Sex Differences in Peripheral Fiber Function, Pain Sensitivity, Central Sensitization, and Descending Inhibition Among Native Americans: Results from the Oklahoma Study of Native American Pain Risk (OK-SNAP)

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INTRODUCTION

- Native Americans (NA) have a higher prevalence of chronic pain than other U.S. minorities and non-Hispanic Whites (NHWs)
- Compared to NHWs, racial and ethnic groups experience more clinical pain including joint pain, migraines, and arthritis
- Meta-analyses have found that females have a higher sensitivity and lower threshold/tolerance to pain than males
- There is a lack of research on sex differences in NAs

OBJECTIVE

- To investigate sex differences in pain processing and pain experience in NAs by examining peripheral nerve fiber function, central sensitization, and descending inhibition

PARTICIPANT CHARACTERISTICS

- Participants were 153 healthy, chronic pain-free NAs from the Oklahoma Study of Native American Pain Risk (OK-SNAP)
- Data collection from 2014-2018
- Exclusion criteria:
  - <18 years old
  - History of cardiovascular, neuroendocrine, musculoskeletal, and neurological disorders
  - Reported chronic pain or acute pain problems
  - BMI > 35
  - Use of antidepressants, anxiolytic, analgesic, stimulant, or antihypertensive medication
  - Current psychotic symptoms or substance use problems
  - And/or an inability to read and speak English
- Female (N = 89, 58.2%), Male (N = 64, 41.8%)
- Average age:
  - F = 31.32 (*SD* = 13.22)
  - M = 29.61 (*SD* = 11.89)

MATERIALS & METHODS

- Procedures were approved by the University of Tulsa, University of Oklahoma Health Sciences, Cherokee Nation, Indian Health Service Oklahoma City Area Office institutional review boards (IRBs)
- Participants provided written informed consent and could withdraw from the study at any point

Peripheral Fiber Function

- CHEPS thermode attached to participants left volar forearm and 5 trials were administered (1 practice and 4 trails averaged)
- Random intertrial interval (25-35 seconds)
- Cool detection threshold
  - Used to assess Aδ fiber function
  - Baseline of 30℃ decreased at 0.5℃/s
  - Participants pressed a button when they first felt the thermode cooling
- Warm detection threshold
  - Used to assess C-fiber function
  - Baseline of 30℃ increased at 0.5℃/s
  - Participants pressed a button when they first felt the thermode warming

Pain Sensitivity

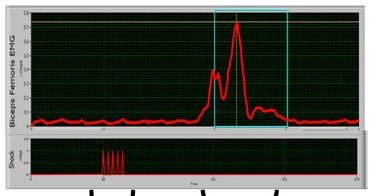
- Assessed by:
  - multiple stimulus modalities representing cutaneous thermal pain (heat pain threshold/tolerance, cold-pressor threshold/tolerance, 2-minutes 10℃ cold water)
  - deep tissue mechanical (pressure pain thresholds)
  - ischemic (ischemia pain threshold/tolerance)
  - electric pain threshold/tolerance

Central Sensitization

- Assessed by:
  - Nociceptive flexion reflex threshold
  - Three-stimulation threshold
  - Temporal summation of nociceptive flexion reflex
  - Temporal summation of electric pain
  - Temporal summation of heat pain

Descending Inhibition of Pain and Spinal Nociception

- NFR is a spinally-mediated protective withdrawal reflex elicited by Aδ fiber activation
- CPM was assessed from painful electric stimulations delivered to the ankle during which participants placed their hands in 26˚C warm water (baseline stimulus) and in painful 10˚C cold water (conditioning stimulus)
- Descending inhibition of spinal nociception assessed from conditioned pain modulation of the nociceptive flexion reflex (CPM-NFR)
- Descending inhibition of pain was assessed from self-report pain ratings (CPM-Pain)



Phase	Conditioned Pain Modulation (CPM)
Baseline	9 stimulations Warm water [26 °C]
Conditioning	9 stimulations Cold water [10 °C]

DATA ANALYSIS

- Outliers were winsorized and replaced with the next nearest nonoutlier value before analysis
- Independent samples t-tests, p <0.05 (2-tailed)

RESULTS

- There were no significant sex differences in peripheral fiber function, central sensitization, or descending inhibition
- Significant sex differences in pain tolerance levels

Variable	Male		Female		*t*	Cohen's *d*
	M	*SD*	*M*	*SD*		
Cool Det Thr (C˚)	745.48	70.38	743.57	78.07	0.142	.026
Warm Det Thr (C˚)	1.53	0.02	1.52	0.02	0.517	.093
Heat Pain Thr (C˚)	43.25	2.46	42.94	2.35	0.719	.130
Cold Pressor Pain Thr (C˚)	1.26	0.21	1.22	0.23	1.088	.196
Ischemia Pain Thr (sec)	1.62	0.35	1.49	0.41	1.968	.353
Elect Pain Thr (mA)	11.00	6.26	11.88	5.94	-0.799	-.145
Pressure Pain – Thumb (kPA)	512.56	232.29	488.23	232.49	0.583	.105
Pressure Pain – Trapezius (kPA)	357.97	151.73	314.28	155.84	1.580	.284
Pressure Pain – Masseter (kPA)	167.07	61.32	152.36	59.16	1.362	.245
Heat Pain Tol (C˚)	46.27	1.52	44.96	1.39	**4.993***	.901
Cold Pressor Pain Tol (C˚)	1.73	0.32	1.60	0.29	**2.327***	.419
Ischemia Pain Tol (sec)	2.23	0.44	2.04	0.44	**2.373***	.426
Elect Pain Tol (mA)	32.21	13.67	30.21	12.32	0.862	.155
NFR Thr (mA)	19.24	10.31	19.33	9.80	-0.050	-.009
Three Pulse Thr (mA)	15.27	5.59	14.33	5.64	0.968	.166
TS-NFR (mA)	0.59	0.47	0.57	0.49	.219	.039
TS-Elect Pain (mA)	2.95	3.94	3.31	4.07	-.485	-.090
CPM-NFR (mA)	0.03	0.45	-0.01	0.35	0.085	.101
CPM-Pain (0-100)	-7.76	7.17	-7.52	9.48	-0.153	-.028

CONCLUSIONS & FUTURE DIRECTIONS

- These findings demonstrate that NA females display lower pain tolerances in response to heat pain, cold pressor pain, and ischemic pain
- Findings are in line with current literature suggesting that the strongest sex differences are in pain tolerance
- Future research should investigate the mechanisms behind these differences

PLAN — Psychophysiology Laboratory for Affective Neuroscience

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