Pain-related Anxiety Promotes Pro-nociceptive Processes in Native Americans

Felicitas A. Huber, Mag., Bethany L. Kuhn, MA, Edward W. Lannon, MA, Shreela Palit, PhD, Michael F. Payne, MA, Natalie Hellman, MA, Cassandra A. Sturycz, MA, Yvette M. Güereca , MA, Tyler A. Toledo, MA, Mara J. Demuth, MA, Burkhart J. Hahn, BA, Joanna O. Shadlow, PhD, & Jamie L. Rhudy, PhD

Department of Psychology, The University of Tulsa, 800 South Tucker Drive, Tulsa, OK 74104

PLAN Psychophysiology Laboratory for Affective Neuroscience

THE UNIVERSITY of TULSA

Introduction

- Chronic pain rates are higher in Native Americans (NA) than the general US population
- The OK-SNAP study addressed mechanisms contributing to this disparity: NAs and non-Hispanic Whites (NHWs) did not differ on any measure of pain processing except higher sensitivity to cold pain
- However, NAs reported greater pain-related anxiety in response to painful QST tasks
- Greater pain-related anxiety may create a vicious cycle for NAs that enhances or initiates chronic pain
- There may be an indirect relationship between NA race and pain processing outcomes that is mediated by pain-related anxiety: **NA —> pain-related anxiety —> pronociception**

Objective

To examine the indirect relationships between race (NHW vs. NA), pain-related anxiety, and quantitative sensory testing (QST) that assesses pain processing.

Participants

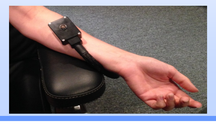
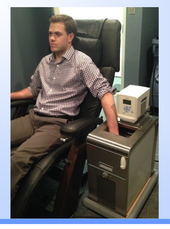
- *N* = 329 healthy, pain-free participants
- **Exclusion criteria:**
  - < 18 years of age
  - BMI > 35
  - Current acute illness, psychotic symptoms, chronic pain condition, or inability to speak/read English
  - Cardiovascular, neurological, and/or circulatory problems
  - Recent use of analgesic, antidepressant, anxiolytic, antihypertensive medications

	NHW (N=150)			NA (N=155)		
Variable	**N**	**M**	**SD**	**N**	**M**	**SD**
Age (years)	150	28.50	13.51	155	30.82	12.79
BMI (kg/m^2)**	149	24.13	3.73	151	25.98	4.52
Mean Arterial Press. (mmHg)**	148	82.82	7.23	149	88.31	9.70
Pain Catastrophizing (PCS; 0-52)	149	9.40	7.44	152	9.78	7.78
Negative Affect (PANAS; 10-50)	149	2.79	2.62	152	3.06	2.58
Positive Affect (PANAS; 10-50)	135	18.12	6.92	134	19.00	7.74
State Anxiety (STAI; 20-80)	149	32.07	7.05	152	33.11	7.19
Poor Sleep Quality (PSQI; 0-3)*	118	0.96	0.63	116	1.26	0.85
Perceived Stress (PSS; 0-40)*	147	13.00	5.87	148	14.46	6.09
Psychological Distress (SCL-90 log GSI)	147	0.11	0.08	148	0.14	0.10
Bodily Pain (SF-36; 0-100)	135	43.53	6.73	135	42.83	7.69
General Health Sc. (SF-36; 0-100)	147	65.32	9.41	149	62.95	11.41
Pain-Related Anxiety (0-100)*	145	36.23	20.96	147	43.71	21.59

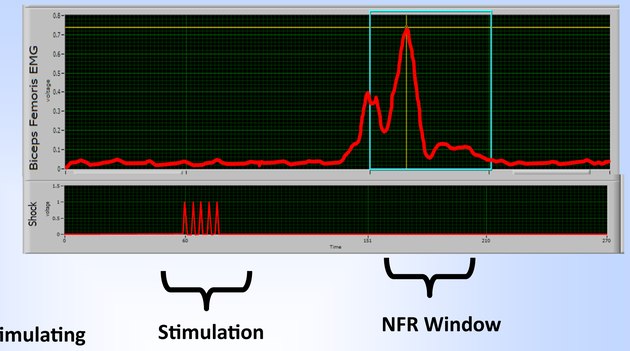
**p* <.05, ** *p* <.001

Experimental Procedure: Pain Tolerance

- **Heat Pain Tolerance:** Temperature when participant rated the heat from a thermal probe as intolerable, or a 51°C max.
- **Cold Pressor Pain Tolerance:** Time (in seconds) until pain was rated as maximum tolerable (on the VAS) or 5 min. max. was reached
- **Ischemia Pain Tolerance:** Time (in seconds) when participant rated ischemia pain as max. tolerable on the VAS (or 25 min max)
- **Electric Pain Tolerance:** Stimulus intensity (in mA) that participant rated as 100 on the visual analog scale (VAS), or a 50 mA max.


Methods: Nociceptive Flexion Reflex (NFR)



- **Numerical Rating:** Pain ratings made following each stimulation (range 0 = no pain to 100 = worst possible pain)
- **Nociceptive Flexion Reflex (NFR):** A spinally-mediated protective withdrawal reflex elicited by Aδ fiber activation
- Size of the reflex correlates with pain ratings and used for within-subject changes in spinal nociception
- **NFR magnitude:** Biceps femoris EMG activity in the 90-150 ms post-stimulus window
- Calculated: **d-score** = mean EMG of 90-150 ms post-stimulation interval **minus** mean EMG of −60-0 ms pre-stimulation interval **divided** by average SD of both intervals

Methods: Conditioned Pain Modulation (CPM)

Phase	CPM
Pretest	5 stimulations
	2 min break
Conditioning	5 stimulations while hand in cold water [10 ˚C]

Data Analysis

- Cold pressor tolerance, ischemia tolerance, and psychological distress were transformed to reduce positive skew
- Outliers were winsorized to the next nearest nonoutlier value
- Independent-samples t-tests or χ^2 analyses were conducted to examine group differences on background variables. If group differences were found, this was considered as a control variable in primary analyses
- PROCESS software (v3.3) was used to conduct bootstrapped mediation analyses from 5000 random samples
- Analyses of CPM of pain and TS-pain controlled for electric stimulus intensity
- Analyses controlled for STAI state anxiety to control for the effects of non-pain-related anxiety
- To examine moderation between pain-related anxiety and pain outcomes, a bootstrapped hierarchical regression analyses in PROCESS was conducted

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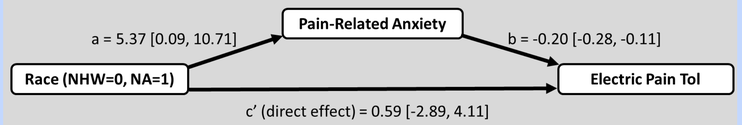
Oklahoma Study of Native American Pain Risk OK-SNAP

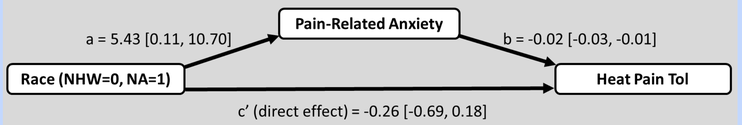
Results

- Pain-related anxiety significantly mediated the relationships between NA race and electric tolerance, heat tolerance, ischemia tolerance, cold pressor tolerance, and CPM of NFR
- Conditioned pain modulation of NFR was calculated from a change score with negative values indicating inhibition and positive values indicating facilitation
- All models controlled for biological sex, BMI, mean arterial blood pressure, sleep quality, perceived stress, and state anxiety

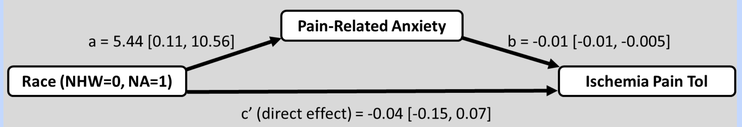
Predicting Electric Tolerance



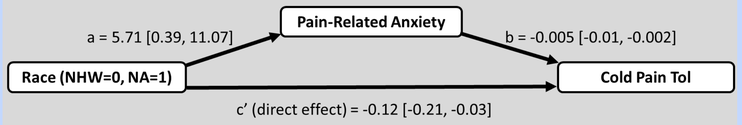
Predicting Heat Tolerance



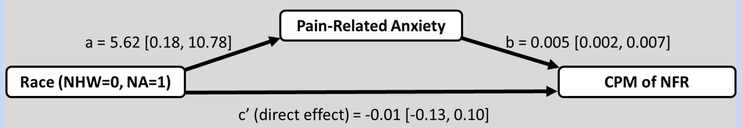
Predicting Ischemia Tolerance



Predicting Cold Tolerance



Predicting CPM of NFR



- Bootstrapped hierarchical regression analyses showed that race did not moderate the relationships between pain-related anxiety and pain outcomes

			95% CI		
Pain DV	**B**	**SE**	**Lower**	**Upper**	**ΔR^2**
Electric Tolerance (mA)	0.0189	0.0407	-0.0616	0.1009	0.0008
Heat Tolerance (C˚)	-0.0070	0.0055	-0.0177	0.0037	0.0060
Ischemia Tolerance (log[s])	-0.0005	0.0012	-0.0029	0.0018	0.0005
Cold Pressor Tolerance (log[s])	-0.0003	0.0011	-0.0024	0.0019	0.0004
CPM of Pain (Δ NRS)	0.0282	0.0259	-0.0220	0.0794	0.0050
CPM of NFR (Δ d-score)	-0.0011	0.0012	-0.0034	0.0012	0.0031

- Relationships between pain-related anxiety and pain outcomes did not differ between NHWs and NAs

Conclusions

- Findings suggest that pain-related anxiety is not a unique mechanism of pain risk for NAs
- However, the greater tendency to experience pain-related anxiety by NAs impairs ability to engage descending modulation of spinal nociception and decreases their pain tolerance
- Pain-related anxiety may promote pro-nociceptive processes in NAs that increase their risk for future chronic pain.