Examining emotional modulation of pain and spinal nociception in Native Americans: A preliminary investigation☆

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A B S T R A C T

Pain problems are more prevalent in Native Americans than in any other group in the U.S., and this might result from group differences in pain modulation. This study was designed to examine emotional modulation of pain and spinal nociception in healthy, pain-free Native Americans (n = 21) relative to non-Hispanic Whites (n = 20). To assess emotional modulation of pain and the nociceptive flexion reflex (NFR, a physiological measure of spinal nociception), participants underwent a well-validated emotional picture-viewing paradigm during which suprathreshold pain stimuli were delivered to the ankle. Compared to Whites, Native Americans reported less pleasure to erotic pictures and failed to show corrugator reactivity to mutilation pictures. Unlike Whites, Native Americans only evidenced pain inhibition in response to erotica, but no pain facilitation (disinhibition) to mutilation pictures. Emotional modulation of NFR was similar in both groups. These preliminary findings suggest that Native Americans failed to disinhibit pain, perhaps due to over-activation of pain inhibitory mechanisms. Chronic over-activation of this system could ultimately exhaust it, thus putting Native Americans at future risk for chronic pain.

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1. Introduction

Previous research indicates that the prevalence of many chronic pain conditions (e.g., severe headaches, rheumatoid and juvenile arthritis, back pain) is higher in Native Americans than in any other group in the United States (Barnes et al., 2010; Deyo et al., 2006; Ferucci et al., 2005; Leake et al., 2008; Mauldin et al., 2004; Rhee, 2000). Additionally, Native Americans have a tendency to minimize their responses to painful conditions (Haozous et al., 2011; Kramer et al., 2002), thus the prevalence rates of chronic pain in this group may be even higher as a result of underreporting. Unfortunately, despite these pain disparities, most of the available research on pain in this population has been limited to epidemiological studies (for a review, Jimenez et al., 2011).

Other ethnic minority groups (e.g., African Americans, Hispanics) also have high rates of chronic pain, and experimental pain studies conducted with these populations have demonstrated that they show lower pain tolerance and enhanced pain sensitivity to noxious stimuli (Campbell et al., 2004, 2005, 2008; Edwards et al., 2001; Edwards and Fillingim, 1999; Rahim-Williams et al., 2007). By contrast, recent evidence suggests that Native Americans have dampened pain sensitivity (Palit et al., in press), such that they have a higher ischemic pain tolerance and lower pain ratings in response to electric stimuli.

In addition, Native Americans showed reduced temporal summation of the nociceptive flexion reflex (NFR) compared to non-Hispanic Whites (Palit et al., in press). The NFR is a withdrawal reflex evoked by suprathreshold electric stimulations to the sural nerve at the ankle. When the stimulus is intense enough to activate nociceptive Aδ fibers, a lower limb withdrawal reflex is elicited and the reflex can be quantified from electromyogram (EMG) of the biceps femoris (hamstring) muscle (Sandrini et al., 2005). Because the NFR requires the activation of Aδ fibers, it is a nociceptive (pain-related) response. Research has demonstrated that the stimulus intensity that elicits the NFR (i.e., NFR threshold) correlates highly with pain threshold, and the size/magnitude of the NFR correlates with suprathreshold stimulus intensity and pain ratings (Sandrini et al., 2005; Skjøsvold and Ramadan, 2002); therefore, both NFR threshold and NFR magnitude are used as indices of spinal nociception. Although the reflex arc does not rely on supraspinal centers, the NFR can be modulated from brain-to-spinal cord circuitry (Rhudy et al., 2005; Sandrini et al., 2005). Temporal summation of NFR is the progressive increase in the magnitude of the reflex that occurs in response to a series of constant-intensity, suprathreshold stimulations (Arendt-Nielsen et al., 1994, 2000), and temporal summation of NFR is used as a measure of spinal neuron (central) sensitization (You et al., 2003, 2004). Thus, our observation that temporal summation of NFR is reduced in Native Americans suggests that the incoming pain signal is dampened at the level of the spinal cord before reaching the brain (Palit et al., in press). These surprising results imply that hypoalgesia in Native
Americans may stem from a central process (dampening of pain signals), not just report bias.

Given that other ethnic groups are hyperalgesic (have enhanced pain sensitivity) but Native Americans are hypoalgesic (have reduced pain sensitivity), this suggests that the mechanisms that promote chronic pain risk in Native Americans may be different from those in other ethnic groups. Indeed, various factors play a role in pain perception (e.g., amount of nociceptive input, pain sensitivity, degree of central sensitization). But one important, relatively understudied, mechanism is the activation of descending pain modulatory processes. For example, descending inhibitory processes keep nociceptive signaling in check to minimize its impact on the body, whereas descending facilitatory (disinhibitory) processes can amplify pain signaling to increase pain detection and promote recuperation following injury (Millan, 2002; Walters, 1994). One study found that African Americans had a reduced capacity to engage descending inhibition (Campbell et al., 2008), which is consistent with studies indicating that African Americans are hyperalgesic on measures of pain sensitivity. At this time, there have been no published studies on pain modulation in Native Americans.

1.1. Why hypoalgesia might be a risk factor for pain in Native Americans: a hypothesis

Individual differences in pain sensitivity, central sensitization, and pain modulation are believed to be normally distributed in humans, thus reflecting natural variability in these processes (depicted as a normal distribution of pain tolerance in Fig. 1) (Diatchenko et al., 2005; Edwards, 2005). People in the middle of the distribution have a balance between ascending nociceptive input and descending inhibition. Individuals with this “healthy” balance can appropriately detect and manage pain, which is likely to put them at a lower risk of injury and development of chronic pain.

However, individuals in either tail of this distribution may be at a higher risk for chronic pain. The left tail is characterized by low pain tolerance (greater pain sensitivity), enhanced central sensitization, and less effective pain inhibition. For these individuals, the balance is shifted towards greater nociceptive input (and less descending inhibition) resulting in hyperalgesia and risk for chronic pain (Edwards, 2005; Peters et al., 1992; Staud et al., 2001). Based on the available data (Campbell et al., 2004, 2005, 2008; Edwards et al., 2001; Edwards and Fillingim, 1999; Rahim-Williams et al., 2007), it appears that African Americans and Hispanics fall into this tail of the distribution.

By contrast, persons in the right tail of the distribution have high pain tolerance (lower pain sensitivity), low or no central sensitization, and augmented pain inhibition. Although this profile appears to be advantageous, chronically dampened pain may promote risk for pain-related problems. For example, in the most extreme case, persons with congenital pain insensitivity who cannot experience pain at all have difficulty identifying physical harm, are unable to protect their injuries, and fail to avoid similar physical dangers in the future (Cox et al., 2006). Similarly, persons in the right tail may have a difficult time detecting and preventing tissue damage and/or protecting tissue damage once it has occurred. Furthermore, chronic activation of descending inhibition could be problematic in and of itself, because it could deplete inhibitory resources via disruption of the opioid system (Bruehl et al., 1999; Mayer and Hayes, 1975). Once these inhibitory processes deplete and fail, then pain would go unchecked and persons in the right tail would shift into the left tail of the distribution and become pain sensitive.

Given evidence that pain-free Native Americans have low pain sensitivity (hypoalgesia) and reduced temporal summation of NFR (reduced central sensitization), we have hypothesized that pain risk in Native Americans may partially stem from difficulties detecting physical harm and protecting injuries (Palit et al., in press). However, pain risk may also stem from chronically activated descending pain inhibitory

![Fig. 1. Normal distribution of pain sensitivity in humans depicting hypothetical risk factors for chronic pain.](image-url)
processes that could deplete over time. Findings from a recent study support this notion, suggesting an age-related increase in low back pain in Native Americans (Knox et al., 2012), which would be consistent with age-related depletion of pain inhibitory resources. At this time however, the role of pain inhibitory processes is purely speculative. It is interesting to note that a similar hypothesis was recently proposed by Haack et al. (2012) for the mechanism by which insomnia confers risk for chronic pain. They observed that pain-free persons with primary insomnia had reduced temporal summation of pain and a failure of descending inhibition. Therefore, Native Americans and persons with primary insomnia may share a common risk factor for pain, but the functioning of pain modulatory processes has not been tested in Native Americans.

1.2. Studying differences in pain modulation: emotion as a tool

As alluded to above, pain perception is influenced by both ascending (nociceptive signaling from the periphery to the brain) and descending (top-down processes that inhibit/facilitate the pain signal) pathways. Thus, it is useful to study mechanisms of pain modulation because disruptions in these processes can be indicative of, or confer risk for, chronic pain (Fields et al., 2006; Porreca et al., 2002; Ren and Dubner, 1999). It has been shown that emotion modulates pain via descending pathways, such that positive emotions attenuate pain while negative emotions enhance pain (Keefe et al., 2001; Rhudy and Meagher, 2001). This has been demonstrated in several studies using emotionally-charged pictures, such that pleasant pictures (e.g., erotica) induce positive affect and pain inhibition, whereas unpleasant pictures (e.g., mutilation) induce negative affect and pain facilitation (disinhibition) (de Wied and Verbaten, 2001; Kenntner-Mabiala and Pauli, 2005; Meagher et al., 2001; Rhudy et al., 2008). Using a well-validated picture viewing paradigm to study emotional modulation of pain and nociception (termed Emotional Controls of Nociception, ECON; Rhudy et al., 2008), our laboratory has shown that emotion also modulates the magnitude of the NFR in the same manner, with pleasant pictures inhibiting the reflex and unpleasant pictures enhancing it (Rhudy et al., 2005). Given that NFR is a measure of spinal nociception, this suggests that the ECON paradigm is a useful tool for investigating modulation of spinal nociception in addition to modulation of pain perception.

1.3. The present study

The present study examined whether there were group differences in emotional modulation of pain and spinal nociception using the ECON paradigm in Native Americans and non-Hispanic Whites. Group differences in emotional processing of pictures were also investigated via measures of emotional valence (i.e., subjective valence ratings, corrugator EMG) and arousal (i.e., subjective arousal ratings, skin conductance response). Given our prior observations that Native Americans have dampened pain, we hypothesized that they would show greater inhibition of pain and NFR in response to pleasant pictures (erota) and a failure to enhance (disinhibit) pain in response to unpleasant pictures (mutilation). Furthermore, given the tendency for Native Americans to underreport pain (Haozous et al., 2011; Kramer et al., 2002) and to minimize facial displays of emotion (Chiang, 1993), we also hypothesized that they might demonstrate suppressed emotional responding to the affective picture stimuli (e.g., reduced corrugator EMG responding, lower reports of pleasure/displeasure). These data were collected as part of a comprehensive study of pain processing differences in Native Americans. Other aspects of that study have been published elsewhere (Palit et al., in press), but the data presented here are novel and have not been previously reported.

2. Materials and methods

2.1. Participants

Participants were healthy, pain-free Native Americans ($n = 21, 8$ females) and non-Hispanic Whites ($n = 20, 7$ females) recruited from the Tulsa, OK community via fliers, newspaper ads, and online postings (e.g., Craigslist). Participants were excluded for self-reported health problems, including history of cardiovascular, neurological, and/or circulatory problems, hypertension, and/or chronic pain; recent use of medications that could interfere with testing (e.g., over-the-counter or prescription analgesics, antidepressants, anxiolytics, and/or antihypertensives); being less than 18 years of age; and/or having a body mass index (BMI) greater than 35 (due to difficulty obtaining an NFR for persons with high adiposity). As with other studies of ethnic differences in pain processing (e.g., Campbell et al., 2005; Klatzkin et al., 2007; Mechlin et al., 2011; Rahim-Williams et al., 2007), ethnic/racial status was based on self-report. Further, Native American participants were asked to provide their Certificate Degree of Indian Blood (CDIB) card, which indicates their degree of Native American heredity (i.e., blood quantum) and tribal affiliation. Most provided their CDIB card (95%, $n = 20$) and one self-reported their tribal affiliation and blood quantum. Blood quantum ranged from 5% (3/64) to 100% (4/4), with the mean $= 49\%$ and mode $= 100\%$. Most Native Americans reported having multiple tribal affiliations, with the most common being Cherokee (33.3%), Creek (19.0%), and Choctaw (14.3%). All Native American participants reported having at least one Native American parent. One non-Hispanic White participant reported having only one White parent, but the rest reported having two non-Hispanic White parents (95%). Participants received a $50 honorarium upon completion of the study.

2.2. 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 by using a microphone connected to a 40 W audio amplifier (Radio Shack, Fort Worth, TX; Part #32-2054). All data acquisition, as well as stimuli and questionnaire presentation, were controlled by a PC equipped with dual monitors, A/D board, and LabVIEW software (National Instruments; Austin, TX). One video output from the computer was used to present questionnaires (including pain rating scales) and picture stimuli to the participant, while a second video output was displayed to a second computer monitor in the control room for the experimenter to check physiological signals and experimental progress.

A Digitimer stimulator (DS7; Hertfordshire, England) and bipolar stimulating electrode (Nicolet, 019-401400, Madison, WI) were used to deliver electrical stimuli (train of five $1$ ms rectangular wave pulses at $250$ Hz) to the left ankle over the retromalleolar pathway of the sural nerve. Timing of the stimulations was controlled by a computer (maximum stimulation intensity $= 50$ mA). Physiological signals were collected and amplified by Grass Technologies (West Warwick, RI) Model 15LT amplifiers (with AC Module 15AS4 and Module 15AS4). All physiological signals were sampled at 1000 Hz. An adaptor for the 15AS12 amplifier (Grass, Model SCA1) was used to record skin conductance response (SCR) as a physiological measure of picture-evoked sympathetic arousal (Lang et al., 1993; Rhudy et al., 2006, 2008). Two electrodes filled with isotonic paste (EC33, Grass Instruments) and attached to the volar surface of the index and middle fingers of the non-dominant hand were used to measure SCR. In order to assess the NFR, two electrodes were placed over the biceps femoris muscle of the leg, 10 cm superior to the popliteal fossa, and a common reference electrode was placed over the lateral epicondyle of the femur. Left corrugator supercilius muscle activity was assessed as a physiological signal.
measure of picture-evoked emotional valence using two Ag/AgCl mini-
ature electrodes (Lang et al., 1993). Biceps femoris electromyography
(EMG) was amplified (∼10,000), rectified, and bandpass filtered
(10 Hz–300 Hz) and left corrugator EMG activity was amplified
(∼20,000), rectified, and bandpass filtered (30 Hz–1000 Hz). To apply
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 kΩ were achieved. Electrodes were filled
with conductive gel (EC60; Grass Technologies) and then applied to
the skin using adhesive collars.

2.3. Ratings of painful stimuli

To assess pain intensity in response to electric pain stimuli, partici-
pants used a computer-presented numerical rating scale (NRS) similar
to that used previously in our laboratory (Rhudy et al., 2005, 2013;
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 made ratings by using a computer mouse to slide an indicator
along the line to a position that corresponded to their rating. Each rating
was submitted by pressing the computer mouse button.

2.4. Determination of suprathreshold stimulus intensity

Noxious flexion reflex (NFR) threshold, electric pain threshold,
and 3-pulse threshold were recorded to determine the level of electrical
stimulation delivered during emotional picture-viewing. The suprathreshold stimulus intensity was set at the highest of the follow-
ing: 120% of NFR threshold, 100% pain threshold, or 100% 3-pulse
threshold (all in mA).

2.4.1. Noxious flexion reflex (NFR) threshold

The NFR is a spinally-mediated protective withdrawal reflex used
as a physiological measure of spinal noxious processing (Chan and
Dallaire, 1989; Rhudy et al., 2005; Sandrini et al., 2005; Willer, 1977).
Three ascending–descending staircases of electric stimulations were
used to assess NFR threshold. Each stimulus was delivered to the sural nerve with a varying interval of 8–12 s between stimulations
to reduce predictability. The first ascending–descending staircase started at 0 mA and increased in 2 mA steps until a reflex was
observed. Once an NFR was obtained, the stimulus level was
decreased in 1 mA steps until a reflex was no longer detected. The
second and third ascending–descending staircases used 1 mA steps. A positive reflex was defined as mean biceps femoris EMG
response in the 90–150 ms post-stimulus interval that exceeded
the mean biceps femoris EMG activity during the 60 ms pre-
stimulus baseline interval by at least 1.4 standard deviations
(Rhudy and France, 2007). Immediately following the presentation
of each stimulus, participants used the NRS to rate their experience
of the stimuli. The stimulus intensity (mA) of the two peaks and
two troughs of the last two ascending–descending staircases were
averaged and used to define NFR threshold.

2.4.2. Electric pain threshold assessment

A single, ascending series of electric stimulations were delivered in
order to assess pain threshold. Immediately following each stimulus,
participants rated their pain intensity using the NRS. Stimulation
intensity started at 0 mA and increased in 2 mA steps until a rating of
100 on NRS was achieved. Electric pain threshold was defined as the
level of stimulation (mA) at which point the participant reported an
NRS rating ≥50.

2.4.3. 3-Pulse threshold

To assess 3-pulse threshold, several series of three electrical stimula-
tions at 2.0 Hz (0.5 s interstimulus interval) 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 (described above). The 3-pulse
threshold was defined as the intensity that elicited an NFR in response
to the third stimulus. This procedure was employed because we have
demonstrated elsewhere that participants with low NFR thresholds
(e.g., 3–12 mA thresholds) do not always produce reliable reflexes during
subsequent testing (Terry et al., 2011). To address this problem, we
developed the 3-pulse threshold which requires an NFR to be present
on the 3rd pulse. Setting the stimulus intensity at or above the 3-pulse
threshold ensures reliable reflexes during NFR testing.

2.5. Emotional Controls of Nociception (ECON)

2.5.1. Picture stimuli

Pictures from the International Affective Picture Systems (IAPS)
(Lang et al., 2005) were chosen because they have been used in numer-
ous studies of emotional processing, including studies with participants
from diverse racial and ethnic backgrounds (e.g., Brown et al., 2006;
Rausch et al., 2008). Mutilation (e.g., injured bodies), neutral (e.g.,
household items), and erotic (e.g., couples engaging in sexual acts)
contents were used because they have been shown to elicit the stron-
gest modulation of pain and NFR (Palit et al., 2009; Rhudy et al.,
2010). During the picture-viewing phase, eight pictures per content
were used for a total of 24 pictures. IAPS picture numbers for the contents
were: mutilation (3010, 3051, 3060, 3130, 3150, 3400, 3071,
9405), neutral (7006, 7009, 7010, 7040, 7060, 7080, 7150, 7235)
and erotica (4658, 4659, 4669, 4672, 4677, 4681, 7695, 4800). See next
section for standardized ratings of the pictures.

2.5.2. Subjective responses to pictures

The Self-Assessment Manikin (SAM) was used to assess picture-
evoked subjective responses (Bradley and Lang, 1994). The SAM is a
two-item questionnaire that yields valence/pleasure ratings (unpleas-
ant to pleasant) and arousal ratings (calm to excited) that range from
1 to 9. Greater pleasure or arousal is indicated by higher scores, respec-
tively. Participants used a computerized version of the SAM to rate each
picture immediately after it was presented. Participants responded by
moving an indicator on or between any of the five pictographs and
then submitted their answer by computer mouse. Normative valence
and arousal ratings for the IAPS pictures used in this study were:
Mutilation (valence: M = 1.96, arousal: M = 6.66), neutral (valence:
M = 4.85, arousal: M = 2.51), and erotica (valence: M = 6.50, arous-
al: M = 6.54) (CSEA, 2006).

2.5.3. Nociceptive outcomes during picture viewing

Suprathreshold electric stimulations presented during pictures were
set at the greatest of 120% NFR threshold, 100% pain threshold or 100% 3-pulse threshold. Electric stimuli were delivered during 50% of the pic-
tures to elicit pain and NFRs. Subjective reactions to the suprathreshold stimulations delivered during the pictures were assessed using the NRS
described above. NFR magnitude was used to assess within-subject
changes in spinal nociception during this procedure. NFR magnitude
was calculated in Cohen’s d units [d = (mean EMG of 90 to 150 ms
post-stimulation interval minus mean EMG of −60 to 0 ms pre-
stimulation interval) divided by the average SD of EMG from −60 to
0 ms pre-stimulation and SD of 90 to 150 ms post-stimulation inter-
vals]. The d-score method was chosen because it has previously been
shown to produce a stronger correlation with pain report (i.e., external
validity coefficient) than other NFR scoring methods (e.g., mean EMG,
AUC, peak EMG) (Rhudy and France, 2007; Rhudy et al., 2009).

2.6. Procedure

Interested participants were informed that the aim of the study was to
“assess pain processing differences in Native Americans.” All proce-
dures were approved by The University of Tulsa Institutional Review
Board (IRB). At the start of the testing session, the experimenter provided a thorough overview of the experiment, obtained informed consent, and screened the participant for inclusion/exclusion. Participants were then provided instructions on the NRS for rating pain and the SAM for rating pictures. Next, participants were instrumented for physiological recording. Participants then underwent ischemia pain testing (reported elsewhere) in which a blood pressure cuff was inflated around their arm until they could no longer tolerate it. After ischemia pain testing, there was a 15–20 min break to allow participants to recover, then NFR threshold, electric pain threshold, and 3-pulse threshold were assessed as described above. Next, participants underwent temporal summation (TS) testing (reported elsewhere) which involved delivering five series of three suprathreshold electric stimulations (with a 0.5-s interstimulus interval) to the sural nerve of the ankle. After another short break, emotional modulation of pain/NFR was tested using ECON. Results from ischemia threshold/tolerance, NFR threshold, electric pain threshold/tolerance testing, and temporal summation of pain/NFR have been reported elsewhere (Palit et al., in press); therefore, they will not be mentioned further.

To assess emotional modulation of pain and NFR, 24-affectively charged pictures were presented on a computer screen for 6 s each in pseudorandom order with the limitation that no more than two pictures of the same content could be shown consecutively. Suprathreshold electric stimuli were delivered 3–5 s after picture onset during 50% of the pictures (4 per content). Inter-picture intervals ranged from 12–22 s and electric stimuli were delivered during six intervals, 11 to 21 s after interval onset, to reduce stimulus predictability. Thus, a total of 18 electric stimulations were delivered during the picture-viewing phase. After each picture, participants used the SAM to rate their emotional response to every picture (and the NRS to rate the electric stimulus if one occurred). To ensure that a picture or stimulation was not delivered during a rating period, the computer automatically paused the experiment until the participant submitted their ratings by computer mouse. Throughout testing, participants were seated comfortably in a recliner with the foot rest extended (knee angle approximately 160°). The instructions given to participants about the ECON procedure were kept to a minimum in order to reduce the chance of experimental demand. Specifically, participants were told, “Please keep your eyes on the screen throughout testing as the pictures are shown. At random times during and in between picture viewing you will receive electric stimulations to your ankle. You will be asked to rate the intensity of the stimulation using the sliding scale and you will also be asked to rate your emotional reactions to the pictures.” However, they were not told that pictures were meant to influence pain. Participants were provided their honorarium after completion of the study.

2.7. Statistical analyses

To analyze group differences in background variables, chi-square analyses were used for nominal variables and independent-samples t tests were used for interval/ratio scale variables. Levene’s test was performed to test the homogeneity of variance assumption. If violated, degrees of freedom for t-tests were adjusted.

Given that the ECON paradigm involves multiple within-subject data points (data were in “long form”), the SPSS MIXED procedure was used to maximize statistical power in the analyses of valence ratings, arousal ratings, SCR, corrugator EMG, pain ratings, and NFR magnitude. Linear mixed model ANOVAs which use maximum likelihood estimation were used and the repeated measures variance–covariance structure was modeled using an autoregressive (AR1) structure. Picture content (mutilation, neutral, erotic) was entered as a within-subjects variable and group (Native American, non-Hispanic White) was entered as a between-subjects variable. Fisher’s LSD comparisons were used for all follow-up tests. The α level was set at p < .05 (two-tailed), except for mean contrasts associated with emotional modulation of pain/NFR. Given the number of prior studies showing emotional modulation of pain/NFR (e.g., Rhudy and Bartley, 2010; Rhudy et al., 2005, 2008, 2010), directional hypotheses were made (i.e., mutilation > neutral > erotica) so one-tailed tests were used for these comparisons only.

3. Results

3.1. Participant characteristics

Participant characteristics are reported in Table 1. There were no group differences in sex, years of education, body mass index, or blood pressure. However, there were group differences in age such that, compared to non-Hispanic Whites, Native Americans were older. To address whether age was a confound, it was entered as a covariate in analysis of variance (ANOVA) models.

No significant group differences were found in systolic or diastolic blood pressures (see Table 1). There was a significant main effect of picture content ([F(2, 867.50) = 872.02, p < .001], but this was qualified by a significant Content × Group interaction. For both groups, mutilation pictures were more unpleasant than neutral and erotica (ps < .001), and erotica was more pleasant than neutral (p < .001). However, non-Hispanic Whites were more unpleasant than neutral and erotica (ps < .001), and erotica was more pleasant than neutral (p < .001). However, non-Hispanic

Table 1

| Participant characteristics by group. | Non-Hispanic Whites (n = 20) | Native Americans (n = 21) | | | | | | | | |
| | M | SD | M | SD | p-Value | Cohen’s d |
| Sex (% female) | 35% (n = 7) | | 38% (n = 8) | | .84 | |
| Age (years) | 33.60 | 11.99 | 41.24 | 13.76 | .04 | .59 |
| Education (years) | 16.18 | 2.67 | 14.69 | 2.54 | .08 | .57 |
| Body mass index (kg/m²) | 27.27 | 4.01 | 25.33 | 5.48 | .21 | .41 |
| Systolic blood pressure (mm Hg) | 123.10 | 15.30 | 121.81 | 13.45 | .78 | .09 |
| Diastolic blood pressure (mm Hg) | 79.69 | 13.04 | 76.33 | 9.11 | .34 | .30 |

Note. Percentages of female participants are reported for sex.
Whites rated the erotic pictures as more pleasant than Native Americans \((p < .001)\). There were no group differences in valence ratings of mutilation or neutral pictures \((p > .20)\).

### 3.2.2. Corrugator EMG

There was no main effect of group \((p = .29)\), but there was a significant main effect of picture content \(F(2, 280.82) = 5.02, p = .007\) that was qualified by a significant Group \(\times\) Content interaction \(F(2, 281.65) = 5.28, p = .006\). This indicated that non-Hispanic Whites showed an increase in corrugator activity during mutilation pictures compared to neutral and erotic pictures \((p < .001)\), but no significant difference in corrugator activity during erotic versus neutral pictures \((p = .52)\). Interestingly, Native Americans did not evidence any differences in corrugator activity based on picture content during emotional picture-viewing \((p > .26)\).

### 3.2.3. Arousal ratings

There was not a main effect of group on arousal ratings \((p = .49)\), but there was a significant main effect of picture content \(F(2, 873.65) = 270.38, p < .001\) that was qualified by a significant Group \(\times\) Content interaction \(F(2, 873.52) = 4.75, p = .01\). For both groups, mutilation and erotic pictures were rated as more arousing than neutral pictures, and erotic pictures were rated as more arousing than mutilation pictures \((p < .001)\). But, none of the simple effects of group were significant \((p > .20)\); thus groups did not differ in their subjective arousal to the pictures.

### 3.2.4. Skin conductance response (SCR)

There were no significant main effects of group or content on SCR \((p > .34)\), meaning SCR was not impacted by the emotionally-charged pictures (not higher during mutilation or erotic pictures). This is similar

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**Fig. 2.** Emotional valence (valence ratings, corrugator EMG) and arousal (arousal ratings, skin conductance response [SCR]) reactions to pictures during pain testing. \(p < .05\).

**Fig. 3.** Emotional modulation of pain (left graph) and nociceptive flexion reflex (NFR; right graph).
to our prior studies that have inconsistently found picture-evoked SCR during pain testing (e.g., Rhudy and Bartley, 2010; Rhudy et al., 2005, 2006), ostensibly due to pain-evoked sympathetic arousal that overshadows the picture-evoked sympathetic arousal.

3.3. Emotional modulation of pain and NFR

3.3.1. Suprathreshold stimulus intensity

The average stimulation intensity used during picture-viewing was 33.08 mA (SD = 16.08) for Native Americans and 28.92 mA (SD = 13.24) for non-Hispanic Whites, which was not significantly different, \( t(39) = 90, p = .37 \). Therefore groups did not differ in the stimulus intensity used during ECON procedures.

3.3.2. Pain ratings

Analysis of pain ratings did not reveal a main effect of group \((p = .30)\). There was a significant main effect of picture content \(F(2, 298.88) = 35.84, p < .001\); however, this was qualified by a significant Content × Group interaction \(F(2, 298.39) = 10.74, p < .001\) (Fig. 3). Non-Hispanic Whites had significantly higher pain ratings during mutilation pictures compared to both neutral and erotic pictures \((p < .01)\), and significantly lower pain ratings during erotica compared to neutral \((p < .001)\). By contrast, Native Americans had significantly lower pain ratings during erotica than mutilation \((p = .004)\) and neutral \((p = .03)\), but pain ratings were not higher during mutilation than neutral \((p = .23)\). Together these data indicate that non-Hispanic Whites had pain inhibition by erotica and pain facilitation (disinhibition) by mutilation, whereas Native Americans showed pain inhibition by erotica, but failed to evidence significant disinhibition by mutilation.

3.3.3. Nociceptive flexion reflex (NFR) magnitudes

Analysis of NFR magnitude revealed only a significant main effect of picture content \(F(2, 392.33) = 4.40, p = .01\) (Fig. 3). NFR magnitudes were higher during mutilation pictures than during neutral \((p = .003)\) and erotic pictures \((p = .01)\), but NFR magnitudes were not different during erotica and neutral \((p = .32)\). There was no main effect of group \(F(1, 39.64) = 0.25, p = .62\) or a Content × Group interaction \(F(2, 392.33) = 0.15, p = .86\) indicating that there were no group differences in modulation of NFR.

Given that erotica failed to inhibit NFR in either group, it was decided to conduct an exploratory analysis to ensure that emotional modulation of NFR was associated with the linear trend of valence modulation, rather than the quadratic trend of arousal modulation. To do so, a linear mixed model was created that included group, a linear trend, a quadratic trend, and interactions between group and each trend. This analysis found that the linear trend was significant \(F(1, 410.52) = 4.24, p = .04\), but not the quadratic trend \(F(1, 377.63) = 1.63, p = .20\). Further, neither the Linear Trend × Group \(F(1, 414.18) = 0.74, p = .39\) nor the Quadratic Trend × Group \(F(1, 410.02) = 0.05, p = .82\) interaction was significant. Thus, emotional valence modulation best characterizes the effect in both groups.

4. Discussion

4.1. Emotional processing in Native Americans

This study examined emotional modulation of pain and spinal nociception in Native Americans using a picture-viewing paradigm (ECON) to examine whether differences in pain modulation might contribute to the dampened pain sensitivity previously noted (Palit et al., in press). In both groups, mutilation pictures were rated as more unpleasant than neutral and erotic pictures, whereas erotic pictures were rated as more pleasant than neutral pictures. Also, both mutilation and erotic pictures were rated as more arousing than neutral pictures. Together, this demonstrates that, subjectively, the emotion manipulation was successful across groups.

Nonetheless, there were some group differences in emotional reactivity. Compared to non-Hispanic Whites, Native Americans rated erotic pictures as slightly less pleasant and failed to activate their corrugator muscle to a significant degree during mutilation pictures. Indeed, non-Hispanic Whites showed the typical corrugator EMG activation in response to mutilation pictures compared to neutral and erotic pictures (e.g., Bradley et al., 2001), but corrugator activity did not differ across picture contents in the Native American group. Together, this suggests that Native Americans may underreport reactivity to pleasurable stimuli and limit their facial reactivity to unpleasant stimuli as compared to non-Hispanic Whites. Both differences could contribute to the impression that Native Americans are stic (at least in the outward expression of emotion) and are consistent with prior research indicating that Native Americans underreport pain (another emotional experience) (Haozous et al., 2011) and limit facial expressions of emotions (Chiang, 1993). It is interesting that there were no group differences in ratings of mutilation (depictions of physical injuries and people in pain), perhaps reflecting a willingness to express their verbal displeasure about other people's pain, but not their own. However, it is important to point out that we cannot determine from our study whether these group differences are limited to erotic and mutilation stimuli given that we only used these two specific contents to represent pleasant and unpleasant stimuli, respectively.

Neither group demonstrated increased sympathetic arousal (SCR) in response to mutilation or erotic pictures, which contradicts prior studies of emotional picture-viewing (e.g., Lang et al., 1993). However, this observation is consistent with several of our prior ECON studies (e.g., Rhudy and Bartley, 2010; Rhudy et al., 2005, 2006) and we believe that this reflects the fact that sympathetic arousal evoked by pain and pain anticipation overshadows any picture-evoked sympathetic arousal.

4.2. Modulation of pain and spinal nociception in Native Americans

Consistent with prior research conducted on healthy participants (e.g., Rhudy et al., 2010), erotic pictures inhibited pain whereas mutilation pictures disinhibited/facilitated pain, but only in non-Hispanic White participants. In contrast, erotica inhibited pain in Native Americans, but mutilation did not facilitate pain. This could be indicative of a failure to turn off ongoing inhibitory processes (i.e., disinhibition) while viewing mutilation pictures. This is further suggested by the non-significant trend for Native Americans to have overall lower pain ratings relative to the non-Hispanic Whites (Fig. 2; note that Native American pain ratings are all near the level of erotica in the White group). Thus, if the pain signal is tonically dampened in Native Americans, then it might be difficult to disinhibit during mutilation, or to engage relatively greater inhibition during erotica. However, it is important not to over interpret non-significant group differences in pain. So, this is pure speculation until this notion can be tested in a study with greater statistical power and that examines other pain inhibitory mechanisms (e.g., conditioned pain modulation) (Yamitsky, 2010).

Interestingly, there were no group differences in emotional modulation of NFR. Mutilation pictures disinhibited/facilitated NFR relative to neutral and erotica in both groups. It is a bit surprising that erotica failed to inhibit NFR in either group, but it is noteworthy that the effect of emotion on NFR is generally weaker than the effect of emotion on pain (e.g., Rhudy et al., 2005, 2006). To further ensure that emotional valence modulation of NFR was present, we conducted an exploratory analysis that examined whether a linear trend (valence modulation) or a quadratic trend (arousal modulation) best fit the data, as is commonly done in the startle literature (e.g., Bradley et al., 1990; Vrana et al., 1988). This revealed that the linear trend best fit the data and did not interact with group, suggesting that emotional valence modulation was present in both groups. However, further research is
needed to determine whether erotica-inhibition of NFR can be observed in Native Americans.

The finding that emotional modulation of NFR was not different in the Native American group is somewhat contrary to our previous study that revealed group differences in another form of modulation of spinal nociception (i.e., temporal summation of NFR was dampened in Native Americans) (Palit et al., in press). However, temporal summation of NFR and emotional modulation of NFR are mediated by different mechanisms and thus provide different information about central processing of pain. Temporal summation is a measure of temporary central sensitization that is elicited via repeated activation of peripheral nociceptive fibers and results in temporary hyperexcitability of dorsal horn neurons (Herrero et al., 2000; Mendell and Wall, 1965; Rhudy et al., 2011; Terry et al., 2011). Thus, temporal summation of spinal nociception is a peripherally-driven process and does not require supraspinal input. On the other hand, emotional modulation of NFR is an affective process that involves communication between supraspinal centers and the dorsal horn. Indeed, emotional modulation of spinal nociception and temporal summation of spinal nociception can be induced in parallel without the two interacting with each other. For example, our laboratory has shown that if you deliver a series of 3 electrical stimulations (instead of 1) during emotional pictures, there is temporal summation of NFR, and there is an emotional valence modulation of NFR, but there is no emotional modulation of temporal summation of NFR (Rhudy et al., 2012). Put another way, that study found that picture valence modulated the overall size of the NFR, and there was a positive slope in NFR across the 3-pulse series indicative of temporal summation, but the positive slope did not vary by picture valence. This provides evidence that the two mechanisms are separate; descending modulation can impact the NFR (and thus spinal nociception) without having an impact on temporal summation of spinal nociception.

Therefore, it is possible that the group differences were found in temporal summation of NFR, but not emotional modulation of NFR, because dorsal horn neurons can sensitize without descending inhibition/facilitation from the brain’s emotion centers. Together, these data suggest that descending inhibition of spinal nociception by emotion does not explain the dampened temporal summation of NFR we previously observed in Native Americans (Palit et al., in press). Moreover, it suggests that multiple mechanisms may contribute to chronic pain risk in this population. Native Americans may have over-engaged supraspinal inhibition of pain and also a local dampening of spinal dorsal horn neurons that put them at risk for pain, even though emotional modulation of NFR is intact. Additionally, it is worth noting that other factors not addressed here (e.g., psychosocial, genetic, cultural) may play a role in pain risk in this group.

It could be argued that differences in emotional reactivity to mutilation pictures (no corrugator activity) in Native Americans could partly explain why mutilation did not disinhibit/facilitate pain in this group; i.e., perhaps the mutilation pictures did not manipulate emotion to the same degree in the Native American group. However, this cannot fully explain the group differences, because groups did not differ in how displeasing (valence) or arousing they rated the mutilation pictures. Moreover, mutilation pictures also disinhibited/facilitated NFR in both groups. It is also worth noting that reduced valence ratings of erotica in Native Americans also cannot explain the group differences we noted, because Native Americans still evidenced pain inhibition during these erotic pictures.

4.3. Potential implications

Given evidence that Native Americans have a high prevalence of pain conditions and are hypoalgesic (Palit et al., in press), we hypothesized that they are in the right tail of the distribution of Fig. 1 and have over-active inhibitory processes that put them at risk for pain. Our findings partially confirm this hypothesis. Native Americans were not able to facilitate pain while watching mutilation pictures, suggesting a failure to release pain inhibition (disinhibition). If true, this could eventually exhaust valuable pain inhibitory processes, placing them at greater risk for developing chronic pain over time. Such evidence may inform treatments for chronic pain in this group. Psychological management of pain often focuses on techniques (e.g., relaxation, guided imagery) aimed at reducing the experience of pain and increasing descending pain inhibition. However, given that Native Americans are hypoalgesic and may have chronically engaged descending inhibition, it may be beneficial to use new or modified interventions that could help them bring pain into awareness in order to improve detection, avoid harm, and promote recuperative behaviors. At the same time, individuals could still be taught the necessary therapeutic skills to effectively cope with pain. Such methods could aid in prevention of further injury as well as reducing distress and functional impairment that can result from chronic pain. Techniques such as mindfulness and biofeedback could be adapted to this end.

4.4. Study limitations

Although this study had several strengths (e.g., first study examining modulation of pain and spinal nociception in Native Americans, use of well-validated methodology, examination of physiological outcomes, powerful analytic methods), a few limitations are worth noting. First, the group sizes in our study were small. This study was originally conceptualized as a pilot study with a targeted N = 50 (25 per group), as power analysis determined that this would provide adequate power when using traditional GLM approaches to data analysis (Palit et al., in press). However, due to funding limitations, we were not able to achieve this final sample, so we tried to overcome this problem by using statistically powerful linear mixed model analyses. This greatly improved statistical power (as denoted by the denominator degrees of freedom in the results). Nonetheless, our ability to detect group differences on some outcomes may have been impacted. Second, this was a sample of healthy individuals, thus the external validity of the study may be limited as we cannot generalize the findings to individuals with health issues (e.g., chronic pain or illness). However, this selection criteria did allow us to avoid potential health confounds. Therefore, future studies should replicate these findings in a larger, more diverse sample, including those with chronic health conditions. Third, it is important to note that this study examined experimental pain which may not generalize to clinical pain. Similarly, the effect of affective pictures used to elicit emotions may not have the same effects as prolonged clinical emotional states (e.g., depression). Fourth, groups were defined on the basis of self-reported ethnicity/race, so our ability to make claims about heredity is limited. Fifth, age was significantly different between groups and may have confounded group differences. Preliminary analyses were run with age as a covariate, however, age was not a significant covariate in any model, nor did adding it change the results. Even so, it would be beneficial for future studies to replicate these results with age-equivalent samples. Sixth, it is possible that response bias and/or experimental demands may have influenced our results, especially given that group differences were found for voluntary responses (e.g., pain), but not involuntary responses (e.g., NFR). However, bias/demands cannot completely explain pain processing differences in Native Americans because we have previously reported that they show reduced temporal summation of NFR (a physiological outcome), suggesting that nociceptive processing is dampened in that group (Palit et al., in press). Finally, emotional modulation of pain/NFR was assessed after other pain tests. Thus, there may be an effect of stimulus pre-exposure on our findings, but because participants were provided breaks in between pain tests to help them recover, this should not have significantly impacted emotional modulation outcomes.
4.5. Summary

The present study extends our previous finding that Native Americans have dampened pain responsivity by providing evidence that this group is unable to disinhibit pain in the context of unpleasant emotional stimuli. In addition, Native Americans also showed reduced facial expressions (as assessed by corrugator EMG) in response to unpleasant pictures and reduced response in pleasure to pleasant pictures. This is consistent with a stoic response style and this group’s underreport of pain (Haozous et al., 2011). If replicated in a larger sample, the findings from this study could help inform treatments to reduce the risk of chronic pain in this population and ultimately help reduce pain disparities.

References


Bradley, M.M., Coddington, M., Cuthbert, B.N., Lang, P.J., 2001. Emotion and motivation I: facial expressions (as assessed by corrugator EMG) in response to unpleasant pictures and reduced response in pleasure to pleasant pictures. This is consistent with a stoic response style and this group’s underreport of pain (Haozous et al., 2011). If replicated in a larger sample, the findings from this study could help inform treatments to reduce the risk of chronic pain in this population and ultimately help reduce pain disparities.

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