low back pain limitation (*n* = 31)		Severe low back pain (*n* = 39)		Chronic low back pain (*n* = 69)		Low back pain with disability (*n* = 31)	
		No low back pain at baseline (n = *1,160*)									
Catastrophizing											
Lowest tertile	373	1§		1§		1§		1§		1§	
Middle tertile	380	0.9	0.6, 1.5	0.7	0.3, 1.8	1.0	0.4, 2.5	1.3	0.7, 2.5	1.9	0.7, 5.9
Highest tertile	345	1.2	0.8, 1.9	1.4	0.6, 3.7	2.2	1.0, 5.0	2.1	1.1, 3.9	3.1	1.1, 8.7

Replicated by Linton, 2005

Risk Factor for Poor (Pharmacologic) Tx Outcomes

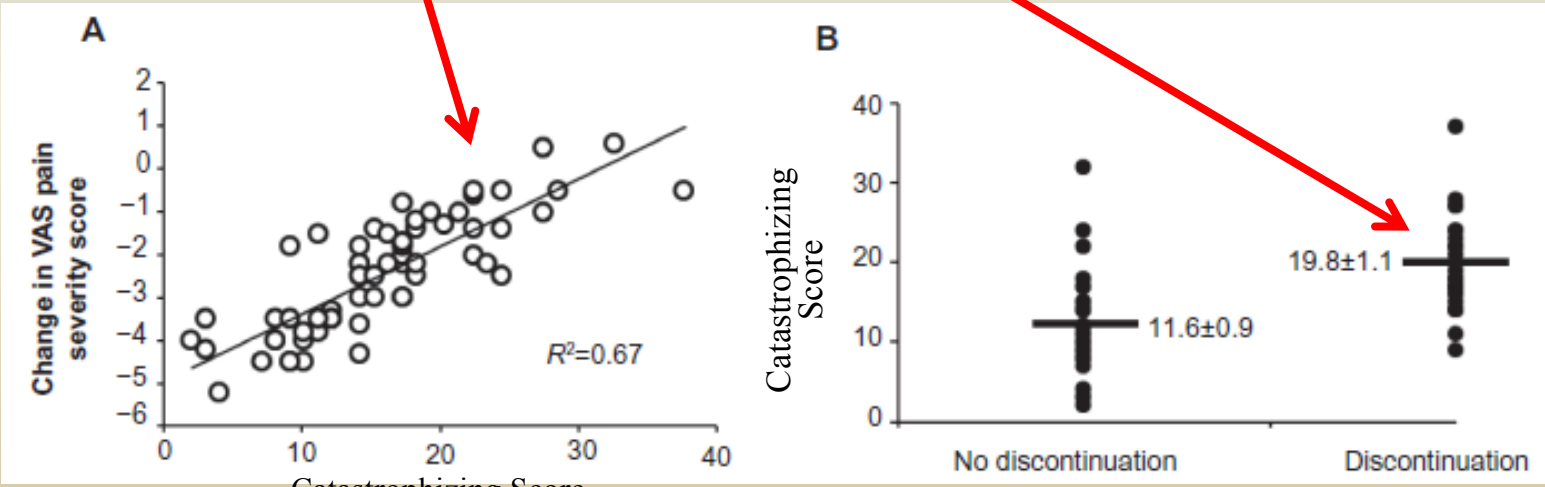
Journal of Pain Research
Dovepress
open access to scientific and medical research
Open Access Full Text Article
ORIGINAL RESEARCH

The importance of catastrophizing for successful pharmacological treatment of peripheral neuropathic pain

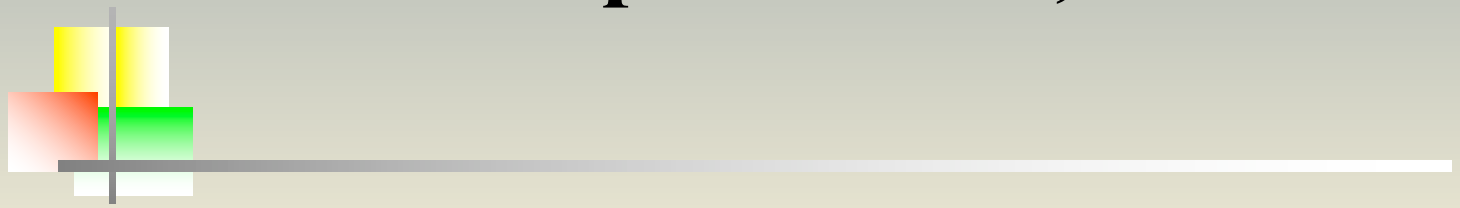
Cory Toth
Shauna Brady
Melinda Hatfield

Table 3 Medication interventions provided to patients

	Number of patients receiving specific medication	Initial medication daily dose	Final medication daily dose	Discontinuations
Amitryptyline	25 (40%)	15.[illegible]±5.2 mg	37.3±12.7 mg	14/25 (56%)
Nortryptyline	10 (16%)	25.5±11.3 mg	55.7±13.3 mg	5/10 (50%)
Gabapentin	17 (27%)	667.0±[illegible]12.3 mg	1,562.7±147.8 mg	7/17 (41%)
Pregabalin	10 (16%)	120.5±[illegible]2.3 mg	363.3±78.8 mg	4/10 (40%)



Catastrophizing's Links with Other Elements of "Centralized" Chronic Pain (e.g., Impaired Pain Modulation, Widespread Pain, Side Effects, Etc.)



Catastrophizing & Pain Sensitivity

PAIN

The relationship between catastrophizing and altered pain sensitivity in patients with chronic low-back pain

Samantha M. Meints[a,*], Ishtiaq Mawla[b], Vitaly Napadow[a,b], Jian Kong[b,c], Jessica Gerber[b], Suk-Tak Chan[b], Ajay D. Wasan[d], Ted J. Kaptchuk[e], Christina McDonnell[a], Junie Carriere[a], Bruce Rosen[b], Randy L. Gollub[b,c], Robert R. Edwards[a]

Table 2

Independent *t* tests for QST Outcomes.

Outcome	Group	Mean	SD	t	d
Two-point discrimination—finger	HC	3.16	1.53	−1.83	0.37
	CLBP	3.78	1.83		
Two-point discrimination—back	HC	34.53	15.42	−2.26*	0.45
	CLBP	41.73	16.69		
P40 pressure	HC	201.94	79.81	2.83**	0.50
	CLBP	165.69	64.66		

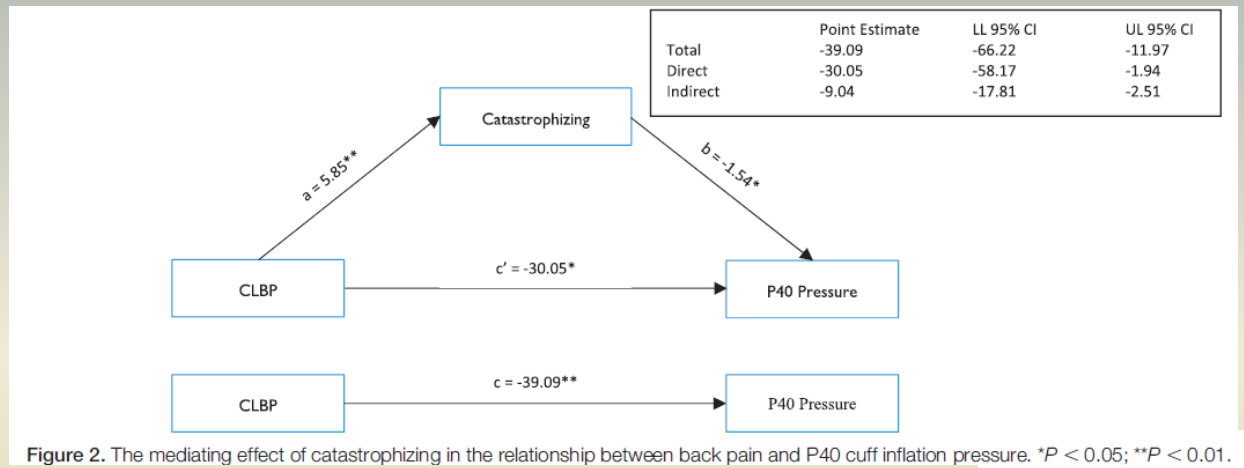
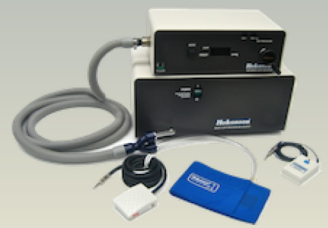


Figure 2. The mediating effect of catastrophizing in the relationship between back pain and P40 cuff inflation pressure. *$P < 0.05$; **$P < 0.01$.



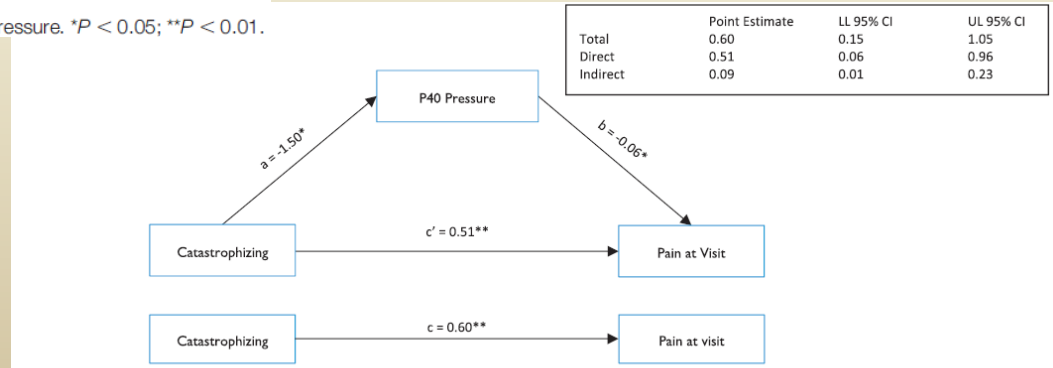


Figure 4. The mediating effect of pain sensitization (as measured by P40 cuff inflation pressure) in the relationship between catastrophizing pain rating at time of visit controlling for opioid use and depression. *$P < 0.05$; **$P < 0.01$.

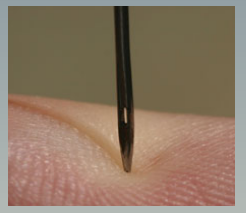
Catastrophizing & Temporal Summation

(Anesthesiology 2014; 121:1292-301)

Distraction Analgesia in Chronic Pain Patients

The Impact of Catastrophizing

Kristin L. Schreiber, M.D., Ph.D., Claudia Campbell, Ph.D., Marc O. Martel, Ph.D., Seth Greenbaum, B.A., Ajay D. Wasan, M.D., M.Sc., David Borsook, M.D., Ph.D.,| Robert N. Jamison, Ph.D., Robert R. Edwards, Ph.D.



Patients with chronic MSK pain, categorized as high catastrophizers (n=76) or low catastrophizers (n=69). Temporal summation assessed using a series of 10 stimuli administered with punctate probes:

The Journal of Pain, Vol 8, No 1 (January), 2007: pp 2-10
Available online at www.sciencedirect.com

ELSEVIER

Original Reports

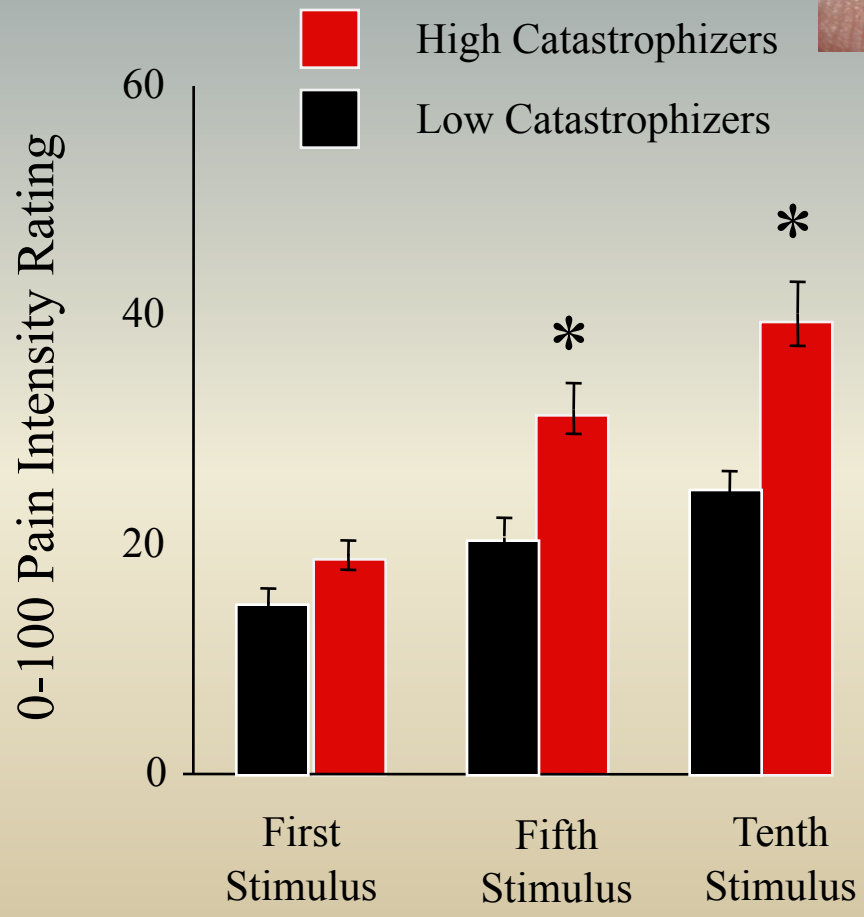
Sex and Pain-Related Psychological Variables Are Associated With Thermal Pain Sensitivity for Patients With Chronic Low Back Pain

Steven Z. George,* Virgil T. Wittmer,† Roger B. Fillingim,‡ and Michael E. Robinson§

Pain-related Catastrophizing in Healthy Women Is Associated With Greater Temporal Summation of and Reduced Habituation to Thermal Pain

Robert R. Edwards, PhD, Michael T. Smith, PhD,* Gregory Stonerock, BA,† and Jennifer A. Haythornthwaite, PhD**

(*Clin J Pain* 2006;22:730–737)



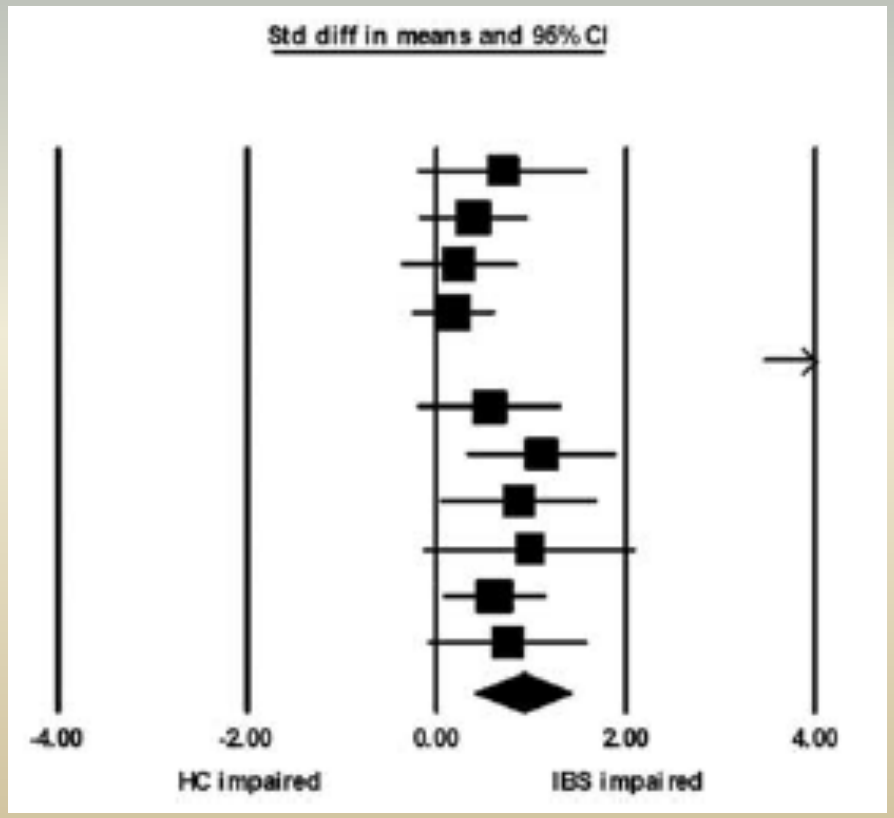
Catastrophizing &CPM

(*J Clin Gastroenterol* 2019;53:399–408)

Conditioned Pain Modulation (CPM) is Reduced in Irritable Bowel Syndrome

A Systematic Review and Meta-Analysis of CPM and the Role of Psychological Factors

Anna Marcuzzi, PhD,†‡ Rosemary J. Chakiath, PhD,*†‡*
Philip J. Siddall, PhD,†§ John E. Kellow, PhD,†‖ Julia M. Hush, PhD,¶
Michael P. Jones, PhD,# Daniel S.J. Costa, PhD,†‡*
and Paul J. Wrigley, PhD†‡*



"In addition, reduced CPM responses were significantly correlated with higher anxiety, stress, and pain catastrophizing (r=0.38)."

"It is noteworthy that Piche and colleagues showed that group differences in CPM responses were no longer significant when psychological factors were accounted for in the analysis. PCS was however found to independently predict CPM effect and mediate increased pain-related anxiety occurring during CPM."

Catastrophizing and Opioid-Induced CPM impairment?

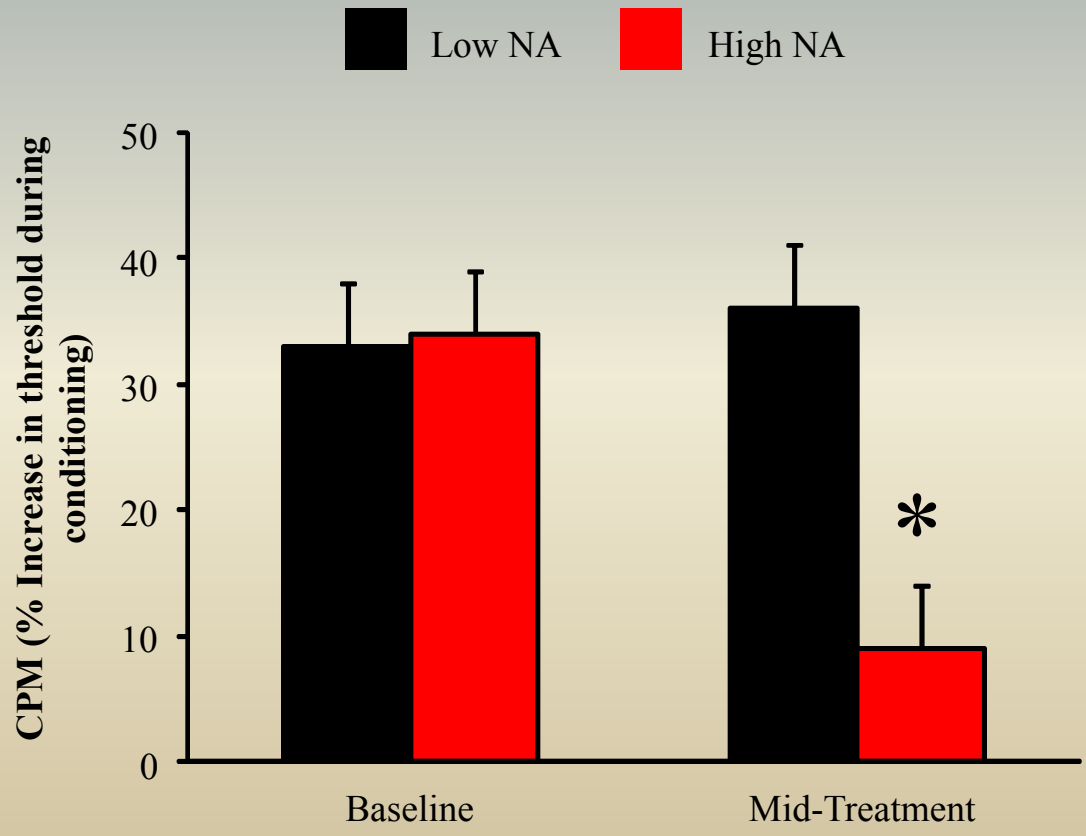
Changes in Pain Sensitivity and Pain Modulation During Oral Opioid Treatment: The Impact of Negative Affect

Pain Medicine 2016; 17: 1882–1891
doi: 10.1093/pm/pnw010

R.R. Edwards, PhD,* A.J. Dolman, BS,*
E. Michna, MD, JD, MPH,* J.N. Katz, MD, MS,†
S.S. Nedeljkovic, MD,* D. Janfaza, MD,*
Z. Isaac, MD,‡ M.O. Martel, PhD,*
R.N. Jamison, PhD,§ and A.D. Wasan, MD, MSc¶

6-month study of oral opioid treatment in patients with chronic radicular LBP.

Patients high in NA and catastrophizing (elevated scores on the HADS, PCS etc) report less opioid analgesia AND show decrements in CPM during treatment.



Catastrophizing and Widespread Pain

American Pain Society
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PUBLISHED BY ELSEVIER
The Journal of Pain, Vol 15, No 11 (November), 2014: pp 1156-1165
Available online at www.jpain.org and www.sciencedirect.com

An Experimental Approach to Examining Psychological Contributions to Multisite Musculoskeletal Pain

Nils Georg Niederstrasser,* P. Maxwell Slepian,† Tsipora Mankovsky-Arnold,‡ Christian Larivière,§ Johan W. Vlaeyen,* and Michael J. L. Sullivan‡

Clin Orthop Relat Res (2015) 473:3894–3902
DOI 10.1007/s11999-015-4575-4
Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

CLINICAL RESEARCH

Is There an Association Between Whole-body Pain With Osteoarthritis-related Knee Pain, Pain Catastrophizing, and Mental Health?

Amish J. Dave MD, Faith Selzer PhD, Elena Losina PhD, Kristina M. Klara BS, Jamie E. Collins PhD, Ilana Usiskin BS, Philip Band PhD, David F. Dalury MD, Richard Iorio MD, Kirk Kindsfater MD, Jeffrey N. Katz MD, MSc

Catastrophizing Is Associated with Clinical Examination Findings, Activity Interference, and Health Care Use Among Patients with Temporomandibular Disorders

J OROFAC PAIN 2005;19:291–300

Differing Psychologically Derived Clusters in People With Chronic Low Back Pain are Associated With Different Multidimensional Profiles

Martin Rabey, M.Manip.Th., Anne Smith, PhD, Darren Beales, PhD, Helen Slater, PhD, and Peter O'Sullivan, PhD

(*Clin J Pain* 2016;32:1015–1027)

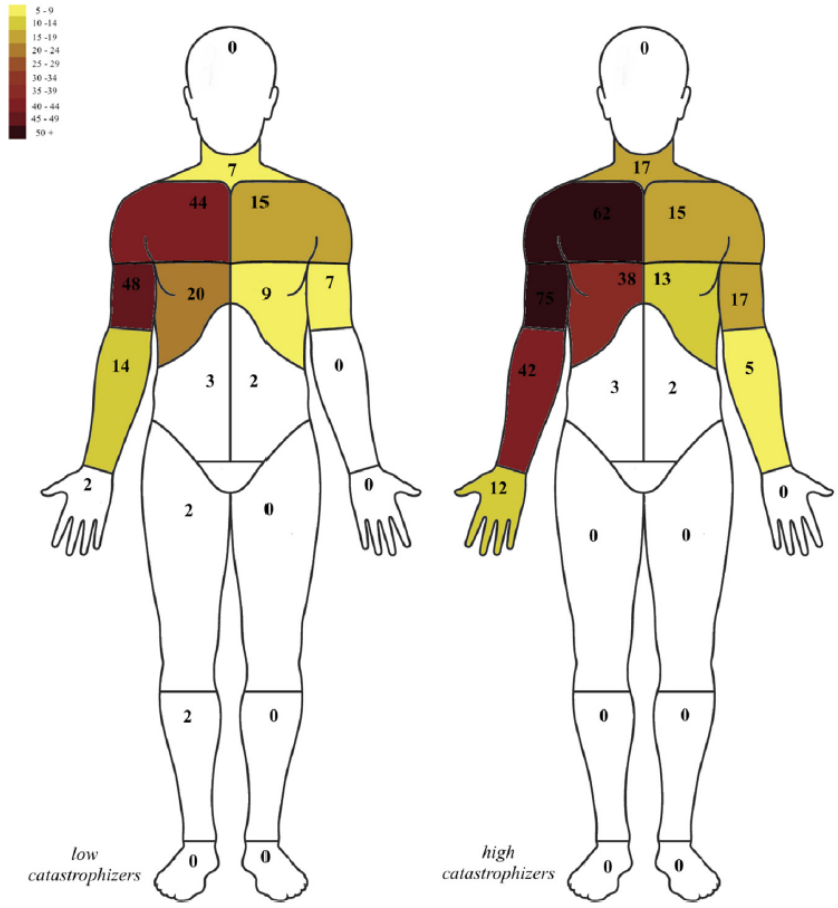


Figure 1. Percentage of high and low catastrophizers reporting pain after DOMS induction. Percentages are summed for the front and back of the body drawing.

Side Effects

Among 200 patients using opioids:
Catastrophizing → Side Effects → Disability

General Section
Research Paper
OPEN
PAIN REPORTS

Influence of opioid-related side effects on disability, mood, and opioid misuse risk among patients with chronic pain in primary care

Robert N. Jamison[a,*], Kathleen Dorado[a], Anna Mei[a], Robert R. Edwards[a], Marc O. Martel[b]

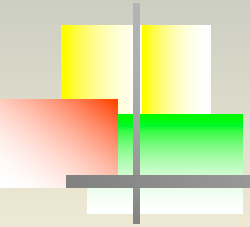
Table 4

Follow-up questionnaires comparison scores between those reporting many medication-related side effects (n = 84) and those reporting few medication-related side effects at 6 months (n = 88).

Variable	All patients (N = 172)	High side effects (n = 84)	Low side effects (n = 88)	*P*
Interference*				
Routine daily	6.7 ± 2.6	7.3 ± 2.4	6.1 ± 2.6	$t = 3.1$†
Social	6.5 ± 3.0	7.2 ± 2.6	5.9 ± 3.2	$t = 2.9$†
Outdoor/rec.	7.0 ± 2.8	7.3 ± 2.6	6.6 ± 2.9	NS
Sleep	6.2 ± 3.1	6.9 ± 2.6	5.7 ± 3.4	$t = 2.9$†
Appetite	4.4 ± 3.3	4.9 ± 3.3	3.9 ± 3.2	$t = 2.1$‡
Work	6.8 ± 3.0	7.8 ± 2.4	5.9 ± 3.1	$t = 4.7$§
Mood	6.2 ± 2.7	6.9 ± 2.5	5.5 ± 2.8	$t = 3.6$§
HADS anxiety	9.3 ± 4.5	10.1 ± 4.1	8.5 ± 4.7	$t = 2.3$‡
HADS depression	9.3 ± 4.2	10.4 ± 3.4	8.2 ± 4.7	$t = 3.4$†
HADS total	18.5 ± 7.7	20.4 ± 6.5	16.7 ± 8.3	$t = 3.1$†
PCS	23.1 ± 13.6	27.6 ± 13.3	18.6 ± 12.5	$t = 4.4$§
PDI	43.9 ± 16.0	49.3 ± 10.6	38.5 ± 18.6	$t = 4.4$§
COMM	10.1 ± 8.2	12.9 ± 9.2	7.5 ± 6.2	$t = 4.3$§

Unique Prediction???

Mixed Findings . . .



Mediational Role in Post-op Pain

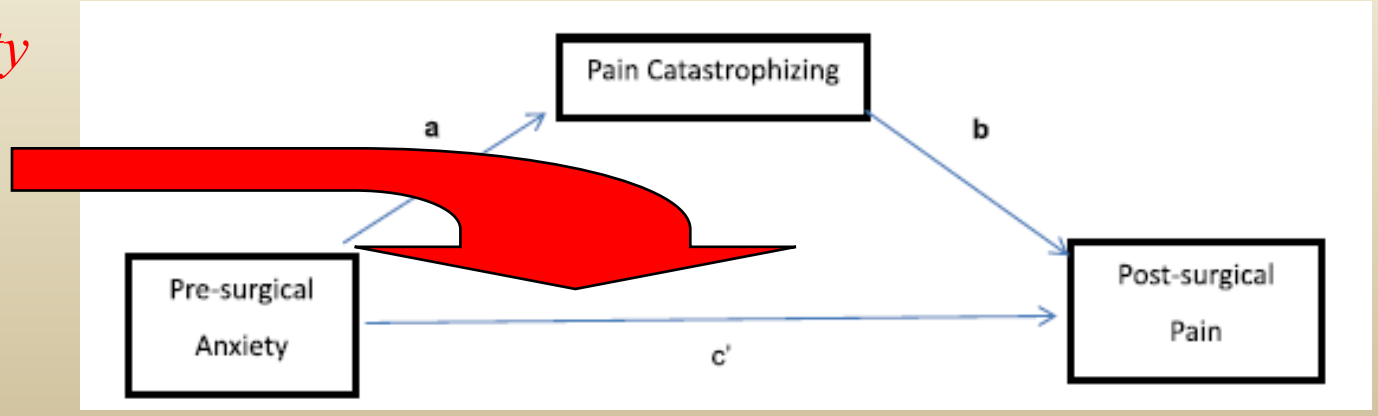
The mediating role of pain catastrophizing in the relationship between presurgical anxiety and acute postsurgical pain after hysterectomy

Patrícia R. Pinto [a,b,c,d], Teresa McIntyre [e], Armando Almeida [b,c,*], Vera Araújo-Soares [d,f]

PAIN® 153 (2012) 218–226

A consecutive sample of 203 women was assessed before and 48 hours after hysterectomy. Younger age, pre-surgical pain (OR = 2.50, p <.05), pain due to other causes (OR = 4.39, p = .001), and pain catastrophizing (OR = 3.37, p = .001) emerged as the main predictors of pain severity in multivariate logistic regression.

P-value for pre-surgical anxiety without catastrophizing in the model= .001. P> .3 once catastrophizing is added (full mediation).



But in Other Cases . . .

Original Research Article

Prediction of Pain and Opioid Utilization in the Perioperative Period in Patients Undergoing Primary Knee Arthroplasty: Psychophysical and Psychosocial Factors

Christopher R. Abrecht, MD,* Marise Cornelius, BS,† Albert Wu, MD,† Robert N. Jamison, PhD,† David Janfaza, MD,† Richard D. Urman, MD, MBA,† Claudia Campbell, PhD,‡ Michael Smith, PhD,‡ Jennifer Haythornthwaite, PhD,‡ Robert R. Edwards, PhD,† and Kristin L. Schreiber, MD, PhD†

Table 2 Predictors of average pain scores from POD0–2: results of linear regression

	Variable	Pearson Correlation *R*	Univariate Linear Regression		Multiple Linear Regression			
							Block Model	
			Adj R^2	*P*	Beta	*P*	Adj R^2	*P*
Block 1: Demographic	Age	−0.274	0.067	0.002	−0.028	0.100	0.163	<0.001
	Female gender	0.220	0.041	0.014	0.588	0.023		
	BMI	0.199	0.032	0.026	0.043	0.044		
Block 2: Previous pain	Average pain (BPI)	0.444	0.190	<0.001	0.126	0.116	0.234	0.007
	Widespread Pain Index	0.297	0.088	0.001	0.009	0.880		
Block 3: Psychosocial	Catastrophizing (PCS)	0.287	0.074	0.002	−0.001	0.965	0.245	0.232
	Somatization (BSI)	0.209	0.036	0.020	0.080	0.265		
	Sleep hours	−0.300	0.082	0.001	−0.097	0.388		
	Anxiety	0.102	0.002	0.266				
	Depression	0.081	−0.002	0.376				
Block 4: Psychophysical	Trapezius pressure pain threshold	0.038	0.008	0.676			0.344	<0.001
	Patella pressure pain threshold	−0.040	−0.008	0.685				
	Conditioned pain modulation	0.015	−0.010	0.888				
	Temporal summation of pain	0.342	0.109	<0.001	0.027	0.001		
	Painful after-sensations	0.199	0.031	0.035				
Block 5: Surgical, anesthetic	Number of previous knee surgeries	0.272	0.067	0.002	0.210	0.006	0.386	0.023
	Number of nonortho-pedic surgeries	−0.003	−0.008	0.970				
	Tourniquet time	0.098	0.002	0.098				
	Surgical time	0.040	−0.006	0.659				
	Anesthetic type	0.048	0.004	0.217				
	Intraop opioid	0.194	0.030	0.030	0.001	0.795		

BMI = body mass index; BPI = Brief Pain Inventory; BSI = Brief Symptoms Inventory; PCS = Pain Catastrophizing Scale; POD = postoperative day.

Different Elements of SA May Uniquely Predict Different Outcomes

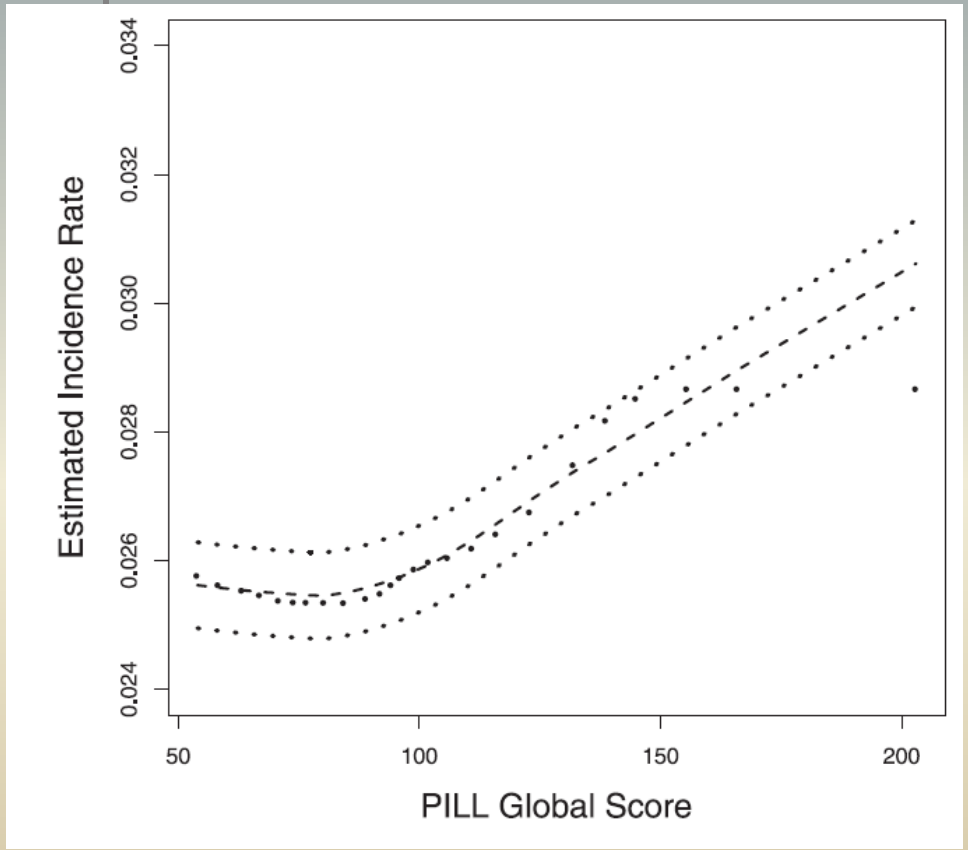
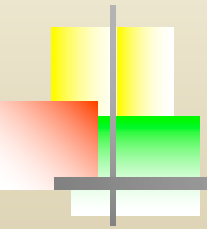


Figure 4. Partial dependence plots for selected psychosocial variables, which show the estimated TMD incidence rate for several possible values of each variable after adjusting for all other OPPERA variables. See Supplementary Figure 7 for a version of this figure with the *y*-axes redrawn to show additional detail.

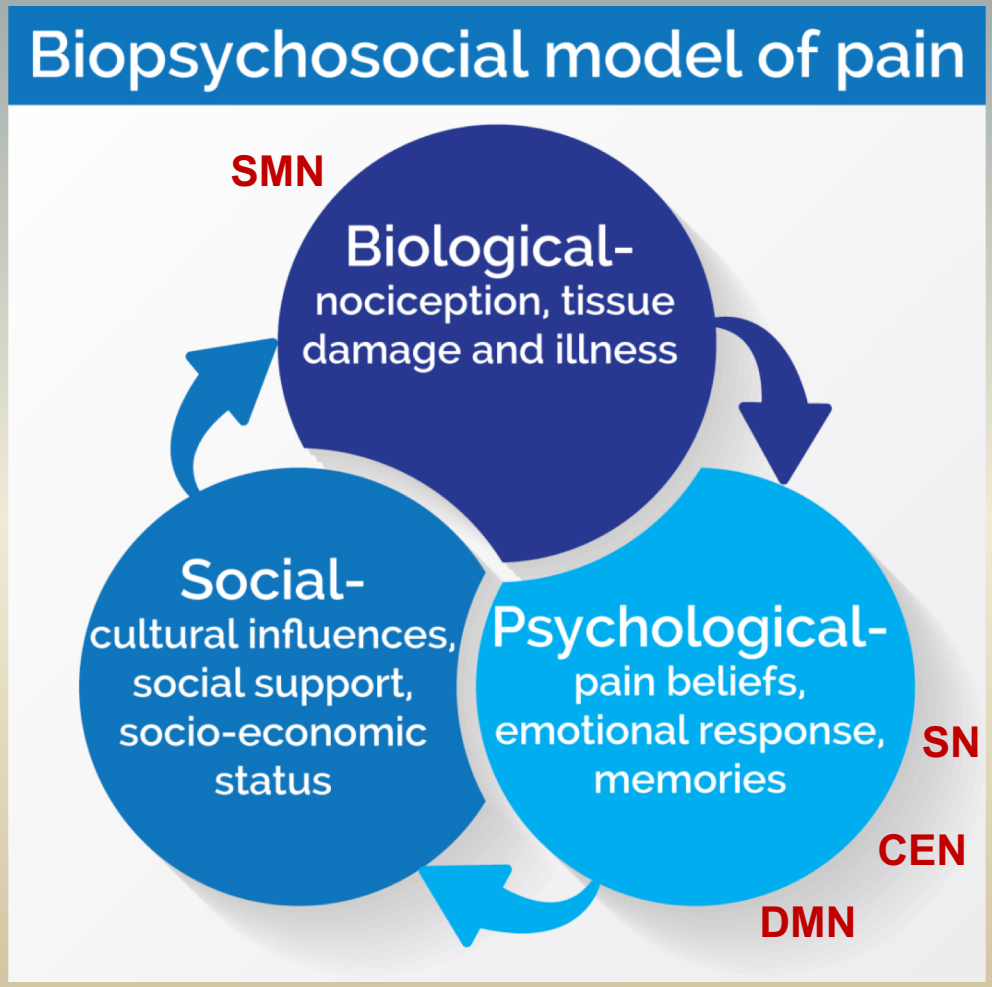
Table 4. Putative TMD Risk Factors With the Largest Importance Scores (by Domain)

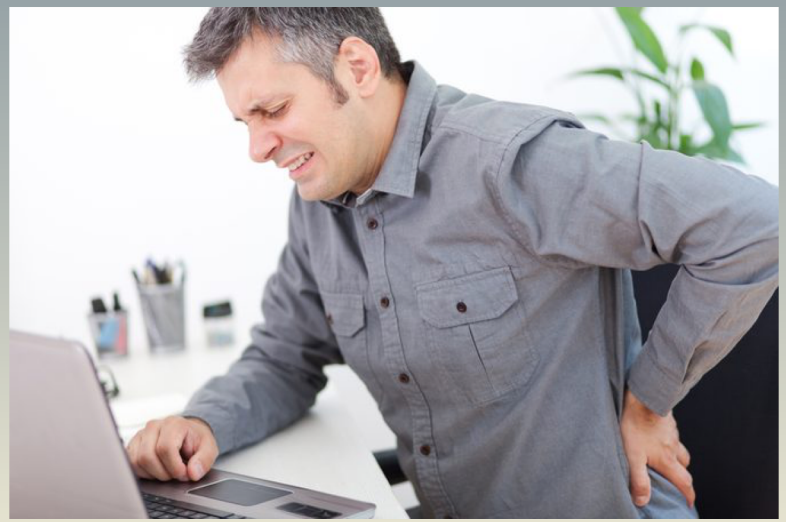
Domain	Variable	Importance Score	Rank
Autonomic	HRV: total power (color-word Stroop)	19.1	15
	Average mean arterial pressure (pain-affect Stroop)	16.2	17
	Average mean arterial pressure (color-word Stroop)	15.8	19
	Average heart rate—ECG (pain-affect Stroop)	12.6	22
	HRV: total power (pain-affect Stroop)	10.8	28
Clinical	Count of nonspecific orofacial symptoms	92.9	2
	Oral parafunction sum score (OBC)	66.0	5
	Could not open mouth wide in the last month	54.1	6
	No. of palpation sites with pain (right masseter)	50.0	8
	Ever had orthodontic procedures	29.3	12
Demographic	Age	51.6	7
	Marital status	44.7	9
	Race	25.1	13
	Lifetime U.S. residence	12.4	23
	Satisfaction with financial situation	5.5	58
Health status	Count of 20 comorbid conditions	100.0	1
	Bodily pain (SF-12v2)	80.6	4
	General health (SF-12v2)	31.8	11
	No. of different types of headaches in the last year	16.1	18
	Sleep latency (PSQI)	12.7	21
Pain sensitivity	Pressure pain threshold (masseter)	5.8	53
	Heat pain ratings of 10 stimuli: area under curve (48°C)	4.2	62
	Pressure pain threshold (trapezius)	3.7	66
	Thermal pain single stimulus rating (46°C)	3.6	67
	Thermal pain single stimulus rating (48°C)	3.5	68
Psychosocial	Somatic symptom reporting (PILL)	42.4	10
	Catastrophizing—magnification (PCS)	10.4	30
	EPQ Lie scale	9.9	31
	Anxiety (SCL-90-R)	9.7	32
	Mood—clearheaded/confused (POMS-Bi)	6.5	46

As the biopsychosocial model of pain would lead you to expect, there is quite a bit of overlap between seemingly-different mechanisms/risk factors/contributors to the experience of chronic pain



fMRI studies suggest that brain networks may differentially link to the ***multi-dimensional*** aspects of chronic pain





Gatchel, et al. The biopsychosocial approach to chronic pain. 2007. Psychological Bulletin. 133(4), 581-624.

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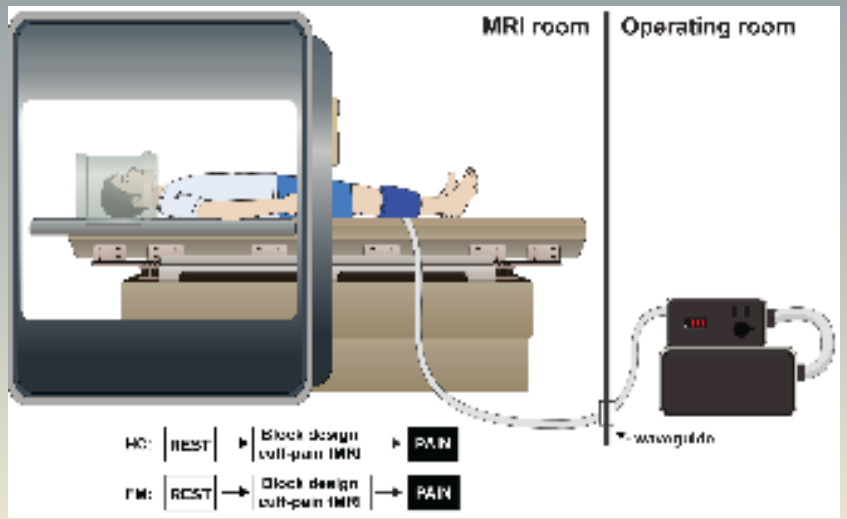
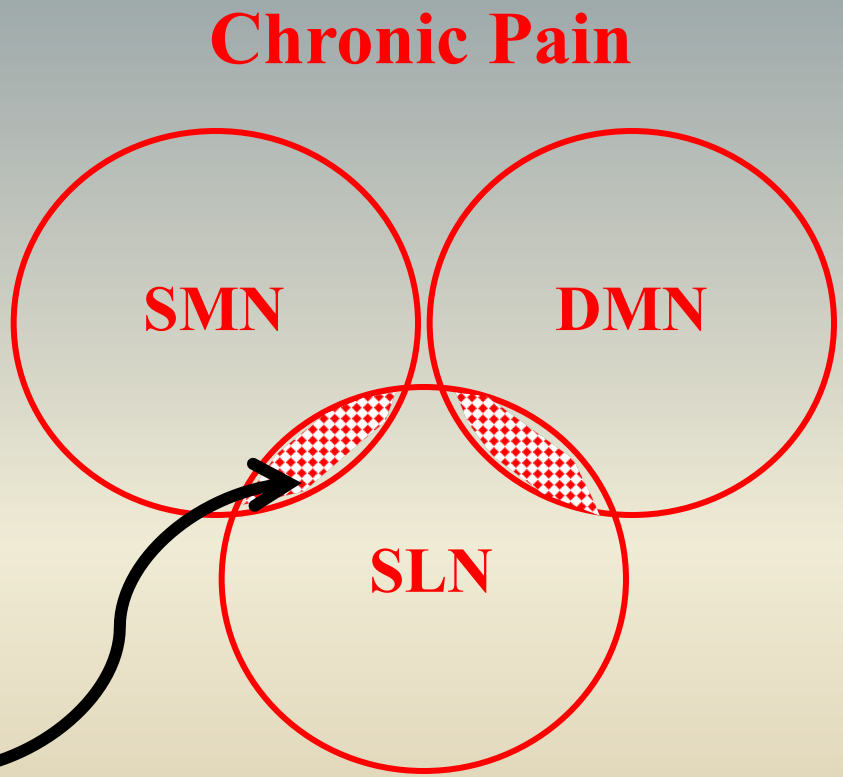
Chronic Pain → Blurred Network Connectivity in the context of painful stimulation





Saliency directed toward the location and intensity of evoked pain

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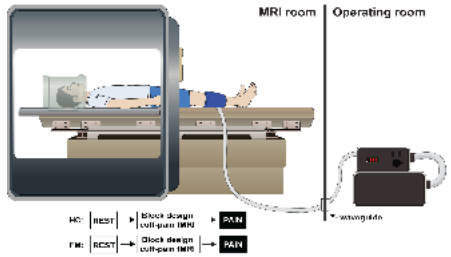
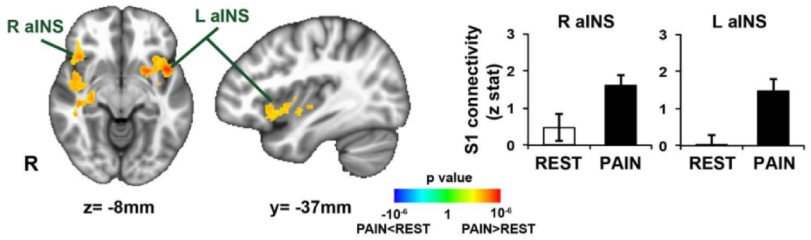
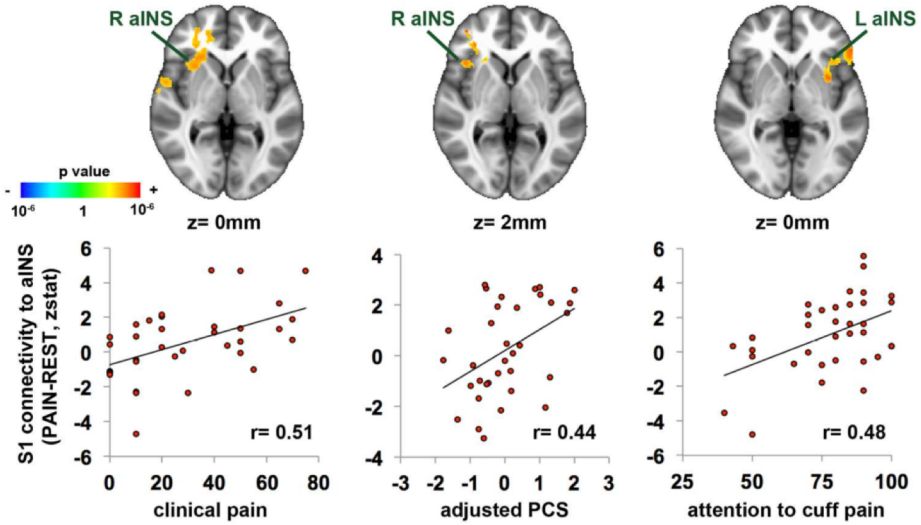
Sustained pain alters insula to S1 connectivity in FM (which is related to PCS and TS and attention to pain)



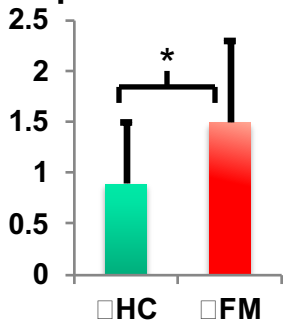
A. FM $S1_{leg}$ connectivity: PAIN vs. REST



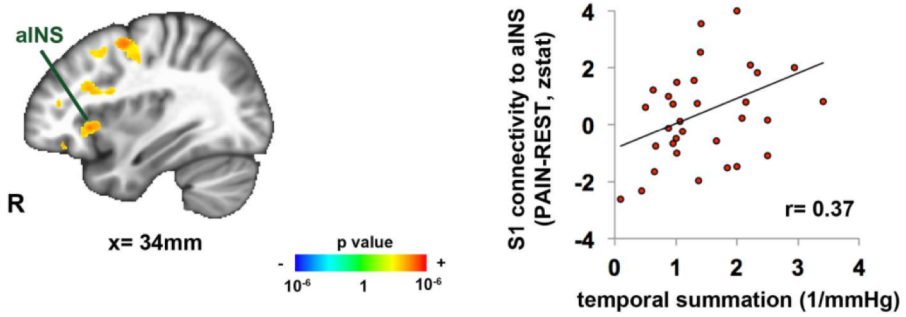
B. PAIN altered $S1_{leg}$ connectivity vs. clinical/behavioral measures



C. Temporal Summation



FM: PAIN altered $S1_{leg}$ connectivity vs. temporal summation



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Kim et al., A & R 2015

Other Neurobiological Substrates: Microglia?

Brain, Behavior, and Immunity 75 (2019) 72–83

Contents lists available at ScienceDirect

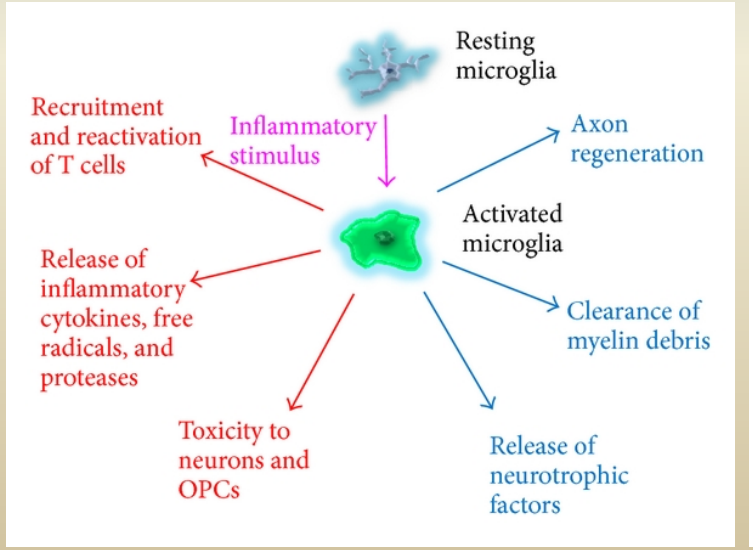
Brain, Behavior, and Immunity

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

Brain glial activation in fibromyalgia – A multi-site positron emission tomography investigation

Daniel S. Albrecht[a,1], Anton Forsberg[b,1], Angelica Sandström[c,d], Courtney Bergan[a], Diana Kadetoff[c,d,e], Ekaterina Protsenko[a], Jon Lampa[f], Yvonne C. Lee[g,h], Caroline Olgart Höglund[i], Ciprian Catana[a], Simon Cervenka[b], Oluwaseun Akeju[j], Mats Lekander[c,d,k], George Cohen[l], Christer Halldin[b], Norman Taylor[l], Minhae Kim[l], Jacob M. Hooker[l], Robert R. Edwards[m], Vitaly Napadow[a,m], Eva Kosek[c,d,e,*,2], Marco L. Loggia[a,*,2]

PET brain scan using TSPO ligand [11C]PBR28. Comparison of fibromyalgia patients and controls at 2 sites



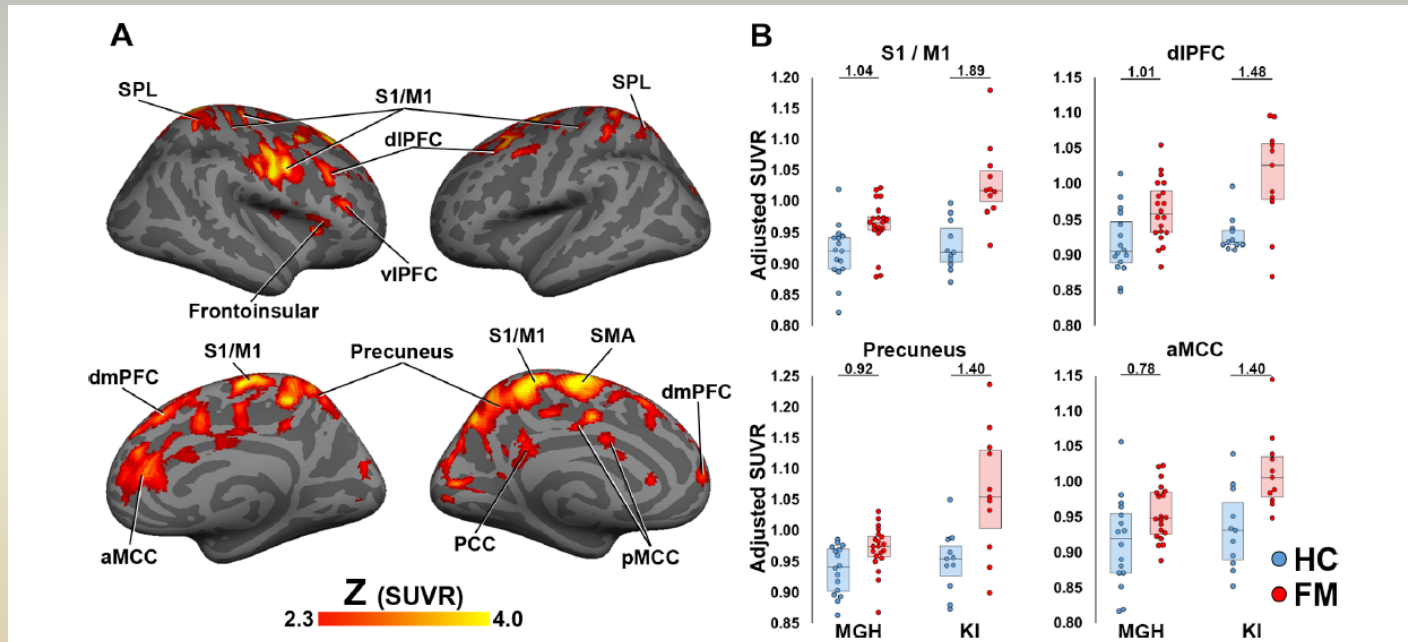


Fig. 2. Voxelwise group differences in [^{11}C]PBR28 SUVR *A*. Surface projection maps displaying areas with significantly elevated [^{11}C]PBR28 SUVR in FM patients compared to controls (FM – n = 31; HC – n = 27), in voxelwise analyses (KI + MGH sample). *B*: average ± standard deviation SUVR extracted from several of the clusters identified as statistically significant in the voxelwise SUVR analysis. Data from individual research sites (MGH or KI) are displayed separately, and the number above each ROI pairing corresponds to the effect size (Cohen's *d*) of PET signal differences between FM patients and controls for each site. These data show that overall SUVR group differences, while larger for the KI dataset, are elevated in FM patients compared to controls in both datasets when evaluated independently. pMCC – posterior middle cingulate cortex, aMCC – anterior middle cingulate cortex. All data have been adjusted for genotype and injected dose.

Affective Factors & Microglial Activation

Molecular Psychiatry
https://doi.org/10.1038/s41380-019-0433-1

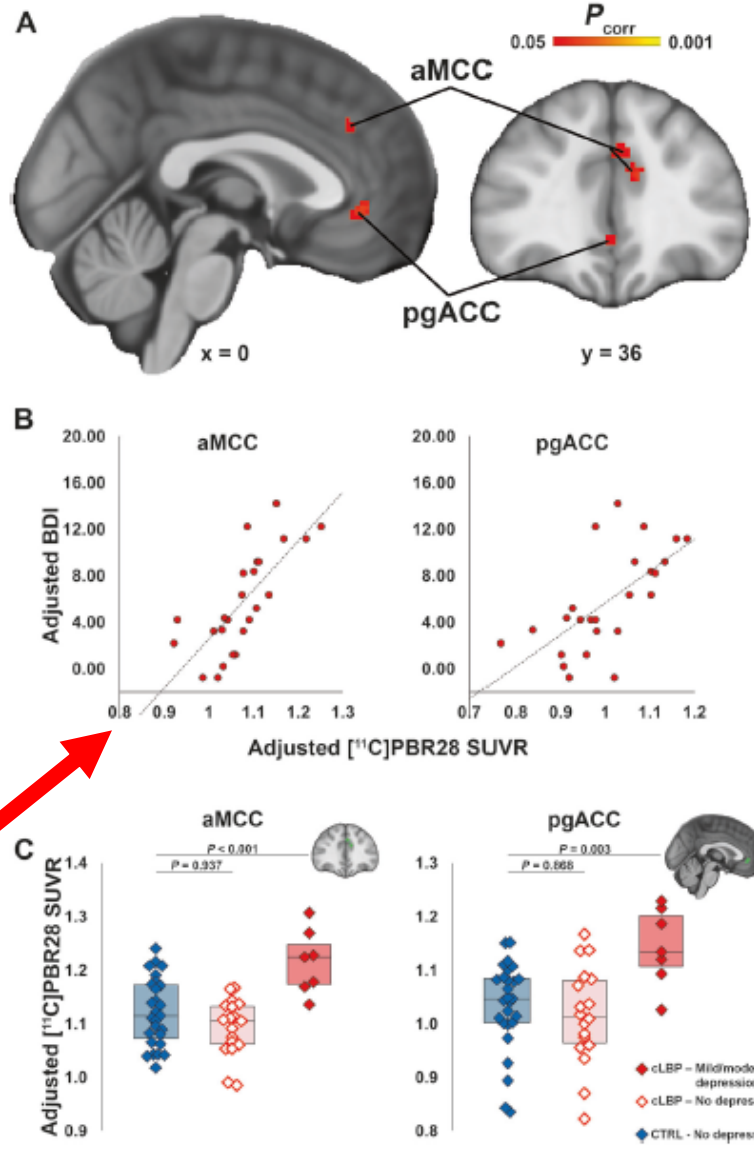
ARTICLE

The neuroinflammatory component of negative affect in patients with chronic pain

D. S. Albrecht[1] · M. Kim[1] · O. Akeju[2] · A. Torrado-Carvajal[1] · R. R. Edwards[3] · Y. Zhang[2] · C. Bergan[1] · E. Protsenko[1] · A. Kucyi[1,4] · A. D. Wasan[5] · J. M. Hooker[1] · V. Napadow[1,3] · M. L. Loggia[1]

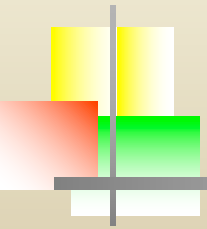
25 patients with chronic pain and 27 healthy control subjects scanned with PET using the second-generation TSPO ligand [11C]PBR28. PET signal was positively associated with BDI scores in patients, and significantly elevated in patients with mild-to-moderate depression compared with controls, in anterior middle and pregenual anterior cingulate cortices (aMCC, pgACC).

Fig. 2 Voxelwise [^{11}C] PBR28 signal is associated with depressive symptoms and elevated in patients with mild-to-moderate depression. **a** Results from the voxelwise analysis showing clusters where [^{11}C]PBR28 SUVR is significantly positively associated with BDI. **b** For visualization purposes, average SUVR from the aMCC and pgACC clusters in panel (**a**) are plotted against BDI, both adjusted for *TSPO* polymorphism. **c** Results from the ANCOVA analysis comparing average aMCC and pgACC SUVR between cLBP patients with little-to-no depression, mild-to-moderate depression, and controls. *P*-values represent results from post-hoc Dunnett's tests comparing both patient subgroups against to controls. All values have been adjusted for age, injected dose, and *TSPO* polymorphism



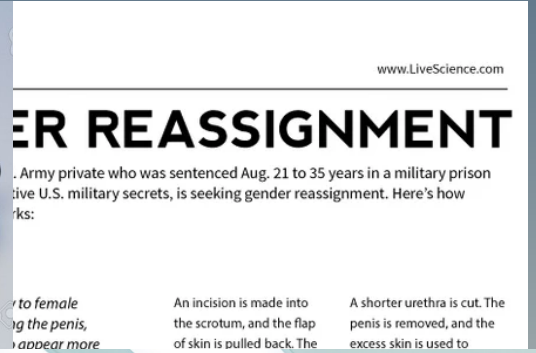
Very strong correlations with BDI

The various elements of Somatosensory Amplification (e.g, somatization, sensitization, pain facilitation, diminished inhibition, hypervigilance, anxiety, negative mood, catastrophizing, etc.) all appear to inter-relate with one another and perhaps have common neurobiological substrates




CYCLE OF
DECONDITIONING
Injury, accident, ageing, inactivity
Pain inhibits the stabilising muscles
Protective response - modified movement patterns
Muscle wasting and loss of strength
Increased susceptibility of recur
and re-injury


ISOLATION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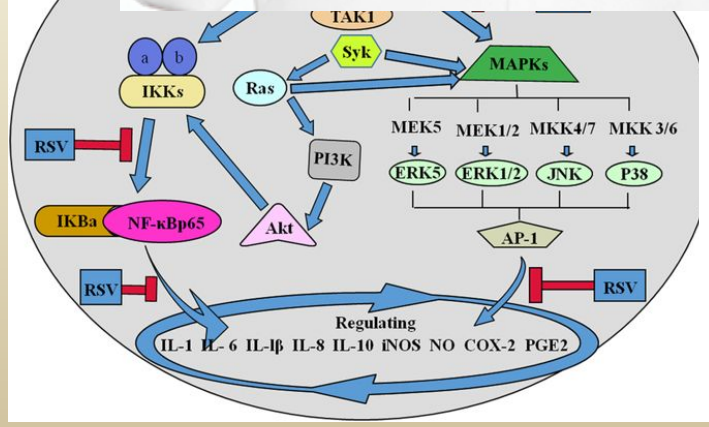
ER REASSIGNMENT
. Army private who was sentenced Aug. 21 to 35 years in a military prison
ive U.S. military secrets, is seeking gender reassignment. Here's how
rks:
An incision is made into the scrotum, and the flap of skin is pulled back. The
A shorter urethra is cut. The penis is removed, and the excess skin is used to


6 WAYS
to Survive


Season

NOCEBO
EFFECTS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MKK 3/6
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ERK1/2
JNK
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IKBa
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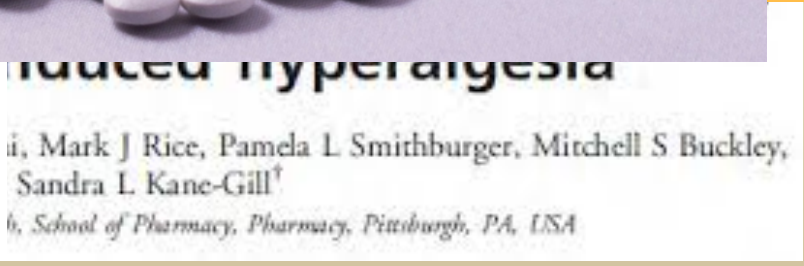
DEPRESSED


duced Hyperalgesia
i, Mark J Rice, Pamela L Smithburger, Mitchell S Buckley,
Sandra L Kane-Gill†
, School of Pharmacy, Pharmacy, Pittsburgh, PA, USA

Conclusions

- SA has not been well-defined, and the term is not widely used.
- It shares space with other more-commonly used terms for constructs that have proven to be important predictors of pain outcomes (somatization, sensitization, catastrophizing, etc.).
- These constructs are all inter-related. For example, catastrophizing is associated with amplified TS and diminished CPM . . .
- It seems a good bet that these various related/overlapping constructs share neurobiological substrates (e.g., hyper-connectivity between the salience network and sensory networks, elevated indices of microglial activation, etc.).
- It is probable that different elements of SA predict different outcomes.
- Should we be measuring and analyzing these things separately (e.g., PILL + PCS + STAI + QST + fMRI + PET +++++++++)?

Thanks to Colleagues

BWH& MGH:

Bob Jamison, Ph.D.
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Mina Lazaridou, Ph.D.
Vitaly Napadow, Ph.D.
Marco Loggia, Ph.D.

Ajay Wasan at UPMC