

Exploring Pain Processing Differences in Native Americans

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Objective: Several chronic pain conditions are more prevalent in Native Americans than in any other group in the United States; however, little has been done to identify factors contributing to this disparity. The study presented here was designed to examine whether there were pain processing differences in Native Americans relative to non-Hispanic White controls. **Methods:** Participants were healthy, pain-free Native Americans ($n = 22$, 8 females) and non-Hispanic Whites ($n = 20$, 7 females). Pain processing was assessed from electric pain threshold/tolerance, ischemia pain threshold/tolerance, nociceptive flexion reflex threshold (NFR; an electrophysiological measure of spinal nociception), pain ratings of suprathreshold electric stimuli, and temporal summation of pain and NFR (an electrophysiological measure of spinal cord sensitization). The institutional review board approved all procedures. **Results:** Compared to non-Hispanic Whites, Native Americans had dampened pain perception (higher ischemia pain tolerance, higher electric pain threshold, lower ratings of electric stimuli). Additionally, temporal summation of NFR was reduced in Native Americans, suggesting sensitization was reduced at the spinal level. **Conclusions:** Findings suggest Native Americans have dampened pain and pain signaling, perhaps due to overactivation of descending pain inhibition mechanisms. Given research indicating that other ethnic groups at risk for chronic pain (e.g., African Americans) show enhanced pain and enhanced central sensitization on experimental pain measures, chronic pain risk could be different for Native Americans, thus emphasizing the need for different treatment interventions.

Keywords: ethnic differences, pain sensitivity, pain modulation, nociception, central sensitization

Research indicates that Native Americans have a high prevalence of severe headaches, rheumatoid arthritis, juvenile arthritis, chronic joint symptoms, back pain, neck pain, face pain, jaw pain, and dental pain (Barnes, Adams, & Powell-Griner, 2010; Deyo, Mirza, & Martin, 2006; Ferucci, Templin, & Lanier, 2005; Leake, Jozzy, & Uswak, 2008; Mauldin, Cameron, Jeanotte, Solomon, & Jarvis, 2004; Rhee, 2000), and most of these prevalence rates tend to be higher than in any other U.S. group (Barnes et al., 2010; U.S. Department of Health and Human Services [USDHHS], 2010). Despite these apparent health disparities, there is an appalling lack of research on pain in this population. Indeed, a recent review found less than 30 studies published in the last 31 years on pain in Native Americans, with most focusing on pain epidemiology (Jimenez, Garrouette, Kundu, Morales, & Buchwald, 2011). What is more, actual rates of pain in Native Americans may be underestimated because research suggests Native Americans tend to minimize their pain complaints, have a stoic response to pain, and may evidence a general unwillingness to discuss pain (Barkwell,

2005; Haozous, Knopf, & Brant, 2011; Kramer, Harker, & Wong, 2002). Given that pain results in tremendous health care utilization, economic burden, disability, and loss of productivity (Loeser, Butler, Chapman, & Turk, 2000), these data on Native Americans are alarming and point to the need for additional research within this population.

A Brief Overview of Pain and Pain Processing

Pain and pain behaviors are normally adaptive. For example, exposure to a noxious stimulus (e.g., stepping on a tack) elicits an immediate withdrawal reflex (i.e., a nociceptive flexion reflex, NFR) that protects the limb from tissue damage. Additionally, ascending spinal cord pathways relay the pain signal to several brain regions (e.g., thalamus, somatosensory cortices, insula, anterior cingulate cortex) that collectively contribute to pain experience (Apkarian, Bushnell, Treede, & Zubieta, 2005; Tracey & Mantyh, 2007). Via these processes, pain helps protect from immediate injury, helps identify when tissue damage is present, promotes learning to avoid future injury, and encourages recuperative behaviors after injury (e.g., rest, protection of damaged site) (e.g., Donaldson et al., 2003; Walters, 1994). However, when pain outlasts the injury or noxious event (e.g., chronic back pain), it no longer serves these adaptive functions.

Pain is not only influenced by the ascending pain signal but also by brain-to-spinal cord (descending) mechanisms that regulate the ascending signal (Fields, Basbaum, & Heinricher, 2006; Millan, 2002). Thus, when taken together, pain can be amplified by (a) increasing painful input, (b) sensitization within central nervous system (CNS) pain pathways, and/or (c) a reduction in descending

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pain inhibition (disinhibition). These amplification processes may even contribute to the initiation and/or maintenance of chronic pain. Indeed, human studies suggest that chronic pain (e.g., fibromyalgia) is associated with heightened CNS reactivity (central sensitization) to painful input (Price, Long, & Huitt, 1992; Sarlani & Greenspan, 2005; Staud, Vierck, Cannon, Mauderli, & Price, 2001), and both animal and human studies suggest that disrupted descending modulatory mechanisms can promote chronic pain (e.g., Neugebauer, Li, Bird, & Han, 2004; Porreca, Ossipov, & Gebhart, 2002; Ren & Dubner, 1999; Zambreau, Wise, Brooks, Iannetti, & Tracey, 2005).

The factors that contribute to pain disparities in Native Americans are likely to be manifold (e.g., genetic, physiological, cultural, behavioral), but studying reactions to experimental pain in this group may identify pain processing differences that contribute to pain disparities. To date, no published study has assessed experimental pain in Native Americans, but experimental techniques have been used to study pain in other ethnic groups.

Pain Processing Differences in Other Ethnic Groups

Experimental studies of pain processing have consistently found that, compared with non-Hispanic Whites, pain is enhanced (e.g., lower pain tolerance, higher ratings of pain) in otherwise healthy, pain-free African Americans and Hispanics (e.g., Campbell, Edwards, & Fillingim, 2005; Edwards, Doleys, Fillingim, & Lowery, 2001; Mechlin, Heymen, Edwards, & Girdler, 2011; Rahim-Williams et al., 2007; Woodrow, Friedman, Siegel, & Collen, 1972). These group differences do not appear to be due to an increased willingness to report pain because African Americans tend to have lower NFR thresholds—a physiological measure of spinal nociception (pain signaling) (Campbell et al., 2008b). Further, Mechlin et al. (2011) examined the degree of spinal cord sensitization in African Americans using a technique called temporal summation of pain (TS-pain) and found greater sensitization (enhanced CNS hyper-reactivity) than non-Hispanic Whites. Thus, these minority groups have enhanced pain, perhaps because of enhanced central sensitization.

Although the experience of experimental pain can be quite different than the experience of clinical pain, the two are correlated (Arendt-Nielsen & Yarnitsky, 2009; Edwards et al., 2001; Fillingim, Maixner, Kincaid, Sigurdsson, & Harris, 1996). It is important to note that prospective studies have shown that responses

to experimental pain can predict future clinical pain. For example, higher experimental pain sensitivity assessed before surgery predicted increased postoperative pain after caesarean section (Grano, Lowenstein, Yarnitsky, Tamir, & Zimmer, 2003), anterior cruciate ligament repair (Werner, Duun, & Kehlet, 2004), and cholecystectomy (Bisgaard, Klarskov, Rosenberg, & Kehlet, 2001). Thus, the enhanced pain sensitivity noted in African Americans and Hispanics may place them at risk for future development of chronic pain. Indeed, these minority groups have a higher prevalence of clinical pain syndromes than non-Hispanic Whites (USDHHS, 2010). This relationship between experimental pain sensitivity and chronic pain risk may also be true of Native Americans.

The Study Presented Here

The study presented here assessed experimental pain in Native Americans and non-Hispanic Whites to identify factors that might contribute to chronic pain risk in Native Americans. Given the relationship between enhanced experimental pain and central sensitization and chronic pain risk in other minority groups, we hypothesized that Native Americans would have enhanced pain sensitivity (e.g., lower pain thresholds/tolerances) and central sensitization (enhanced TS-pain) compared with non-Hispanic Whites. To ensure that any observed group differences were not solely due to differences in pain reporting, we also assessed physiologic outcomes (NFR threshold, temporal summation of NFR). Finally, we assessed pain coping styles to determine whether group differences in pain were associated with these variables.

Methods

Participants

Participants were healthy, pain-free Native Americans ($n = 22$, 8 females) and non-Hispanic Whites ($n = 20$, 7 females) recruited via fliers, newspaper ads, and online postings (e.g., Craigslist) from the Tulsa, OK, community (see Table 1). As with most all studies of ethnicity/race and pain (e.g., Campbell et al., 2005; Edwards et al., 2001; Klatzkin, Mechlin, Bunevicius, & Girdler, 2007; Mechlin et al., 2011; Rahim-Williams et al., 2007), group status was based on self-reported racial/ethnic identity. However,

Table 1
Participant Characteristics by Group

Characteristic	Non-Hispanic Whites ($n = 20$)		Native Americans ($n = 22$)		p	Cohen's d
	M	SD	M	SD		
Sex (% female)	35% ($n = 7$)		36% ($n = 8$)		0.93	
Age (years)	33.60	11.99	41.14	14.39	0.07	-0.57
Education (years)	16.18	2.67	14.25	3.23	0.04	0.65
BMI (kg/m^2)	27.41	3.86	25.28	5.18	0.14	0.46
Psychological distress (SCL-90-R)	1.43	0.39	1.33	0.26	0.37	0.28
Quality of life (SF-36)	79.00	15.44	80.91	14.93	0.69	-0.13
Systolic blood pressure (mmHg)	123.10	15.30	121.63	13.16	0.74	0.10
Diastolic blood pressure (mmHg)	79.69	13.04	76.23	8.90	0.33	0.32

Note. Percentages of female participants are reported for sex. SCL-90-R = Symptom Checklist 90 Revised; SF-36 = Short-Form Health Survey.

Native American participants were also asked to provide their Certificate of Degree of Indian Blood (CDIB) card, which indicates their degree of Native American heredity (i.e., blood quantum) and tribal affiliation. Most (91%, $n = 20$) provided their CDIB card, and the other two self-reported their tribal affiliation and blood quantum. Blood quantum ranged from 5% (3 of 64) to 100% (4 of 4), $M = 49\%$, mode = 100%. All Native American participants reported having at least one Native American parent and 59% ($n = 13$) reported having two. One White participant reported having one non-Hispanic White parent, but the rest (95%) reported having two. Most Native American participants reported multiple tribal affiliations, with the most common affiliations being Cherokee (23.8%), Creek (16.7%), and Choctaw (9.5%). All participants provided verbal and written informed consent. Participants were excluded for being less than 18 years of age; self-reported health problems, including a history of cardiovascular, neurological, and/or circulatory problems; hypertension; chronic pain; reported recent use of medications that could interfere with testing (e.g., over-the-counter or prescription analgesics, antidepressants, anxiolytics, and/or antihypertensives); or having a body mass index (BMI) greater than 35 (due to difficulty obtaining an NFR for persons with high adiposity). Participants received a \$50 honorarium upon completion of the study.

Apparatus, Electrode Application, and Signal Acquisition

All testing procedures were completed in an electrically shielded and sound-attenuated experiment room. Experimenters monitored participants from an adjacent room via a video camera with a microphone that was connected to an LCD television. Participants wore sound-attenuating headphones, and experimenters communicated with participants using a microphone connected to a 40-W audio amplifier (Radio Shack, Fort Worth, TX; Part #32-2054). Data acquisition was controlled by a computer with dual monitor capacity, A/D board (PCI-6071E; National Instruments, Austin, TX), and LabVIEW software (National Instruments). Participants used one computer monitor to complete electronic questionnaires and to make pain ratings whereas experimenters used a second monitor to observe physiological signals. A Digitimer stimulator (DS7, Hertfordshire, England) and bipolar stimulating electrode (Nicolet, 019-401400, Madison, WI) were used to deliver electrical stimuli to the left ankle over the retromalleolar pathway of the sural nerve. Stimulation timing was controlled by computer (maximum stimulation intensity = 50 mA).

To apply electromyographic (EMG) and stimulating electrodes, the skin was first cleaned with alcohol and exfoliated using Nuprep gel (Weaver and Company, Aurora, CO) until impedances below 5 k Ω were achieved. Electrodes were filled with conductive gel (EC60; Grass Technologies) and then applied to the skin using adhesive collars. To assess NFR, two electrodes were placed over the ipsilateral biceps femoris muscle, 10 cm superior to the popliteal fossa, and a common reference electrode was placed over the lateral epicondyle of the femur. EMG was sampled at 1000 Hz, amplified ($\times 10,000$), and bandpass filtered (10–300 Hz) using Grass Technologies (West Warwick, RI) model 15LT amplifiers.

Background Variables

BMI was calculated using each participant's height and weight as measured by a medical scale. Resting blood pressure was recorded using a Critikon Dinamap PRO 100 Monitor (Tampa, FL) four times before experimental testing began. The Symptom Checklist-90-Revised (SCL-90-R) was used to measure psychological distress. The SCL-90-R is a reliable and valid questionnaire that consists of a list of 90 items asking about psychological problems. Respondents rated these items using a 5-point Likert scale (0 = *not at all*, 4 = *extremely*). The Global Severity Index (GSI) of the SCL-90-R was used to measure overall psychological distress (Derogatis, 1983, 1994). The general health scale from the Short-Form Health Survey (SF-36) was used to measure quality of life. This is a 5-item reliable and valid scale that measures the person's general perception of their health (McHorney, Ware, Lu, & Sherbourne, 1994; Ware & Sherbourne, 1992). Higher scores reflect an individual's belief that his or her health is excellent.

Pain Coping

The Coping Strategies Questionnaire (CSQ) was administered to assess individual differences in pain coping styles. The CSQ is a reliable and valid 50-item questionnaire (Rosenstiel & Keefe, 1983) that measures six cognitive pain coping strategies (diverting attention, reinterpreting pain sensations, coping self-statements, ignoring pain sensations, praying or hoping, catastrophizing) and two behavioral pain coping strategies (increasing behavioral activities, increasing pain behavior). Each subscale comprised six items and participants responded on a 7-point Likert-type scale (0 = *never do that*, 6 = *always do that*).

Pain Outcomes

Ratings of Painful Stimuli. To assess pain intensity in response to ischemia and electric pain stimuli, participants used a computer-presented numerical rating scale (NRS) similar to that used in prior studies (e.g., Rhudy, Williams, McCabe, Nguyen, & Rambo, 2005; Terry et al., 2011). The NRS ranged from 0 to 100, with the following labels: 0 (*no pain*), 50 (*painful*), and 100 (*most intense pain imaginable*). Participants used a computer mouse to slide an indicator along the scale to make ratings.

Ischemia Pain Assessment. The ischemia pain task emulates musculoskeletal pain. During this task, participants completed a set of hand exercises for 2 min at 50% of their maximum grip strength (as determined at the beginning of the study using a dynamometer) using the nondominant hand. The arm was then elevated for 15 s to allow blood to drain from the arm. Next, forearm blood flow was occluded by inflating a blood pressure cuff to 220 mm/Hg around the upper arm. While the cuff was inflated, participants were instructed to continuously rate pain intensity using the NRS described previously. Ischemia pain threshold was defined as the time (in seconds) from blood occlusion to the point at which the participant reported an NRS rating of 50 or greater. Ischemia pain tolerance was defined as the time (in seconds) until the individual reported it was the maximum pain he or she could tolerate (NRS rating = 100). Maximum time was set at 25 min to ensure participant safety.

NFR Threshold Assessment. The NFR is a spinally mediated protective reflex primarily elicited by A δ pain fiber activation (see

Figure 1; Sandrini et al., 2005). The stimulation intensity that reliably elicits the NFR (i.e., NFR threshold) correlates highly with pain threshold (e.g., $r = .70$; Willer, 1977), and the size of the reflex correlates with subjective pain intensity (e.g., $r = .84$; Chan & Dallaire, 1989; Rhudy et al., 2005). Therefore, NFR is used as a physiologic measure of spinal nociception (Sandrini et al., 2005).

To measure NFR threshold, three ascending-descending staircases of electric stimulations were delivered (Rhudy & France, 2007). Each stimulus consisted of a train of five 1-ms rectangular wave pulses at 250 Hz delivered to the sural nerve with a varying interval of 8–12 s between electric stimulations to reduce habituation and predictability. The first ascending-descending staircase started at 0 mA and increased in 2-mA steps until an NFR was obtained. The presence of the reflex was defined as a mean biceps femoris EMG response in the 90- to 150-ms poststimulus interval that exceeded the mean biceps femoris EMG activity during the 60-ms prestimulus baseline interval by at least 1.4 standard deviations (Rhudy & France, 2007). Once an NFR was obtained, the stimulus level was decreased in 1-mA steps until an NFR was no longer detected. The second and third ascending-descending staircases repeated this procedure but used 1 mA steps. NFR threshold was defined as the average stimulus intensity (mA) of the two peaks and two troughs of the last two ascending-descending staircases. Immediately after the presentation of each electric stimulus, participants used the NRS to rate their pain intensity. Suprathreshold pain ratings were defined as the average pain ratings of the stimuli that occurred at the two peaks and two troughs of the last two ascending-descending staircases.

Electric Pain Assessment. Pain threshold and tolerance were assessed using a single, ascending series of electrical stimulations (Rhudy et al., 2009). Stimulus parameters and interstimulus intervals (ISIs) were the same as during NFR testing. Immediately following each stimulus, participants rated their pain intensity on the NRS. Stimulation intensity started at 0 mA and increased in 2 mA steps until *electric pain tolerance* was reached (NRS rating = 100). *Electric pain threshold* was defined as the intensity of stimulation (mA) at which point the participant reported pain (NRS rating ≥ 50). Maximum intensity was set at 50 mA to ensure participant safety.

TS-Pain and NFR. TS-pain is the progressive increase in pain ratings in response to a series of constant-intensity, painful stimulations (Price, 1972). TS-pain is believed to result from a temporary hyperexcitability of spinal cord neurons (e.g., Mendell & Wall, 1965), which is thought to be an indicator of central sensitization and chronic pain risk (Li, Simone, & Larson, 1999; Woolf, 1983). In some circumstances, pain perception can diverge from measures of pain signaling in the spinal cord (Danziger et al., 1998; Rhudy, Williams, McCabe, Rambo, & Russell, 2006). For this reason, it is advantageous to measure temporal summation of NFR (TS-NFR; the progressive increase in NFR magnitude across series of painful stimulations, see Figure 1) to get a better measure of the sensitization of spinal cord neurons (Arendt-Nielsen, Brennum, Sindrup, & Bak, 1994).

The stimulus intensity during temporal summation testing was individually calibrated to each participant's three-pulse threshold (see Figure 1). To assess three-pulse threshold, several series of

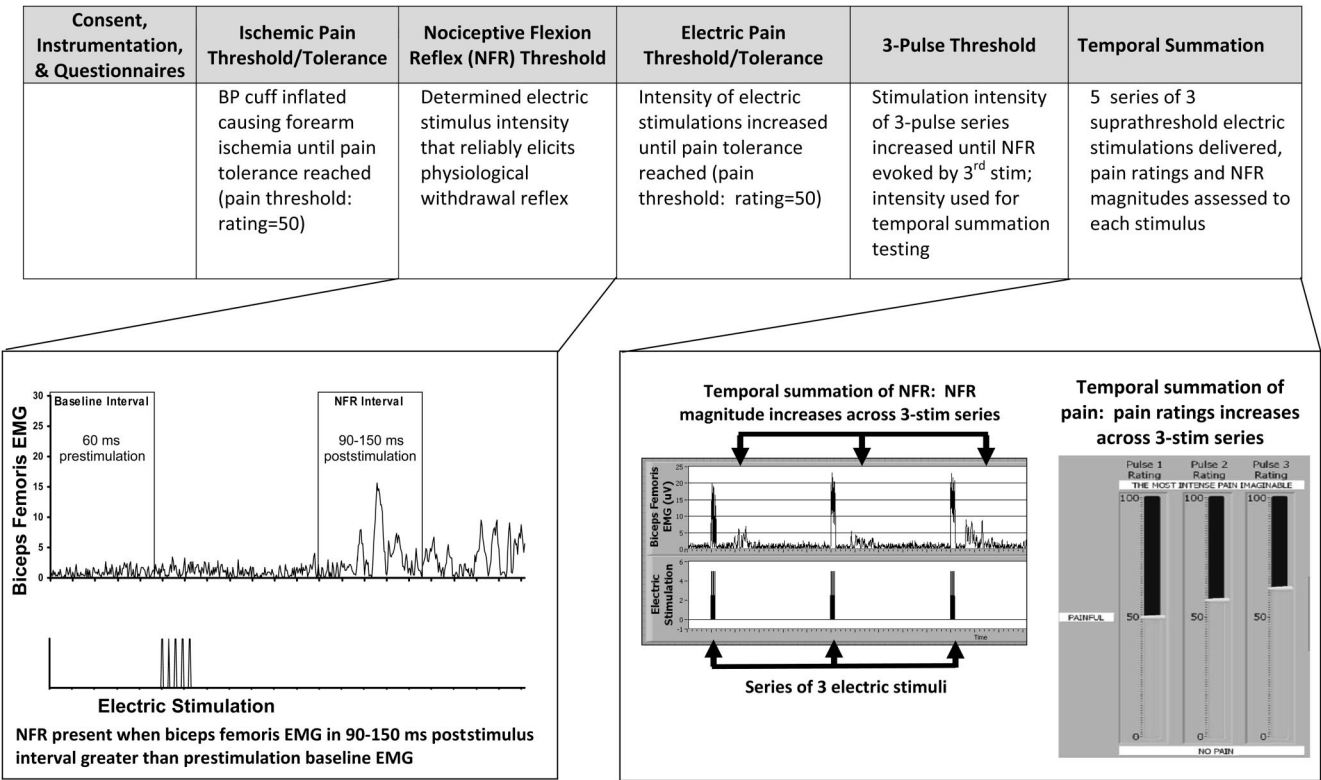


Figure 1. Experimental protocol.

three electrical stimulations with a 0.5-s ISI were delivered. The stimulus intensity of the first series started at 80% NFR threshold and increased by 1 mA until the third stimulus in the series evoked an NFR according to the definition used in NFR threshold testing. This stimulus intensity (mA) was defined as the three-pulse threshold. This was used because participants with low NFR thresholds (e.g., 3–10 mA) do not always produce reliable reflexes during temporal summation testing (Terry et al., 2011). However, when the stimulus intensity is set at or above the three-pulse threshold, this problem is alleviated.

To assess TS-pain and TS-NFR, five series of three suprathreshold electrocutaneous stimuli with a 0.5 s-ISI were delivered (Terry et al., 2011). Immediately following each series, pain ratings were assessed from computer-presented NRSs displaying three separate scales (one for each stimulus in the series). These ratings were used to assess TS-pain. To assess TS-NFR, biceps femoris EMG was recorded during each stimulus series. NFR magnitude was calculated by subtracting the mean prestimulus baseline EMG from the mean EMG in the 90- to 150-ms post-stimulation interval after each stimulus (Terry et al., 2011). Eight NFRs were excluded from analysis (1.3%) because there was contamination (e.g., voluntary muscle contraction) in the prestimulation EMG (defined as mean EMG > 10 μ V).

Procedure

Figure 1 illustrates the experimental procedures. All procedures were approved by The University of Tulsa Institutional Review Board (IRB). The experimenter provided a thorough overview of the experiment, obtained informed consent, and screened the participant for inclusion/exclusion criteria. Participants were then instrumented for physiological recording. The procedures in the single testing session proceeded in the following order: questionnaire administration, ischemia pain threshold/tolerance testing, NFR threshold testing, electric pain threshold/tolerance testing, and temporal summation of pain/NFR. To allow participants time to recover from the ischemia tolerance task, there was a 15- to 20-min break immediately after it. Between other tasks there were breaks that lasted 2–5 min during which participants heard instructions regarding the next task. Throughout all phases, participants were seated comfortably in a reclining chair with the foot rest extended (knee angle approximately 160°). When the study was over, participants were provided their honorarium.

Statistical Analyses

The α level was set at $p < .05$ (two-tailed) for all analyses. To analyze group differences in background variables, pain coping variables, and pain sensitivity (except temporal summation), independent samples t tests were conducted and Levene's test was performed to test the homogeneity of variance assumption. If violated, degrees of freedom were adjusted.

Given that temporal summation testing involved multiple data points (three stimuli per series \times five series), the SPSS MIXED procedure was used to analyze TS-pain and TS-NFR and maximize statistical power. Data were arranged in long form (i.e., each participant contributed 15 rows of data; three stimuli per series \times five series). In these two MIXED models, maximum likelihood estimation was used and the repeated measures covariance was modeled by an autoregressive (AR1) structure. Stimulus number (Stim1, Stim2, Stim3) was entered as a within-subjects variable to assess changes in pain/NFR across the three-stimulation series (i.e., temporal summation) and group (Native American, White) was entered as a between-subjects variable.

Results

Participant Characteristics

Participant characteristics are reported in Table 1. There were no group differences in sex, age, BMI, psychological distress, quality of life, or resting blood pressure. However, compared with non-Hispanic Whites, Native Americans reported fewer mean years of education (note: all participants except one Native American reported having at least a high school education).

Pain Coping

There were no significant group differences on any coping strategy (see Table 2).

Pain Outcomes

One Native American participant did not achieve an NFR threshold before reaching the 50-mA stimulus intensity maximum; therefore, this participant was excluded from analysis of NFR threshold and TS-NFR. Contrary to hypotheses, Native Americans

Table 2
Means, SD, and Cohen's d Values for Group Comparisons for Pain Coping Styles

CSQ Pain Coping Variables	Non-Hispanic Whites		Native Americans		p	Cohen's d
	M	SD	M	SD		
Diverting attention (0–36)	18.15	8.16	15.82	9.47	0.40	0.26
Reinterpretation of pain sensations (0–36)	14.35	8.22	13.59	9.10	0.78	0.09
Coping self-statements (0–36)	23.85	8.11	24.41	6.64	0.81	–0.08
Ignoring sensations (0–36)	17.75	6.31	16.18	7.70	0.48	0.22
Praying/hoping (0–36)	9.50	6.46	10.36	6.96	0.68	–0.13
Catastrophizing (0–36)	5.10	6.32	3.41	4.03	0.30	0.33
Increasing behavioral activities (0–36)	14.70	5.99	12.86	7.45	0.39	0.27
Increasing pain behaviors (0–36)	14.70	5.57	15.64	7.20	0.64	–0.15

Note. CSQ = Coping Strategies Questionnaire.

showed lower pain sensitivity than non-Hispanic Whites on most pain outcomes (see Table 3). Specifically, they had significantly higher ischemia pain tolerances, higher electric pain thresholds, and lower suprathreshold pain ratings. Although nonsignificant, the means for ischemia pain threshold and electric pain tolerance were also in the direction of lower pain sensitivity.

The stimulus intensity used during temporal summation testing did not differ between the two groups: $M_{\text{Whites}} = 19.92$ mA ($SD = 8.62$) versus $M_{\text{NA}} = 19.71$ mA ($SD = 9.08$), $p = .99$; therefore, any group differences noted in temporal summation cannot be attributed to stimulus intensity differences. As noted in Figure 2, analysis of TS-pain indicated that both groups experienced a progressive increase in pain across the three-pulse series (stimulus number main effect: $F(2, 513.45) = 11.26$, $p < .001$; all pairwise comparisons p values $< .05$). Moreover, Native Americans rated the stimuli as less painful than non-Hispanic Whites (group main effect: $F(1, 47.94) = 7.13$, $p = .01$, $d = 0.70$). The Group \times Stimulus Number interaction was nonsignificant, $F(2, 513.45) < 1$. These results indicate that the perception of painful electric stimuli was dampened in Native Americans, but that both groups had a similar pain summation.

In the analysis of TS-NFR (see Figure 2), there was a significant main effect of group, $F(1, 102.58) = 5.03$, $p = .03$, and stimulus number, $F(2, 311.54) = 32.41$, $p < .001$, but these effects were qualified by a significant Group \times Stimulus Number interaction, $F(2, 311.54) = 8.36$, $p < .001$. Contrasts for the simple effect of group found that Native Americans had a lower NFR magnitude at stimulus 2 ($p = .014$, $d = 0.51$) and stimulus 3 ($p < .001$, $d = 0.40$), but not stimulus 1 ($p = .35$, $d = 0.19$). Therefore, summation of NFR was reduced in Native Americans providing physiological evidence that they have reduced spinal cord sensitization.

Exploratory Analyses: Potential Confounding by Background Variables

Analyses indicated that groups differed on education, and the effect sizes for age and BMI were of moderate size (close to $d = 0.50$). Thus, to explore whether these variables could contribute to group differences in pain outcomes, zero-order correlations were first conducted between these variables and all pain outcomes. There were significant correlations between ischemia pain tolerance and age ($r = .33$, $p = .03$), electric pain threshold and age ($r = .40$, $p = .009$), and suprathreshold pain ratings and education ($r = .34$, $p = .03$). All other correlations were nonsignificant. To follow-up on these significant relationships, hierarchical regres-

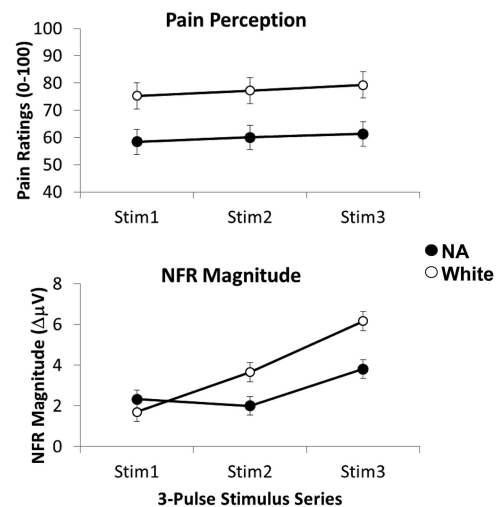


Figure 2. Temporal summation of pain (upper figure) and temporal summation of the nociceptive flexion reflex (lower figure). NA = Native American; NFR = nociceptive flexion reflex.

sions were conducted in which the background variable was entered in step 1 and group was entered in step 2. These analyses indicated group was still a significant predictor of ischemia pain tolerance after controlling for age (step 2 $\Delta R^2 = .09$, $p = .047$) and of suprathreshold pain ratings after controlling for education (step 2 $\Delta R^2 = .09$, $p = .046$). However, group was no longer a significant predictor of electric threshold after controlling for age (step 2 $\Delta R^2 = .04$, $p = .15$). Therefore, age may partially account for group differences in electric pain threshold.

Discussion

This study examined pain processing in Native Americans using experimental methods. Contrary to hypotheses, pain was reduced in Native Americans compared with non-Hispanic Whites on some pain outcomes. Native Americans had higher electric pain thresholds, higher ischemia pain tolerances, and lower ratings of suprathreshold electric stimuli (during NFR threshold and temporal summation testing). Group differences in electric pain tolerance, ischemia pain threshold, and NFR threshold were nonsignificant. The lack of group differences in NFR threshold indicate that this protective reflex is evoked by similar stimulus levels in the two

Table 3
Means, SD, and Cohen's d Values for Group Comparisons of Pain Outcomes

Outcome	Non-Hispanic Whites		Native Americans		p	Cohen's d
	M	SD	M	SD		
Ischemic pain threshold (s)	90.30	122.51	267.14	401.00	0.06	-0.68
Ischemic pain tolerance (s)	210.15	206.22	540.77	544.97	0.01	-0.88
NFR threshold (mA)	22.21	12.28	19.89	11.75	0.54	0.19
Suprathreshold pain ratings (0-100)	76.08	18.04	53.56	34.33	0.01	0.86
Electric pain threshold (mA)	15.50	6.61	22.82	14.34	0.04	-0.70
Electric pain tolerance (mA)	34.70	13.41	36.00	13.66	0.76	-0.10

Note. Degrees of freedom (and thus p values) were adjusted when the homogeneity of variances assumption was not passed. NFR = nociceptive flexion reflex.

groups. However, Native Americans demonstrated reduced TS-NFR. Given that TS-NFR is a physiologic measure of spinal sensitization, this suggests that pain signaling is dampened within the spinal cord before it is relayed to the brain. Consistent with this, pain ratings during temporal summation were considerably lower in Native Americans relative to non-Hispanic Whites (see Figure 2). Physiologic evidence provided by TS-NFR also indicates that group differences in pain perception are not fully explained by group differences in reporting style. This is important given evidence that Native Americans may under-report pain (Barkwell, 2005; Haozous et al., 2011; Kramer et al., 2002).

One potential explanation for these group differences in pain perception and spinal cord sensitization could be group differences in descending inhibition. Indeed, pain perception is determined by several factors including the level of painful input, the amount of CNS sensitization, and the degree of activation of descending (brain-to-spinal cord) pain inhibitory mechanisms. Some have suggested that enhanced pain sensitivity in African Americans is due to underactivation of descending inhibition because one study found that African Americans demonstrated less pain inhibition than non-Hispanic Whites on an experimental measure of descending inhibition (Campbell et al., 2008a). Thus it is possible that overactivation of descending inhibition results in dampened pain and reduced spinal cord sensitization in Native Americans. Alternatively, group differences in pain could be explained by psychosocial factors (eg, perceived discrimination, ethnic identity) as has been noted in other studies of pain in ethnic minorities (Edwards, 2008; Rahim-Williams et al., 2007). Future studies are needed to examine these possibilities.

Group differences in pain processing are not likely to be explained by differences in pain coping strategies because groups did not differ on subscales of the Coping Strategies Questionnaire (see Table 2). Moreover, exploratory analyses were conducted to examine whether age, BMI, or education contributed to group differences in pain because group differences on these three background variables had moderate effect sizes. These analyses indicated that age may partially explain the group difference in electric pain threshold but not other pain outcomes.

Potential Implications

Native Americans, African Americans, and Hispanics have a high risk of chronic pain, but African Americans and Hispanics have higher pain sensitivity. Thus, the mechanisms that contribute to chronic pain in Native Americans may be different than these other groups. Pain sensitivity, central sensitization, and descending inhibition are normally distributed in humans and reflect natural variation in pain processing (depicted by hypothetical normal distribution of pain tolerance in Figure 3; e.g., Diatchenko et al., 2005; Edwards, 2005). Persons in the middle of the distribution have a healthy balance between descending inhibition and ascending nociception. They can detect tissue damage and are able to engage descending inhibition when necessary to manage pain. As a result, these persons may be at lower chronic pain risk.

However, deviations from “normal” pain processing may confer risk for chronic pain. Individuals in the left tail of the distribution of Figure 3 are pain sensitive (e.g., low pain tolerance). They have higher pain sensitivity, enhanced central sensitization, reduced ability to inhibit pain, and higher risk for chronic pain (Edwards,

2005; Peters, Schmidt, Van den Hout, Koopmans, & Sluiter, 1992; Staud et al., 2001). For these individuals, incoming pain signals (ascending nociception) and descending inhibition are out of balance, with the result being enhanced pain and chronic pain risk.

Individuals in the right tail of the distribution in Figure 3 are pain insensitive (e.g., high pain tolerance). Although experiencing less pain can seem beneficial, chronically dampened pain may actually confer risk for future pain-related problems. In extreme cases, persons who cannot experience pain at all (i.e., congenital pain insensitivity) have difficulty detecting physical harm, are less likely to protect injuries, and fail to learn to avoid future danger (Cox et al., 2006). Likewise, those in the right tail of the distribution may be at risk for chronic pain because they have a difficult time detecting and preventing tissue damage and/or protecting tissue damage once it has occurred. Further, chronic overactivation of descending pain inhibition may promote chronic pain by exhausting pain inhibitory resources, perhaps through a disruption of the opioid system (Bruehl, McCubbin, & Harden, 1999; Mayer & Hayes, 1975). Once there is a failure of descending pain inhibition, incoming pain signals will go unchecked, and these individuals may move from the right tail of the distribution into the left tail to become pain sensitive. The notion that inhibitory resources are depleted over time in Native Americans is consistent with recent evidence that Native Americans show the greatest age-related increase in low back pain incidence (Knox, Orchowski, & Owen, 2012).

Thus, chronic pain risk in Native Americans may be due to problems detecting physical harm (because of low pain sensitivity) and/or overactivation of pain inhibitory mechanisms. If these assertions are correct, then there are several potential implications. First, it means that the mechanisms underlying pain risk in Native Americans is different than other minority groups. Second, clinical interventions may need to be tailored to Native Americans. Whereas most psychological pain techniques focus on decreasing pain and increasing descending pain inhibition (e.g., distraction, pleasant imagery), Native Americans may benefit from new or adapted interventions that focus on bringing pain into awareness and/or directing attention toward pain to improve its detection. For example, mindfulness techniques could be adapted to promote awareness of incoming pain signals while at the same time decreasing pain effect and distress. Third, if Native Americans are chronically hypoalgesic, then this could contribute to inaccurate prevalence rates of pain problems in this population. Finally, it might be possible to develop an objective screening tool to identify individuals at risk for chronic pain (i.e., those with dampened TS-NFR).

Study Limitations

Although our study had several strengths (e.g., first experimental pain study in Native Americans, multiple stimulus modalities, use of physiological outcomes), a few limitations are worth noting. First, sample sizes were small. Given that this study was the first to assess experimental pain in Native Americans, we conceptualized this as a pilot study and targeted $N = 50$ (25 per group), which would have provided power of .61 or greater for effect sizes of d of .65 or greater. This seemed adequate because other studies of ethnicity and pain have found moderate to large effect sizes

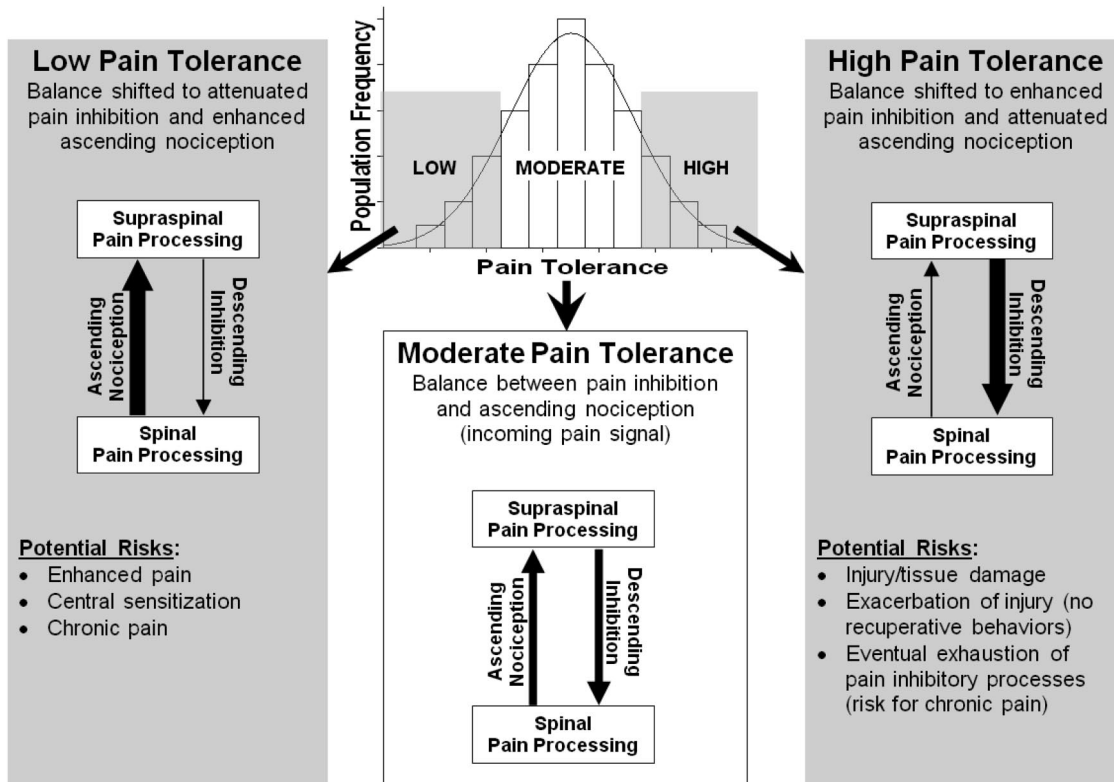


Figure 3. Hypothetical risk factors for chronic pain. Pain sensitivity (e.g., pain tolerance) is normally distributed in humans, and individual differences in pain sensitivity are determined by the relative contribution of the incoming pain signal (nociception) and descending inhibitory processes. It is proposed that those with moderate pain sensitivity (e.g., moderate pain tolerance) have a balance between ascending nociception and descending inhibition that places them at lower risk for chronic pain. By contrast, persons with extremely high pain sensitivity (e.g., those in the left tail of the distribution who have low pain tolerance) and extremely low pain sensitivity (e.g., those in the right tail of the distribution with high pain tolerance) are both at risk for clinical pain because of an imbalance between ascending nociception and descending inhibition.

(Campbell et al., 2005, 2008b; Edwards & Fillingim, 1999). However, we were only able to achieve $N = 42$ total because of funding limitations. This likely reduced our ability to detect some group differences on pain coping and pain sensitivity. Furthermore, small samples sizes meant that we were unable to assess whether variables mediated or moderated ethnic/racial differences in pain sensitivity (e.g., tribal affiliation, blood quantum level, acculturation, biological sex, age, BMI). Second, because our sample comprised healthy individuals, we are unable to generalize to those with health problems. For example, rates of obesity in the general population are higher for Native Americans than Whites (39.6% vs. 26.1%) (USDHHS Office of Minority Health, 2010), yet our samples were similar on BMI. Therefore, our group of Native Americans may not represent well the general population of Native Americans. Furthermore, our results cannot be generalized to persons with chronic pain. However, by limiting our sample to healthy individuals, we were able to rule out many potential confounds. Third, our samples were not perfectly matched on all background variables. Nevertheless, exploratory analyses revealed that group differences in pain were not fully explained by age, BMI, or education. Fourth, we used a fixed order for our pain tasks. Although we tried to allow for ample time in between tasks,

we cannot rule out that carryover effects influenced our conclusions on later tasks. Finally, similar to prior studies, groups were defined largely by self-reported ethnicity/race rather than other factors (e.g., parental ethnicity/race, genetics). This limits our ability to make claims about heredity.

Summary

The study presented here suggests Native Americans have dampened pain sensitivity and reduced central sensitization. Thus, chronic pain risk in Native Americans may be different than in other ethnic minorities, perhaps because of problems detecting physical harm. If these findings are replicated in a larger sample, these observations could inform new interventions tailored to this population and could aid in the reversal of health disparities in pain.

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