PAIN

Racial and ethnic differences in experimental pain sensitivity: systematic review and meta-analysis

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Abstract

Our objective was to describe the racial and ethnic differences in experimental pain sensitivity. Four databases (PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, and PsycINFO) were searched for studies examining racial/ethnic differences in experimental pain sensitivity. Thermal–heat, cold–pressor, pressure, ischemic, mechanical cutaneous, electrical, and chemical experimental pain modalities were assessed. Risk of bias was assessed using the Agency for Healthcare Research and Quality guideline. Meta-analysis was used to calculate standardized mean differences (SMDs) by pain sensitivity measures. Studies comparing African Americans (AAs) and non-Hispanic whites (NHWs) were included for meta-analyses because of high heterogeneity in other racial/ethnic group comparisons. Statistical heterogeneity was assessed by subgroup analyses by sex, sample size, sample characteristics, and pain modalities. A total of 41 studies met the review criteria. Overall, AAs, Asians, and Hispanics had higher pain sensitivity compared with NHWs, particularly lower pain tolerance, higher pain ratings, and greater temporal summation of pain. Meta-analyses revealed that AAs had lower pain tolerance (SMD: -0.90, 95% confidence intervals [CIs]: -1.10 to -0.70) and higher pain ratings (SMD: 0.50, 95% CI: 0.30–0.69) but no significant differences in pain threshold (SMD: -0.06, 95% CI: -0.23 to 0.10) compared with NHWs. Estimates did not vary by pain modalities, nor by other demographic factors; however, SMDs were significantly different based on the sample size. Racial/ethnic differences in experimental pain sensitivity were more pronounced with suprathreshold than with threshold stimuli, which is important in clinical pain treatment. Additional studies examining mechanisms to explain such differences in pain tolerance and pain ratings are needed.

Keywords: Racial/ethnic differences, Pain sensitivity, Meta-analysis, Systematic review

1. Introduction

Chronic pain is a major health problem in the United States, and over 116 million Americans are currently affected.³⁵ It is reported that there are more than 70 million annual visits to health care providers at a cost more than \$600,000 million per year in medical treatment and lost work productivity.³⁵ Also, patients with chronic pain and their families suffer from intangible costs related to pain, such as decreased quality of life and interpersonal stresses.³¹

Racial/ethnic minorities experience greater adverse effects caused by chronic pain, such adverse effects may include that they have lower quality of life,²⁷ higher pain anxiety and

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© 2016 International Association for the Study of Pain http://dx.doi.org/10.1097/j.pain.0000000000000731 depressive symptoms,^{20,27,32} higher limitation of activity and work,⁵ and higher levels of disability.^{54,65} Disparities related to pain management in the United States have been reported; racial/ethnic minorities received lower quality of pain care than non-Hispanic whites (NHWs) in acute, chronic, cancer, and palliative pain care across the lifespan and treatment settings.⁴ Low socioeconomic status, lack of health insurance, limited or delayed access to care/medication, and patient-health care provider communication issues have been reported to be associated with racial/ethnic chronic pain disparities.^{27,46,59}

Studies examining racial/ethnic differences in clinical pain have documented greater levels of clinical pain in racial/ethnic minorities compared with NHWs for various painful conditions, including joint pain, migraine headache, jaw pain, or arthritis.^{15,23,24} Using a representative sample in the United States, Riskowaski⁶⁰ reported higher rates of acute pain in African Americans (AAs) and Hispanics compared with NHWs.

Although there is no consensus regarding the underlying mechanisms to explain the racial/ethnic group differences in clinical pain, several studies have found significant associations between experimental pain sensitivity and clinical pain. Higher experimental pain sensitivity was associated with higher clinical pain sensitivity in older adults with knee osteoarthritis (OA).¹² Lower ischemic pain tolerance in AAs compared with NHWs was associated with higher chronic pain in AA patients with noncancer chronic pain conditions.¹⁵ Temporal summation (TS) of mechanical pain predicted greater clinical pain ratings in adults with knee OA.²⁴ Differences in central pain-inhibitory mechanisms (eg,

A view of pain as a composite of 3 interdependent components—sensory–discriminative, cognitive–evaluate, and affective–motivational features—was proposed by Melzack and Wall and has become a dominant paradigm in the pain and pain management fields.²¹ Pain threshold and pain intensity ratings are commonly considered indicative of the sensory–discriminative feature of pain, whereas tolerance and ratings of unpleasantness are considered indicative of the affective–motivational features of pain. It has been reported that sensory–discriminative components of pain vary relatively little across racial/ethnic groups, whereas affective–motivational components of pain are more sensitive to racial/ethnic differences.^{16,60} Taken together, these results suggest that racial/ethnic differences in experimental pain sensitivity could contribute to the racial/ethnic differences in reported clinical pain.¹⁵

Most previous studies have focused on comparing AAs vs NHWs, as noted previously,⁵⁶ leading to a limited understanding of differences in experimental pain sensitivity among other racial/ ethnic groups. Multiracial Americans, Asians, and Hispanics are rapidly growing populations in the United States,⁶⁶ making it increasingly relevant to examine pain sensitivity in multiple racial/ ethnic groups. Therefore, the purpose of this study was to review the literature evaluating differences in experimental pain sensitivity among multiple racial/ethnic groups.

2. Methods

2.1. Search strategy and data sources

A systematic review of the literature was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. 41,48 Search strategies were developed and adapted for PubMed, EMBASE (Elsevier), the Cochrane Central Register of Controlled Trials (Cochrane Library), and PsycINFO (EbscoHOST). Three categories of terms (pain, race/ethnicity, and experimental modalities and measures) were identified and combined to retrieve articles that included at least 1 term from each group. Both subject headings and freetext searching were used in all databases. Explosion, which applies all narrower terms underneath the subject heading automatically, was used to ensure a comprehensive search of ethnic and racial groups. No limits were applied for date or language in the initial search. The full search strategy for PubMed is provided in Appendix I (available online as supplemental digital content at http://links.lww.com/PAIN/A351).

Inclusion criteria for articles were as follows: full-text, published, peer-reviewed, English-language studies, studies of experimental pain sensitivity, published between January 2000 and February 2016, and limited to human subjects. Exclusion criteria were studies that did not use any type of experimental pain stimuli to evoke pain or did not compare pain sensitivity measures by racial/ethnic groups.

Two authors (H.J.K. and G.S.Y.) independently reviewed all retrieved titles after duplicates were removed. Selected abstracts were reviewed by the 2 reviewers independently, and full-text articles were selected on agreement that the article met the inclusion and exclusion criteria. Data extraction was conducted by one reviewer (H.J.K.) with a self-developed structured codebook and confirmed by the other reviewer (G.S.Y.) (**Fig. 1**).

Risk of bias in reporting racial/ethnic differences in experimental sensitivity in individual studies was assessed based on the criteria from the Agency for Healthcare Research and Quality (AHRQ)

guideline. The Agency for Healthcare Research and Quality developed quality assessment criteria of individual studies according to the study design. The assessment criteria for nonexperimental design studies include sample size, methods for selecting participants, methods for measuring exposure variables, methods to deal with design-specific issues such as recall or interviewer bias, and analytical methods to control for confounding factors.¹ After assessment of individual criteria, ratings of "good," "fair," or "poor" can be assigned. Because we focused on racial/ethnic differences in experimental pain sensitivity for this review, most of the studies retrieved were those that used similar study design and methodology (eg, experimental pain sensitivity measurements in a laboratory setting, convenience sampling), and included multiple racial/ethnic samples. Therefore, 4 items were evaluated for each article; sample size (\geq 100 vs <100), clear definition of the racial/ethnic group (provided vs unprovided), description of a standardized study protocol (provided vs unprovided), and control of confounding factors (yes vs no). Total scores ranged from 0 to 4, with a smaller number indicating a higher risk of bias. The quality of reviewed studies was assessed by the 2 reviewers independently (H.J.K. and G.S.Y.), and the ratings of each study were compared. Discrepancy was identified and discussed to arrive at agreement.

2.2. Data analysis

Included studies were classified by pain modality type and racial/ ethnic group comparison (AAs vs NHWs, comparisons among other racial/ethnic groups). We conducted meta-analyses to estimate pooled standardized mean differences (SMDs) and 95% confidence intervals (CIs) between racial/ethnic groups to determine the magnitude of differences on pain sensitivity using Stata (version 13.1, StataCorp LP, College Station, TX). Tolerance, threshold, pain intensity ratings, and pain unpleasantness were examined and compared between the 2 groups (AAs vs NHWs). If

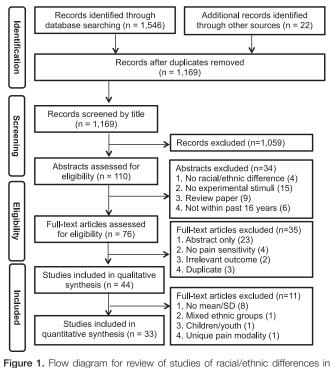


Figure 1. Flow diagram for review of studies of racial/ethnic differences in experimental pain sensitivity.

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Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Comparing AA and NHW									
Campbell et al. ⁷	120 (AA = 62, NHW = 58)	Young healthy adults	54	4	Left hand	Cold-pressor task (5°C)	No difference	NHW > AA	
Cruz-Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	63	4	Hand	Cold-pressor task (16, 12, 8°C)	No difference		AA > NHW (at 16 and 12°C, no difference at 8°C)
Fabian et al. ¹⁷	64 (AA = 11, API = 15, NHW = 26)	Young healthy adults	61	2	Hand	Cold-pressor task (4°C)		No difference	AA = API > NHW
Forsythe et al. ¹⁹	155 (AA = 60, NHW = 95)	Healthy undergraduate students	54	3	Hand	Cold-pressor task (0-2°C)		$\rm NHW > AA$	No difference
Grewen et al. ²⁹	48 (AA = 25, NHW = 23)	Premenopausal women	100	3	Hand	Cold-pressor task (4°C)	No difference	NHW>AA	
Hastie et al. ³⁰	247 (AA = 81, NHW = 87, Hispanic = 79)	Young healthy adults	52	3	Hand	Cold-pressor task (5°C)	No difference	$\rm NHW > AA, Hispanic$	NHW $<$ AA, Hispanics
Klatzkin et al. ³⁷	55 (AA = 32, NHW = 23)	Women with or without histories of depression	100	2	Hand	Cold-pressor task (4°C)		NHW > AA	No difference
Kim et al. ³⁶	617 (AA = 130, Hispanic = 59, API = 67, NHW = 344)		60	4	Hand	Cold-pressor task (2-4°C)		NHW (highest) $>$ AA (lowest)	NHW (lowest)
Mechlin et al. ⁴⁵	106 (AA = 51, NHW/other* = 55)	Healthy adults (18-47)	53	3	Hand	Cold-pressor task (4°C)	No difference	NHW/other $>$ AA	
Mechlin et al.44	84 (AA = 45, NHW = 39)	Young healthy adults	51	3	Hand	Cold-pressor task (4°C)	$\rm NHW > AA$	$\rm NHW > AA$	
Mechlin et al.43	88 (AA = 44, NHW = 44)	Healthy adults (18-45)	50	3	Hand	Cold-pressor task	No difference	$\rm NHW > AA$	No difference
Meints and Hirsh ⁴⁷	190 (AA = 82, NHW = 108)	Healthy undergraduate students	74	3	Hand	Cold-pressor task (2°C)	No difference	NHW > AA	AA < NHW
Rahim-Williams et al. ⁵⁷	206 (AA = 63, Hispanic = 61, and NHW = 82)	Healthy adults	54	4	Left hand	Cold-pressor task (5°C)	No difference	NHW $>$ AA, Hispanics	
Riley et al.58	191 (NHB = 53, and NHW = 138)	Middle-aged and older adults (range: 45-76)	68	4	Hand	Cold water immersion	No difference		No difference
Weisse et al. ⁶⁹	290 (NHW = 193, AA = 97)	Healthy undergraduate students	55	3	Hand	Cold-pressor task (0-2°C)			AA > NHW
Comparing other ethnicities									
Chan et al. ¹¹	57 (FAA = 12, SAA = 21, EA = 24)	Undergraduate students living in the United States	63	3	Hand	Cold-pressor task (0.5-1°C)	No difference	SAA = EA > FAA	FAA>EA
Dawson and List ¹⁴	64 (Middle Easterners = 32, Swedes = 32)	Young healthy adults	50	3	Hand	Cold-pressor task (0-1°C)	No difference	Swedes $>$ Middle Easterners	
Hsieh et al. ³⁴	160 (Chinese = 80, EC = 80)	Healthy undergraduate students living in Canada	52	4	Hand	Cold-pressor task (2-3°C)	No	EC > Chinese	No difference
Hsieh et al. ³³	184 (Chinese = 102, EC = 82)	0	70	4	Hand	Cold-pressor task	anoronoo		$\rm CM = ECM > EC$
Nayak et al. ⁵¹	226 (In India = 119, in United States = 107)	Healthy college students, second or higher generation Americans and Indians in each country	50	4	Hand	Cold-pressor task (0-2°C)		Indians in India $> \mbox{Americans}$ in the United States	

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Authors Sample size Sample characteristics % (F) Rowell et al. ⁶¹ 60 (NHW = 30, Asians = 30) Healthy young adults living in the 50 50	Sample characteristics	% (E) BI	M_M_4	o included of		:		:
			(+_0) nr	% (F) KUB (U-4) SIMULATION METHOD	Method	Threshold	Threshold Tolerance	Katings
				site				
	Healthy young adults living in the	50	2	Hand	Cold-pressor task NHW >	> MHM >	NHW > Asians	No difference
	United States				(4°C)	Asians		
Watson et al. ⁶⁸ 40 (white British = 20, South W	Working professional males living	0	က	Forearms	Contact cold	No		
Asians = 20) in	in the United Kingdom					difference		
Yang et al. ⁷⁰ 58 (Chinese = 29, Danes = 29) University students of each	University students of each	52	ი	Bilaterally in	Bilaterally in Contact cold	Chinese >		
0	country			the		Danes		
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				and mental				
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experimenters and English language; FAA, first-generation Asian American; HC, Hong Kong Chinese; MC, mainland Chinese; NHW, non-Hispanic white; OA, osteoarthritis; ROB⁺, risk of bias; SAA, second-generation Asian American

results of testing multiple body sites for a single pain modality were reported from a study, we selected the most commonly used measurement site (eg, forearm). Also, we chose the first measurement when there were multiple tests over time with a single modality. Heterogeneity across studies was identified by l^2 statistic ($l^2 \ge 50\%$); therefore, the random-effects model was used to get pooled SMDs.⁶ To investigate heterogeneity, we performed subgroup analyses by sex (% of women), sample size, sample characteristics, and pain modalities using random-effects metaregression models (DerSimonian and Laird method), with 95% Cls. We also conducted sensitivity analysis by excluding studies that did not provide definitions of race/ethnicity. The Egger tests of publication bias were performed to assess publication bias.64 Publication bias indicates that small studies with a small or nonsignificant effect may be less likely to be published than studies reporting a large or significant effect.⁶³ P < 0.05 was considered statistically significant (2-tailed).

3. Results

The literature search yielded 1546 articles. Twenty-two articles were also found through Google Scholar and relevant bibliographies. After removal of duplicates, the title screening process identified 110 potentially eligible studies (Fig. 1). After abstracts were screened using the inclusion and exclusion criteria, 44 studies remained for gualitative synthesis.

In regard to the risk of bias of individual studies, most of the studies had a score of 3 or 4, indicating a low risk of bias. All of the studies had a standardized pain sensitivity measure protocol and had controlled for recognized confounding factors (eg, age, sex) in study designs or their analyses. However, more than half of the studies had sample sizes of less than 100, and several studies lacked information about how the researchers defined "race/ethnicity."

Racial/ethnic differences in experimental pain were evaluated using a wide range of stimulus modalities, including pressure, thermal-heat, cold-pressor, electric, ischemic, and chemical experimental pain (eg, capsaicin). Pain sensitivity has been assessed using a number of different outcome measures, including threshold and tolerance, and ratings of pain intensity and/or unpleasantness.

3.1. Qualitative synthesis

The systematic review begins with a summary of pain sensitivity differences comparing AAs and NHWs, and followed by comparisons among other racial/ethnic groups for each pain modality. Forty-four studies were selected for qualitative synthesis.

3.2. Thermal pain

3.2.1. Cold pain stimuli

Twenty-three studies examined racial/ethnic differences in experimental cold pain (Table 1). All studies used some form of the cold-pressor task in which subjects immersed their hand in circulating cold water for a determined period, except for 2 studies that used contact cold.68,70 The sample size of the studies ranged from 40 to 617. The majority of study participants were young healthy adults, but one study examined patients with knee OA¹² and another examined women with or without histories of depression.³⁷ Fifteen studies compared AAs and NHWs. Nine studies reported no difference in cold pain threshold between the 2 groups, whereas 2 studies reported that NHWs

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Studies examining racial/ethnic differences in thermal-heat experimental pain models.

Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Comparing AA and NHW									
Campbell et al. ⁷ Cruz-Almeida et al. ¹²	120 (AA = 62, NHW = 58) 267 (AA = 120, NHW = 147)	Young healthy adults With knee OA, aged from 45 to 85	54 63	4 4	Left ventral forearm Knee and forearm	Contact heat Contact heat	No difference $\rm NHW > AA$	NHW > AA NHW > AA	AA > NHW
Glover et al. ²³	94 (AA = 45, NHW = 49)	With symptomatic knee OA, middle- aged and older adults	74	2	Knee and forearm	Contact heat	NHW > AA (forearm only)	$\rm NHW > AA$	
Goodin et al. ²⁵	130 (AA = 67, NHW = 63)	Older adults with symptomatic knee OA	77	3	Index knee and ipsilateral ventral forearm	Contact heat		NHW > AA	
Goodin et al. ²⁴	225 (AA = 122, NHW = 103)	With knee OA, aged 45 y and above	68	4	Index knee and ipsilateral volar forearm	Contact heat			AA > NHW
Grewen et al. ²⁹ Hastie et al. ³⁰	48 (AA = 25, NHW = 23) 247 (AA = 81, NHW = 87, Hispanic = 79)	Premenopausal women Young healthy adults	100 52		Volar forearms Ventral forearm	Contact heat Contact heat	No difference No difference	NHW > AA No difference	No difference
Kim et al. ³⁶	617 (AA = 130, Hispanic = 59, API = 67, NHW = 344)	Healthy adults	60	4	Ventral forearm	Contact heat			API $>$ AA, Hispanic, NHW
Klatzkin et al. ³⁷	55 (AA = 32, NHW = 23)	Women with or without histories of depression	100	2	Volar forearm	Contact heat	No difference	No difference	AA > NHW
Lu et al. ⁴²	214 (NHW = 98, Hispanic = 58, $AA = 34$, and Asian = 24)	Healthy children (range: 8-18)	49	3	Both volar forearms	Radiant heat		No difference	$\rm NHW = Asian > AA$
Mechlin et al. ⁴⁵	106 (AA = 51, NHW/other* = 55)	Healthy adults (range: 18-47)	53	3	Left volar forearm	Contact heat	No difference	NHW/other $>$ AA	
Mechlin et al.44	84 (AA = 45, NHW = 39)	Young healthy adults	51	3	Left volar forearm	Contact heat	No difference	$\rm NHW > AA$	
Morris et al.49	78 (AA = 40, NHW = 38)	Healthy youth (range: 10-17)	51	2	Nondominant ventral forearm	Contact heat			AA > NHW
Riley et al. ⁵⁸	191 (AA = 53, and NHW = 138)	Middle-aged and older adults (range: 45-76)	68	4	Forearms and knee	Contact heat	No difference	NHW > AA	No difference
Rahim-Williams et al. ⁵⁷	206 (AA = 63, Hispanic = 61, and NHW = 82)	Healthy adults	54	4	Ventral forearm	Contact heat	No difference	NHW > AA, Hispanic	
Sheffield et al.62	51 (AA = 24, NHW = 27)	Healthy adults	49	3	Right volar forearm	Contact heat			AA > NHW
Comparing other ethnicities									
Watson et al. ⁶⁸	40 (white British = 20, South Asians = 20)	Working professional males living in the United Kingdom	0	3	Forearms	Contact heat	White British > South Asians		South Asians $>$ white British
Yang et al. ⁷⁰	58 (Chinese = 29, Danes = 29)	University students living in each country	52	3	Bilaterally in the infraorbital and mental foramen	Contact heat	Danes > Chinese		-

* Other included Indian, Asian, and Hispanic.

AA, African American; AA, African American; API, Asian/Pacific Islanders; NHW, non-Hispanic white; OA, osteoarthritis; ROB⁺, risk of bias.

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Table 3									
Studies examinin	g racial/ethnic difference	es in mechanical-pressur	re exp	perimental	pain models.				
Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Comparing AA and									
NHW									
Cruz-Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	63	4	Knee, ipsilateral quadriceps, trapezius, and dorsal forearm	PA	$\rm NHW > AA$ (only knee)		
Glover et al. ²³	94 (AA = 45, NHW = 49)	With symptomatic knee OA, middle-aged and older adults	74	2	Knee and forearm	PA	NHW > AA		
Goodin et al. ²⁶	149 (AA = 28, Asian = 35, NHW = 86)		52	3	Dorsal forearm and ipsilateral trapezius	PA	forearm: no difference, Trapezius: NHW = Asian $>$ AA		
Hastie et al. ³⁰	247 (AA = 81, NHW = 87, Hispanic = 79)	Young healthy adults	52	3	Bilateral upper trapezius, masseter, and ulna	PA	No difference		
Rahim-Williams et al. ⁵⁷	206 (AA = 63, Hispanic = 61, and NHW = 82)	Healthy adults	54	4	Left upper trapezius, left masseter	PA	No difference		
Riley et al. ⁵⁸	191 (AA = 53, and NHW = 138)	Middle-aged and older adults (range: 45-76)	68	4	Medial joint, lateral joint, quadricep, trapezius, epicondyle	PA	No difference		
Lu et al. ⁴²	214 (NHW = 98, Hispanic = 58, AA = 34, and Asian = 24)	Healthy children (range: 8-18)	49	3	Middle and index finger of each hand	Analgesy-Meter		No difference	No difference
Comparing other									
ethnicities									
Alabas et al. ²	175 (Libyan = 124, white British = 51)	Healthy undergraduate students living in each country	50	4	1st interosseous muscle	PA	Libyans $>$ white British		
Al-Harthy et al. ³	244 (Saudis = 41, Swedes =	Female, temporomandibular	100	4	Right masseter and temporalis	PA	Saudis > Swedes	Swedes > Italians	
	41, Italians = 42 for each case/ control group)	disorder case/control			muscle				
Dawson and List ¹⁴	64 (Middle Easterners = 32 , Swedes = 32)	Young healthy adults	50	3	Right masseter muscle	PA	No difference	Swedes > Middle Easterners	
Gazerani and Arendt- Nielsen ²²	32 (South Indians = 16, white European Danes = 16)	Healthy university students living in Denmark	0	1	Forehead	PA (before and after capsaicin)	White European Danes $> {\rm South}$ Indians	Lactoriolo	
Komiyama et al. ³⁸	88 (Belgian = 44, Japanese = 44)	University students and staff living in each country	50	3	Masseter, thenar muscle	PA	Belgian $>$ Japanese	Belgian > Japanese	Belgian > Japanese
Komiyama et al. ³⁹		University students and staff living in each country	50	3	Masseter muscle	PA	No difference	Sapariooo	oapunooo
Yang et al. ⁷⁰		University students living in each country	52	3	Masseter muscle	PA	Danes > Chinese		

AA, African American; NHW, non-Hispanic whites; OA, osteoarthritis; PA, pressure algometer; ROB⁺, risk of bias.

Table 4

Studies examining racial/ethnic differences in mechanical-ischemic experimental pain models.

Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Alabas et al. ²	175 (Libyan = 124, white British = 51)	Healthy undergraduate students living in each country	50	3	1st interosseous muscle	SETT			Libyans > white British
Campbell et al. ¹⁰	135 (AA = 72, NHW = 63)	Young adults	36	3	Dominant upper arm	SETT			AA > NHW
Campbell et al. ⁷	120 (AA = 62, NHW = 58)	Young healthy adults	54	4	Left arm	SETT	No difference	NHW > AA	
Das Gupta et al. ¹³	152 (Malay = 46, Chinese = 62, Indian = 44)	Healthy university students living in Malaysia	55	3	Arm	SETT		No difference	
Edwards et al. ¹⁵	337 (AA = 68, NHW = 269)	Patients with chronic pain	40	3	Arm	SETT		NHW > AA	AA > NHW
Grewen et al. ²⁹	48 (AA = 25, NHW = 23)	Premenopausal women	100	3	Arm	SETT	No difference	No difference	
Hastie et al. ³⁰	247 (AA = 81, NHW = 87, Hispanic = 79)	Young healthy adults	52	3	Arm	SETT	NHW < AA, Hispanics	NHW > AA, Hispanics	
Klatzkin et al. ³⁷	55 (AA = 32, NHW = 23)	Women with or without histories of depression	100	2	Arm	SETT	No difference	NHW > AA	No difference
Mechlin et al. ⁴⁵	106 (AA = 51, NHW/other* = 55)	Healthy adults (18-47)	53	3	Arm	SETT	No difference	NHW/other > AA	
Mechlin et al. ⁴⁴	84 (AA = 45, NHW = 39)	Young healthy adults	51	3	Arm	SETT	No difference	NHW > AA	
Mechlin et al. ⁴³	88 (AA = 44, NHW = 44)	Healthy adults (18-45)	50	3	Arm	SETT	No difference	NHW > AA	No difference
Palit et al. ⁵²	42 (Native Americans = 22, NHW = 20)	Healthy adults	36	3	Arm	SETT	Native Americans > NHW	Native Americans > NHW	
Rahim- Williams et al. ⁵⁷	206 (AA = 63, Hispanic = 61, and NHW = 82)	Healthy adults	54	4	Left arm	SETT	No difference	No difference	

* Other included Indian, Asian, and Hispanic.

AA, African American; EA, East Asian; NHW, non-Hispanic white; ROB⁺, risk of bias; SETT, submaximal effort tourniquet test.

demonstrated higher thresholds than did AAs.^{37,44} In contrast, 10 of 11 studies comparing cold pain tolerance between AAs and NHWs found that NHWs had higher cold pain tolerance than did AAs, except one study reporting no difference.¹⁷ Suprathreshold cold pain ratings were measured during the cold pressure task (eg, at 30-second intervals) or at the end of the task for some studies. Four of 10 studies indicated that there was no racial/ ethnic difference in suprathreshold pain ratings, whereas 5 studies indicated that AAs had higher pain ratings than did NHWs for cold stimuli and one study reported the opposite result.⁴⁷

Regarding other race/ethnic groups, 10 studies included Asians and 3 studies included Hispanics (**Table 1**). Hispanics showed lower tolerance level and higher pain ratings than did NHWs for all 3 studies.^{30,36,57} Results from studies involving Asian groups were more varied. The ethnicity of Asians and comparison groups was diverse across the studies; 4 studies compared Asians, including Chinese or Koreans, with NHWs,^{11,17,61,68} and 3 studies specifically explored Chinese compared with Danes⁷⁰ and with European Canadian.^{33,34} Nayak et al.⁵¹ examined second-generation Americans with various racial/ethnic backgrounds in the United States and compared them with Indians in India, and Dawson and List¹⁴ compared Middle Easterners with Swedes. Four of 6 studies that examined cold pain threshold indicated no difference, and 4 of 6 studies that examined cold pain tolerance indicated that Asians had a lower pain tolerance than did the comparison groups. Three of 5 studies that examined suprathreshold pain ratings reported higher pain ratings in Asians compared with various racial/ethnic groups (mostly Western).

Experimental cold pain stimulation (mostly the cold-pressor task) was the most commonly used method in studies of racial/ ethnic differences in experimental pain sensitivity. Overall, racial/ ethnic minorities had higher sensitivity measured with tolerance and pain ratings compared with NHWs, whereas differences in threshold were only infrequently observed.

3.2.2. Heat pain stimuli

Eighteen studies examined racial/ethnic differences in experimental heat pain (**Table 2**). All of the studies used some form of contact heat with the exception of one study that used radiant heat.⁴² Contact heat stimuli were commonly delivered using a computer-controlled thermode (eg, Medoc Thermal Sensory Analyzer). The sample size of the studies ranged from 40 to 617. Sample characteristics varied, including patients with knee OA,^{12,23–25} women with/without depression history,³⁷ healthy children,⁴² healthy youth,⁴⁹ and middle-aged and older adults.^{12,23–25,58} Sixteen studies compared AAs and NHWs, 10

Studies examining racial/ethnic differences in mechanical cutaneous experimental pain models.

Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Cruz- Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45-85	63	4	Patella and back of the ipsilateral hand	Calibrated nylon monofilament prick			AA > NHW
Goodin et al. ²⁴	225 (AA = 122, NHW = 103)	With knee OA, aged 45 y and older	68	4	Patella and back of the ipsilateral hand	Calibrated nylon monofilament prick			AA > NHW
Komiyama et al. ³⁸	88 (Belgian = 44, Japanese = 44)	University students and staff living in each country	50	3	Cheek skin, Maxillary gingiva, tongue tip, thenar skin	Filament-prick	Belgian > Japanese (cheek, tongue tip and thenar skin)		Belgian > Japanese (Maxillary gingiva)
Komiyama et al. ³⁸	88 (Belgian = 44, Japanese = 44)	University students and staff living in each country	50	3	Cheek skin, maxillary gingiva, tongue tip, thenar skin	Tactile detection	Belgian > Japanese (cheek and thenar skin)	No difference	No difference
Komiyama et al. ³⁹	56 (Belgian = 28, Japanese = 28)	University students and staff living in each country	50	3	Masseter muscle	Tactile detection and filament-prick pain	Belgian > Japanese		
Riley et al. ⁵⁸	191 (AA = 53, and NHW = 138)	Middle-aged and older adults (range: 45-76)	68	4	Patella and the dorsal surface of the hand	Calibrated nylon monofilament punctuate			AA > NHW
Yang et al. ⁷⁰	58 (Chinese = 29, Danes = 29)	University students living in each country	52	3	Bilaterally in the infraorbital and mental foramen	Pinprick stimuli	Danes > Chinese		

AA, African American; NHW, non-Hispanic white; OA, osteoarthritis; ROB⁺, risk of bias.

of which compared heat pain threshold between the 2 groups. Eight of 10 studies indicated no difference in heat pain threshold between AAs and NHWs, whereas 2 studies of patients with OA^{12,23} reported higher thresholds for NHWs vs AAs. Nine of 12 studies reported higher heat pain tolerance in NHWs than AAs. With respect to suprathreshold heat pain ratings, 5 studies showed higher pain ratings in AAs than in NHWs, 2 studies found no difference, and 1 study found a reverse association in children,⁴² indicating higher pain ratings in NHWs than in AAs.

For other race/ethnic groups, 4 studies included Hispanics^{30,36,42,57} and 4 studies included Asians.^{36,42,68,70} No difference was found in heat pain threshold between Hispanics and NHWs,^{30,57} whereas one study reported lower pain tolerance in Hispanics.⁵⁷ For Asians, 2 studies reported that Asians had lower heat pain thresholds than did NHWs.^{68,70} One study evaluated heat pain tolerance and found no difference among AA, Asian, Hispanic, and NHW children.⁴² With respect to supra-threshold heat pain ratings, Asians produced higher pain ratings compared with Hispanics, AAs, and HNWs,³⁶ and compared with white British⁶⁸ and with AAs.⁴²

Heat pain stimulation was the second most commonly used modality in studies of racial/ethnic differences in experimental sensitivity—frequently using contact heat thermodes. Most studies compared AAs and NHWs and reported higher sensitivity in AAs measured by tolerance and pain ratings, but no differences in threshold among healthy participants.

3.3. Mechanical pain

3.3.1. Pressure pain stimuli

Fourteen studies examined racial/ethnic difference in pressure pain sensitivity (**Table 3**). All of the studies used pressure algometry (eg, Medoc/Somedic digital pressure algometer) with the exception of one study that used an analgesy-meter, which is the device often used to perform paw pressure experiments in rodents.⁴² The sample size of the studies ranged from 32 to 267. Studies included young healthy adults, patients with knee OA,^{12,23} healthy children,⁴² females with temporomandibular disorder,³ and middle-aged and older adults.^{12,23,58} Seven studies compared AAs and NHWs, 6 of which measured threshold. Three of 6 studies reported no difference in pressure pain threshold between AAs and NHWs, whereas the other 3 studies found lower thresholds for AAs. Only one study examined pressure pain tolerance and reported no difference among AA, Asian, Hispanic, and NHW children. This study also evaluated pressure pain ratings and found no difference among the groups.⁴²

For other race/ethnic groups, 3 studies included Hispanics^{30,42,57} and 5 studies included Asians.^{25,38,39,42,70} No difference in pressure pain threshold was found between Hispanics and other racial/ethnic groups (AAs and NHWs).^{30,57} For studies of Asian groups, Goodin et al.²⁶ found higher pressure pain threshold in Asians than in AAs. Several studies evaluated pressure pain sensitivity differences between specific ethnic groups. Yang et al.⁷⁰ compared pressure pain threshold between Chinese and Danes and found that Danes had higher threshold than did Chinese. Komiyama et al. compared Japanese with Belgians in 2 studies.^{38,39} Japanese had lower pressure pain threshold and tolerance than did Belgians in one study, but no differences were found for pain threshold in the second study.³⁹ Alabas et al.² examined pressure pain threshold difference between Libyans and white British and found that Libyans had higher threshold than did white British. Gazerani and Arendt-Nielsen²² examined pressure pain threshold before and after capsaicin exposure and found higher pressure pain threshold in white European Danes than in South Indians both before and after capsaicin exposure. Two studies compared Middle Easterners with Swedes^{3,14} and reported mixed results in pressure pain sensitivity.

Studies examining racial/ethnic differences in pressure pain sensitivity commonly used a pressure algometer, and most of the studies measured thresholds. Results were mixed by participant characteristics (eg, patients with OA) and ethnicities.

3.3.2. Ischemic pain stimuli

Thirteen studies examined racial/ethnic differences in experimental ischemic pain (**Table 4**). These studies used the submaximal effort tourniquet test to induce ischemic pain, which induces pain by occluding a participant's arm using a blood pressure cuff. Although most of the participants of the studies were young healthy adults, one study was conducted with women with/ without a history of depression.³⁷ Ten studies compared AAs and NHWs; overall, no differences were found for threshold, whereas lower tolerance levels were found in AAs. Two studies included Hispanics^{30,57} and reported mixed results on differences in ischemic pain sensitivity. Alabas et al.² compared ischemic pain ratings between Libyans and white British and found that Libyans had higher pain ratings than did white British. Palit et al.⁵² compared Native Americans with NHWs and reported higher threshold and tolerance in Native Americans than in NHWs.

3.3.3. Mechanical cutaneous pain stimuli

Seven studies examined racial/ethnic differences in mechanical cutaneous pain (Table 5). The sample size of included studies

ranges from 56 to 267. Mechanical cutaneous pain was induced using nylon monofilament stimulation to evaluate pricking pain threshold or suprathreshold pain ratings. Three studies compared AAs and NHWs^{12,24,58} and reported higher pain ratings in AAs. Komiyama et al.^{38,39} compared Japanese with Belgians, and found that Japanese had lower thresholds than did Belgians. Yang et al.⁷⁰ compared Chinese with Danes and found that Chinese had lower mechanical cutaneous pain threshold using pinprick stimuli than did Danes. Overall, the results from studies using mechanical cutaneous pain stimuli were mixed and sparse, and comparisons were made among particularly diverse ethnic groups.

3.4. Other pain modalities

3.4.1. Chemical pain stimuli

Two studies examined racial/ethnic difference in chemical pain sensitivity using capsaicin (**Table 6**). Gazerani and Arendt-Nielsen²² reported higher postcapsaicin pain ratings in South Indians compared with white European Danes. Wang et al.⁶⁷ studied differences of pain sensitivity among AAs, East Asians, Hispanics, and NHWs, evaluating heat pain threshold and suprathreshold pain ratings after capsaicin exposure. The authors reported that East Asians demonstrated the highest maximum intensity of postcapsaicin burning or pain sensation, followed by Hispanics, NHWs, and AAs; East Asians and Hispanics had significantly higher ratings compared with AAs.

Table 6

Studies examining racial/ethnic differences in chemical and electrical experimental pain models.

Authors	Sample size	Sample characteristics	% (F)	ROB ⁺ (0-4)	Simulation site	Method	Threshold	Tolerance	Ratings
Chemical pain									
Gazerani and Arendt- Nielsen ²²	32 (South Indians = 16, white European Danes = 16)	Healthy university students living in Denmark	0	1	Forehead	Capsaicin injection			South Indians > white European Danes
Wang et al. ⁶⁷	40 (AA = 10, EA = 10, Hispanic = 10, and NHW = 10)	Healthy adults	50	2	forearms	Application of capsaicin	(Pre–post capsaicin changes) NHW, Hispanic > AA		(Postcapsaicin) EA > AA, Hispanic > AA, AA = NHW
Electrical pain									
Al-Harthy et al. ³	244 (Saudis = 41, Swedes = 41, Italians = 42 for each group)	Female with temporomandibular disorder case/control	100	4	Thumb and index fingers on the right hand	Electrical stimulation	Saudis < Swedes, Saudis < Italians	Saudis > Italians, Swedes > Italians	
Campbell et al. ⁸	58 (AA = 29, NHW = 29)	Healthy young adults	55	3	Left biceps femoris muscle	Electrical stimulation	NHW > AA		No difference
Dawson and List ¹⁴	64 (Middle Easterners = 32, Swedes = 32)	Young healthy adults	50	3	Thumb and index finger	Electrical stimulation	No difference	No difference	
Komiyama et al. ³⁹	56 (Belgian $=$ 28, Japanese $=$ 28)	University students and staff living in each country	50	3	Masseter muscle	Electrical stimulation	Belgian > Japanese		
Palit et al. ⁵²	42 (Native Americans = 22, NHW = 20)	Healthy adults	36	3	lpsilateral biceps femoris muscle, popliteal fossa, lateral epicondyle of the femur	Electrical stimulation	Native Americans > NHW	No difference	NHW > Native Americans

AA, African American; EA, East Asian; NHW, non-Hispanic white; SETT, submaximal effort tourniquet test; ROB⁺, risk of bias.

For pre–post capsaicin heat pain threshold changes, significant decreases were found in NHWs, East Asians, and Hispanics but not in AAs, and the magnitude of changes was greater in NHWs and Hispanics than in AAs.⁶⁷

3.4.2. Electrical pain stimuli

Five studies examined racial/ethnic differences in electrical pain (**Table 6**). Electrical pain was induced using a constantcurrent stimulator. Campbell et al.⁸ reported that AAs demonstrated lower electrical pain threshold than did NHWs, and Komiyama et al.³⁹ reported that the Japanese demonstrated lower electrical pain threshold than did Belgians. Palit et al.⁵² reported higher electrical pain thresholds for Native Americans compared with NHWs, whereas no difference was found in tolerance. Native Americans produced lower pain ratings than did NHWs for constant-current electrical stimuli.⁵² Al-Harthy et al.³ and Dawson and List¹⁴ compared electrical pain threshold and tolerance among Saudis, Swedes, and Italians, and reported mixed results.

3.5. Pain unpleasantness

Eleven studies examined racial/ethnic differences in pain unpleasantness (**Table 7**). Most of the studies evoked cold pain using the cold-pressor task, and measured pain unpleasantness using a visual analogue scale. Greater pain unpleasantness was reported in AAs compared with NHWs in studies of healthy young adults,^{7,10,30,69} whereas no differences was found in other studies.^{19,43,58} One study of elderly adults with knee OA reported greater unpleasantness in AA compared with NHW.¹² In contrast, another study of healthy children reported greater unpleasantness in NHWs than in AAs and Hispanics. Alabas et al.² used pressure and ischemic pain and found that Libyans reported higher unpleasantness for pressure pain compared with British, but no difference for ischemic pain.

3.6. Temporal summation of pain

Seven studies examined racial/ethnic differences in TS of pain (**Table 8**). Brief painful pain stimuli are repetitively delivered to the skin at intervals at or less than 3 seconds. A gradual increase in subjective pain ratings is characteristic of temporal response to repetitive noxious stimuli, and this has been documented using many different stimulus modalities. Temporal summation reflects central nervous system temporal integration processes (often termed "wind-up") and is associated with C-fiber input (eg, second pain) more so than with A-delta fiber input (eg, first pain). Accordingly, TS of pain is commonly used to evaluate central nociception processing.¹⁸ Overall, AAs demonstrated higher TS than did NHWs.^{12,24,43,58} One study reported lower TS for healthy AA youth compared with NHW youth.⁴⁹ Yang et al.⁷⁰ found that

Table 7

Studies examining racial/ethnic differences in pain unpleasantness.

Authors	Sample size	Sample characteristics	Pain stimuli	Method	Results
Alabas et al. ²	175 (Libyan = 124, white British = 51)	Healthy undergraduate students living in each country	Pressure and ischemic pain	VAS (0-100 mm)	Libyans > British for Pressure pain, no differences in Ischemic pain
Campbell et al. ⁷	120 (AA = 62, NHW = 58)	Young healthy adults	Cold pain	0-20 box scales	AA > NHW
Campbell et al. ¹⁰	135 (AA = 72, NHW = 63)	Young adults	Ischemic pain	Standard VRS and Individualized VRS cards (unpleasant descriptors ordered from the least score of 1 to most severe- score of 13)	AA> NHW for Standard verbal rating scale, No difference for individualized verbal rating scale
Chan et al. ¹¹	57 (FAA = 12, SAA = 21, EA = 24)	Undergraduate students living in the United States	Cold pain	VAS (15 cm long)	No difference
Cruz- Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	Cold pain	Verbal rating (0-100)	AA > NHW (at 16 and 12°C, no difference at 8°C)
Forsythe et al. ¹⁹	155 (AA = 60, NHW = 95)	Healthy undergraduate students	Cold pain	VAS (10 cm)	No difference
Hastie et al. ³⁰	247 (AA = 81, NHW = 87, Hispanic = 79)	Young healthy adults	Cold pain	0-100 box scale	AA, Hispanic $>$ NHW
Lu et al. ⁴²	214 (NHW = 98, Hispanic = 58, AA = 34, and Asian = 24)	Healthy children (range: 8-18)	Heat and pressure pain	VAS (10 cm)	$\begin{array}{l} \mbox{Hispanic} < \mbox{NHW} = \mbox{Asian for} \\ \mbox{pressure pain, AA} < \mbox{NHW} = \\ \mbox{Asian for Heat pain} \end{array}$
Mechlin et al. ⁴³	88 (AA = 44, NHW = 44)	Healthy adults (18-45)	Cold pain and ischemic pain	VAS (0-100)	No difference
Riley et al. ⁵⁸	191 (NHB = 53, and NHW = 138)	Middle-aged and older adults (range: 45-76)	Cold pain	A scale from 0 to 100	No difference
Weisse et al. ⁶⁹	290 (NHW = 193, AA = 97)	Healthy undergraduate students	Cold pain	Gracely box scale (numeric 0–20 rating scale: neutral to very intolerable)	AA > NHW

AA, African American; CPT, cold-pressor task; EA, European American; FAA, first-generation Asian American; NHW, non-Hispanic white; OA, osteoarthritis; SAA, second-generation Asian American; VAS, visual analogue scale; VRS, verbal rating scale.

Table 8

Studies examining racial/ethnic differences in experimental pain models of temporal summation.

uthors	Sample size	Sample characteristics	Stimulation site	Method	Summation
Cruz-Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	Knee and forearm	Contact heat	AA > NHW
Cruz-Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	Knee, ipsilateral quadricepts, trapezius, and dorsal forearm	Pressure algometer	AA > NHW
Goodin et al. ²⁴	225 (AA = 122, NHW = 103)	With knee OA, aged 45 y and older	Index knee and ipsilateral volar forearm	Contact heat	AA > NHW
Goodin et al. ²⁴	225 (AA = 122, NHW = 103)	With knee OA, aged 45 y and older	Patella and back of the ipsilateral hand	Calibrated nylon monofilament prick	AA > NHW
Mechlin et al. ⁴³	88 (AA = 44, NHW = 44)	Healthy adults (18-45)	Palm	Contact heat	AA > NHW
Morris et al.49	78 (AA = 40, NHW = 38)	Healthy youth (range: 10-17)	Forearms	Contact heat	AA < NHW
Palit et al. ⁵²	42 (Native Americans = 22, $NHW = 20$)	Healthy adults	Arm	Submaximal effort tourniquet test	No difference
Riley et al. ⁵⁸	191 (AA = 53, NHW = 138)	Middle-aged and older adults (range: 45-76)	Forearms	Contact heat	No difference
Riley et al. ⁵⁸	191 (AA = 53, NHW = 138)	Middle-aged and older adults (range: 45-76)	Knee	Contact heat	AA > NHW
Riley et al. ⁵⁸	191 (AA = 53, NHW = 138)	Middle-aged and older adults (range: 45-76)	Medial joint, lateral joint, quadricep, trapezius, epicondyle	Pressure algometer	${ m AA}>{ m NHW}$ (Knee and Hand)
Yang et al. ⁷⁰	58 (Chinese = 29, Danes = 29)	University students living in each country	Bilaterally in the infraorbital and mental foramen	Pinprick stimuli	Danes > Chinese

AA, African American; NHW, non-Hispanic white; OA, osteoarthritis.

Danes showed higher TS than did Chinese. Another study did not show TS differences between Native Americans and $\rm NHWs.^{52}$

3.7. Conditioned pain modulation

Six studies compared racial/ethnic differences in CPM (Table 9). Conditioned pain modulation refers to reduced pain intensity perception for a test stimulus when also exposed to a painful conditioning stimulus.⁵⁰ Conditioned pain modulation is believed to reflect descending endogenous pain-inhibitory processes, initially called "diffuse noxious inhibitory control," serving to reduce nociceptive signaling originating from elsewhere on the body.⁵³ Diminished CPM was reported for AAs compared with NHWs in one study of healthy adults,⁹ whereas another study reported no

Table 9

uthors	Sample size	Sample characteristics	Stimulation site	Method	Conditioning stimulus	Conditioned pain modulation
Campbell et al. ⁹	57 (AA = 29, NHW = 28)	Healthy young adults	Right arm	Electric pain	Submaximal effort tourniquet procedure	Greater reductions in pain ratings in NHWs compared with AAs
Cruz-Almeida et al. ¹²	267 (AA = 120, NHW = 147)	With knee OA, aged from 45 to 85	Left ventral forearm	Contact heat	Cold water immersion	No significant changes (pre–post) in NHWs, significan increase in pain ratings in AA
Goodin et al. ²⁶	149 (AA = 28, Asian = 35, NHW = 86)	Healthy young adults	Left dorsal forearm or left trapezius	Pressure algometer	Cold water immersion	Significant reductions in pain ratings; No significant difference in CPM effect across ethnic groups
Morris et al. ⁵⁰	78 (AA = 40, NHW = 38)	Healthy youth (range: 10- 17)	Nondominant forearm	Contact heat	Hot water immersion	Greater reductions in pain ratings in AAs than NHWs
Palit et al. ⁵³	88 (AA = 44, NHW = 44)	Healthy adults (18-45)	Left ankle	Electric pain	Picture viewing (mutilation, neutral, and erotic)	NHWs: pain inhibition by erotica and pain facilitation by mutilation; Native Americans: pain inhibition by erotica, no disinhibition by mutilation
Riley et al. ⁵⁸	191 (AA = 53, NHW = 138)	Middle-aged and older adults (range: 45-76)	Left forearm	Contact heat	Cold water immersion	No significant effect of the CPN manipulation in both groups

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Overall (I-squared = 83.3%, p = 0.000)		2013	58	-0.85 (-1.39, -0.32)	
	Subtotal (I-squared = 83.5%, p = 0.000)			-0.03 (-0.28, 0.22)	26.54
NOTE: Weights are from random effects analysis	Overall (I-squared = 83.3%, p = 0.000)			-0.06 (-0.19, 0.07)	100.00
	IOTE: Weights are from random effects analysis				

Figure 2. Meta-analysis on racial/ethnic differences in pain threshold between African Americans and non-Hispanic whites. *Studies with older patients with knee osteoarthritis, **studies with patients with chronic pain, *** studies with older adults.

racial/ethnic differences in CPM in healthy young adults.²⁶ Recently, increased CPM in healthy AA youth compared with NHW youth was reported.⁵⁰ A study of CPM among old adults with knee OA reported a significant increase in pain ratings in AAs—pain facilitation, whereas no significant changes were observed in NHWs.¹² No significant effect of CPM was reported in one study of middle-aged and older AA and NHW adults.⁵⁸ Palit et al.⁵³ examined emotional modulation of pain, and found pain inhibition by erotic picture viewing in both healthy young Native Americans and NHWs. Pain

facilitation by mutilation was found in NHWs, but not in Native Americans. Overall, the findings of racial/ethnic differences in CPM are inconsistent, and it is difficult to draw conclusions regarding the existence of racial/ethnic differences in CPM.

3.8. Quantitative synthesis/meta-analysis

Thirty-three studies that examined differences in experimental pain sensitivity were included in the meta-analysis (Fig. 1). The pooled

SMDs of tolerance, threshold, and pain ratings were estimated by pain modality. Some studies used in the qualitative analysis were omitted from the quantitative analysis as follows: 8 studies were excluded because of insufficient quantitative information in the original article.^{9,13,37,49,50,53,61,62} One study was excluded because it included NHW, Asian, and Hispanic in one group.⁴⁵ Two studies were excluded because their specialized study characteristics (children sample, chemical pain stimulation) made it difficult to conduct subgroup analyses.^{42,67} The Egger test revealed no significant publication bias in the threshold (Egger bias = 0.723, 95% CI = -1.406 to 2.852, P = 0.499), tolerance (Egger bias = -2.25, 95% CI = -4.818 to 0.327, P = 0.085), and pain rating (Egger bias = 2.630, 95% CI = -0.114 to 5.375, P = 0.060) analyses.

In general, the SMDs for threshold were small and not significant (**Fig. 2**, overall SMD = -0.06, 95% Cl = -0.19 to 0.07). The overall effect size of pain tolerance between AAs and NHWs was statistically

significant (SMD = -0.64, 95% CI = -0.80 to -0.48) with high heterogeneity (l^2 = 86.5%). The meta-analytic SMDs for tolerance of each modality (cold pain, heat pain, and ischemic pain) were large and statistically significant individually, whereas SMDs for electrical and pressure pain were not significant (**Fig. 3**). For suprathreshold pain ratings, the individual modality SMDs were medium to large and statistically significant, except in the case of electrical pain (**Fig. 4**, overall SMD = 0.46, 95% CI = 0.30–0.61). In addition, we calculated a pooled SMD for pain unpleasantness, and the results revealed a significant medium effect size for pain unpleasantness as shown in **Figure 5** (SMD = 0.37, 95% CI = 0.19–0.54).

3.9. Sensitivity and subgroup analyses

The sensitivity analyses results (**Table 10**, top) were comparable to the primary analyses results, with both analyses indicating

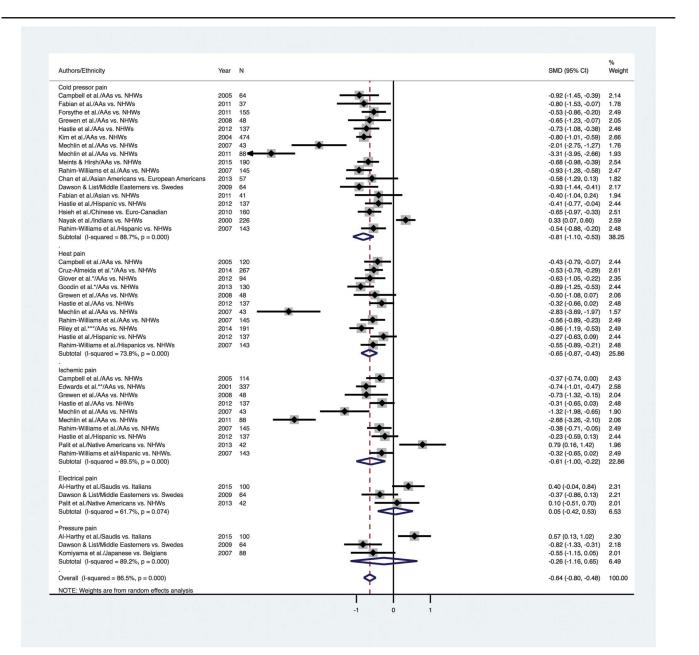


Figure 3. Meta-analysis on racial/ethnic differences in pain tolerance between African Americans and non-Hispanic whites. *Studies with older patients with knee osteoarthritis, **studies with patients with chronic pain, *** studies with older adults.

Authors/Ethnicity	Year		SMD (95% CI)	% Weigh
Cold pain		I		
Chan et al./Asian Americans vs. European Americans	2013	1	1.10 (0.36, 1.84)	2.18
Cruz-Almeida et al.*/AAs vs. NHWs	2014		0.22 (-0.02, 0.47)	4.02
abian et al./AAs vs. NHWs	2011		0.97 (0.23, 1.71)	2.17
abian et al./Asian vs. NHWs	2011		1.04 (0.36, 1.71)	2.38
Forsythe et al./AAs vs. NHWs	2011		0.29 (-0.03, 0.62)	3.72
lastie et al./AAs vs. NHWs	2012		0.45 (0.11, 0.79)	3.66
lastie et al./Hispanic vs. NHWs	2012		0.49 (0.12, 0.85)	3.56
lsieh et al./Chinese vs. Euro-Canadian	2010		0.41 (0.10, 0.73)	3.76
sieh et al./Chinese vs. Euro-Canadian	2011		0.94 (0.57, 1.30)	3.56
Kim et al./AAs vs. NHWs	2004	·	0.46 (0.26, 0.66)	4.14
lechlin et al./AAs vs. NHWs	2011	ī	1.43 (0.96, 1.90)	3.14
leints & Hirsh/AAs vs. NHWs	2015	i	-0.34 (-0.63, -0.05)	3.85
Riley et al.***/AAs vs. NHWs	2014		0.26 (-0.06, 0.58)	3.74
Veisse et al./AAs vs. NHWs	2005		0.67 (0.30, 1.04)	3.55
Subtotal (I-squared = 80.4%, p = 0.000)		\diamond	0.54 (0.32, 0.75)	47.42
Electrical pain				
Campbell et al./AAs vs. NHWs	2008		-0.21 (-0.75, 0.33)	2.86
Palit et al./Native Americans vs. NHWs	2013		-0.81 (-1.44, -0.18)	2.53
Subtotal (I-squared = 50.5%, p = 0.155)			-0.49 (-1.07, 0.10)	5.39
leat pain				
Campbell et al./AAs vs. NHWs	2005		0.72 (0.35, 1.10)	3.53
Goodin et al.*/AAs vs. NHWs	2014		0.41 (0.15, 0.68)	3.94
lastie et al./AAs vs. NHWs	2012		0.06 (-0.28, 0.39)	3.67
lastie et al./Hispanic vs. NHWs	2012		0.20 (-0.16, 0.56)	3.58
Kim et al./AAs vs. NHWs	2004		-0.04 (-0.24, 0.16)	4.15
Riley et al./AAs vs. NHWs	2014		0.13 (-0.18, 0.45)	3.75
Subtotal (I-squared = 69.4%, p = 0.006)		\diamond	0.23 (0.01, 0.45)	22.61
schemic pain				
Alabas et al./Libyans vs. White British	2013		0.82 (0.34, 1.29)	3.12
Campbell et al./AAs vs. NHWs	2004		0.28 (-0.25, 0.82)	2.88
Edwards et al.**/AAs vs. NHWs	2001		0.28 (0.01, 0.55)	3.93
lechlin et al./AAs vs. NHWs	2011		1.94 (1.44, 2.45)	2.98
Subtotal (I-squared = 91.3%, p = 0.000)			0.82 (0.09, 1.55)	12.92
Nechanical cutaneous Pain		<u>i</u>		
Cruz-Almeida et al.*/AAs vs. NHWs	2014		0.50 (0.26, 0.75)	4.01
Goodin et al.*/AAs vs. NHWs	2014		0.49 (0.23, 0.76)	3.94
Riley et al.***/AAs vs. NHWs	2014	-	0.80 (0.47, 1.13)	3.71
Subtotal (I-squared = 19.1%, p = 0.290)			0.57 (0.40, 0.75)	11.65
Overall (I-squared = 82.6%, p = 0.000)			0.46 (0.30, 0.61)	100.00
NOTE: Weights are from random effects analysis				
		-1 0	1	

Figure 4. Meta-analysis on racial/ethnic differences in pain intensity ratings between African Americans and non-Hispanic whites. *Studies with older patients with knee osteoarthritis, **studies with patients with chronic pain, *** studies with older adults.

significant effect sizes for tolerance and pain ratings, but a nonsignificant effect size for threshold. Regarding the subgroup analyses, the SMDs did not differ statistically by the percentage of women, sample characteristics (young healthy adults vs patients with chronic pain), or pain modality. Accordingly, subgroup effects based on sex, sample characteristics, and pain modalities did not explain the high heterogeneity found in the primary analysis. However, the SMDs of tolerance and pain ratings were significantly larger for studies with a small sample size (n < 100) compared with studies with a larger sample size (n \ge 100). The SMD of tolerance in AAs was significantly larger than in Asians and other ethnic groups.

4. Discussion

This study provides an update on racial/ethnic differences in experimental pain sensitivity by incorporating the most recent literature. Reviewed studies examined racial/ethnic differences in experimental pain sensitivity using various types of stimulus modalities with multiple pain sensitivity measures. Overall, we found that racial/ethnic minorities had higher pain sensitivity compared with NHWs, specifically showing lower pain tolerance, higher pain intensity and unpleasantness ratings, and greater TS of pain, regardless of stimulus modality. This analysis is generally consistent with that previously been reported regarding racial/ ethnic differences in pain sensitivity.⁵⁶ This study adds to the literature by providing analyses that allow for a quantitative comparison of racial/ethnic differences across various stimulus modalities and pain measures.

The meta-analysis of studies comparing AAs and NHWs found large estimated SMDs for pain tolerance, moderate to large SMDs for suprathreshold pain intensity ratings and unpleasantness, but no significant pooled SMDs in pain threshold. A previous review on racial/ethnic differences in experimental pain sensitivity also indicated that the effect sizes were consistently moderate to large for pain tolerance but small to moderate for pain threshold, whereas limited data were available for suprathreshold pain ratings.⁵⁶ The current review found medium to large effect sizes not only for tolerance but for both suprathreshold intensity and unpleasantness ratings. These results

uthors	Year	Ν	SMD (95%	% 6 Cl) Weight
old pain				
han et al.	2013	36	0.59 (-0.12	2, 1.30) 4.47
ruz-Almeida et al.*	2014	267	0.21 (-0.03	3, 0.45) 12.68
orsythe et al.	2011	155	0.21 (-0.11	1, 0.53) 10.62
lastie et al.	2012	137	0.47 (0.13	, 0.81) 10.22
lastie et al.	2012	119	0.56 (0.20	, 0.93) 9.63
lechlin et al.	2011	88	• 1.08 (0.63	, 1.53) 7.96
Veisse et al.	2005	129	-0.00 (-0.3	6, 0.35) 9.81
ubtotal (I-squared = 6	67.0%, p =	0.006)	0.41 (0.17	, 0.65) 65.39
leat pain				
ampbell et al.	2005	118	0.63 (0.26	, 1.00) 9.56
iley et al.***	2014	191	0.26 (-0.06	6, 0.58) 10.77
ubtotal (I-squared = 5	5.7%, p =	0.133)	0.43 (0.07	, 0.80) 20.33
schemic pain				
labas et al.	2013	88	0.28 (-0.18	3, 0.74) 7.74
ampbell et al.	2004	59	-0.08 (-0.6	61, 0.45) 6.53
ubtotal (I-squared = 0	0.0%, p = 0	.318)	0.13 (-0.22	2, 0.47) 14.28
verall (I-squared = 57	7.1%, p = 0	.010)	0.37 (0.19	, 0.54) 100.00
075 11/1				
OTE: Weights are from	m random	effects analysis		

Figure 5. Meta-analysis on racial/ethnic differences in pain unpleasantness ratings between African Americans and non-Hispanic whites. *Studies with older patients with knee osteoarthritis, **studies with patients with chronic pain, *** studies with older adults.

suggest that racial/ethnic differences in experimental pain sensitivity are more pronounced in suprathreshold pain experiences than in thresholds. This may be important because suprathreshold pain measures have been reported to be among the most relevant experimental pain tasks to clinical pain.^{7,15}

Greater experimental pain sensitivity among females compared with males has been frequently reported.²⁸ Enhanced experimental pain sensitivity in patients with chronic pain has also been reported.^{40,55} Subgroup analyses in the current report revealed that racial/ethnic differences did not vary significantly according to sex or sample characteristics (healthy adults vs patients with chronic pain). In regard to experimental pain modality, one study documented that racial/ethnic differences in cold pain responses were more prominent than in heat pain.³⁶ Al-Harthy et al.³ also reported that mechanical pain responses differed more than did electrical pain responses among different race/ethnic groups. However, the results of this study suggest that racial/ethnic differences in experimental pain sensitivity are more frequently found across multiple pain modalities than within a single modality.

In our analyses, there was a variance in racial/ethnic differences by ethnicity, specifically for tolerance. For example, the SMD for comparing AAs and NHWs was significantly higher compared with those of Asians or other ethnic groups vs NHWs. It is difficult to draw a conclusion because the majority of the studies found in this review compared AAs and NHWs, and there were relatively few studies of other ethnic groups, including Asians and Hispanics. More studies are needed in these racial/ethnic groups to test the variance in subgroup racial/ethnic differences in experimental pain sensitivity.

Sample size was another significant factor in subgroup differences of the pooled SMDs of tolerance and pain intensity rating, indicating that small studies reported large effects. This result could be partially explained by publication bias. Publication bias is more frequent in small-sample studies than in large sample studies because a small study that does not demonstrate significant effects is unlikely to be published.⁶³

We included racial/ethnic differences in dynamic responses to experimental pain stimulation, which were measured by TS and CPM. In addition to the racial/ethnic differences in basal pain sensitivity, our analysis revealed that AAs exhibited higher TS among patients with OA, ¹² young healthy adults, ⁴³ and elderly, ⁵⁸ suggesting an upregulated central nociceptive processing system among AAs than among NHWs. Deficient pain inhibition has been reported as a significant predictor of the severity of clinical pain, which supports that pain modulation capacity has an important role in chronic pain.¹² Although reduced pain-inhibitory function, measured by CPM, has been suggested as a potential Table 10

Subgroup and sensitivity analyses of the selected studies on racial/ethnic differences in experimental pain sensitivity.

	Tolerance		Threshold		Pain intensity rating	
	SMD (95% CI)	Sig,* P	SMD (95% CI)	Sig*	SMD (95% CI)	Sig*
Primary analysis	-0.64 (-0.80 to -0.48)		-0.06 (-0.19 to 0.07)		0.46 (0.30 to 0.61)	
Sensitivity analysis						
Excluding studies of no definition of race/ethnicity	-0.45 (-0.59 to -0.31)		-0.05 (-0.18 to 0.08)		0.38 (0.25 to 0.51)	
Subgroup analysis						
% of women		0.446		0.751		0.594
Ethnicity						
AAs vs NHWs	-0.90 (-1.10 to -0.70)	Ref. group	0.08 (-0.24 to 0.08)	Ref. group	0.44 (0.26 to 0.61)	Ref. group
Asians vs NHWs	-0.34 (-0.85 to 0.17)	0.010	-0.25 (-0.62 to 0.11)	0.786	0.80 (0.44 to 1.16)	0.422
Hispanics vs NHWs	-0.39 (-0.53 to -0.26)	0.323	-0.06 (-0.18 to 0.07)	0.776	0.34 (0.06 to 0.62)	0.792
Others vs NHWs	-0.04 (-0.54 to 0.46)	0.006	0.31 (-0.34 to 0.97)	0.077	0.02 (-1.58 to 1.61)	0.306
Sample size						
<100	-0.99 (-1.41 to -0.57)	0.001	-0.08 (-0.37 to 0.21)	0.947	0.72 (0.06 to 1.37)	0.004
≥100	-0.44 (-0.58 to -0.30)		-0.06 (-0.19 to 0.07)		0.38 (0.25 to 0.50)	
Sample characteristics						
Young healthy adults	-0.64 (-0.82 to -0.45)	0.862	-0.03 (-0.18 to 0.11)	0.417	0.48 (0.28 to 0.68)	0.478
Patients with chronic pain	-0.67 (-0.82 to -0.52)		-0.33 (-0.54 to -0.13)		0.38 (0.27 to 0.49)	
Pain modality						
Cold pain	-0.81 (-1.10 to -0.53)	Ref. group	-0.00 (-0.22 to 0.22)	Ref. group	0.54 (0.32 to 0.75)	Ref. group
Electrical pain	0.05 (-0.42 to 0.53)	0.954	-0.31 (-0.93 to 0.30)	0.085	-0.49 (-1.07 to 0.10)	0.030
Heat pain	-0.65 (-0.87 to -0.43)	0.449	-0.25 (-0.51 to 0.01)	0.406	0.23 (0.01 to 0.45)	0.703
Ischemic pain	-0.61 (-1.00 to -0.22)	0.230	0.33 (-0.07 to 0.73)	0.284	0.82 (0.09 to 1.55)	0.131
Pressure pain	-0.26 (-1.16 to 0.65)	0.669	-0.03 (-0.28 to 0.22)	0.815		
Mechanical cutaneous pain			-0.64 (-1.00 to -0.29)	0.216	0.46 (0.30 to 0.61)	0.195

* Random-effects meta-regression models (with 95% confidence interval [CIs]) were conducted to explore the subgroup differences (DerSimonian and Laird).

AA, African American; NHW, non-Hispanic white; SMD, standardized mean difference.

contributing factor to the racial/ethnic differences in clinical pain response,⁹ the evidence found in current review in this regard is sparse and inconclusive. Future research is needed to address how these pain modulatory systems differ across racial/ethnic groups and affect clinical pain response.

Several limitations in this review, and its component studies, should be noted. First, the results of the present analyses are likely influenced by several methodological limitations of the reviewed studies. Most of the studies recruited a "convenience sample" rather than a systematic representation of a population. For example, several studies recruited participants from a university campus or from clinics. Heterogeneity of Asian populations, including the countries of the participants, was relatively high. For example, some studies included people with origins from many different Asian countries with no distinction, whereas others recruited only Asians with specific backgrounds. Similar inconsistent recruitment is also a limitation for the studies examining differences between Hispanic and non-Hispanic groups. Furthermore, experimenter characteristics and language proficiency of both participants and experimenter could influence the results of these studies. Finally, although most of the studies included age and sex as confounding factors in their study, socioeconomic factors (eg, education and income) were not considered in most of the studies.

Second, heterogeneity across the studies was considerably high, and the samples were diverse in age and context. As noted above, the characteristics of the "Asian" and "Hispanic" cohorts could vary greatly across studies. Furthermore, some studies compared ethnic groups with Asians living in their home country, whereas most recruited those living locally, usually either in the United States or Europe. For studies conducted in the United States or Europe, there was typically no distinction made between first-generation or later-generation AAs, Asians, or Hispanics, which could have a large impact upon study results because of cultural factors. $^{11,51}\,$

5. Conclusions

We have systematically reviewed the scientific literature addressing racial and ethnic differences in experimental pain sensitivity. Our review included studies using various types of stimulus modalities and pain measures. Despite considerable heterogeneity across studies, racial/ethnic minorities generally showed higher pain sensitivity compared with NHWs. Racial/ethnic minorities commonly had lower pain tolerance and higher pain ratings across all pain modalities; however, differences in pain threshold were most often statistically not significant. Given the reported relationship between experimental pain sensitivity and clinical pain severity, health care providers who serve multiple racial/ethnic groups should consider these differences when they implement pain management programs. Further research is required to identify the biopsychosocial factors underlying racial/ ethnic differences in pain sensitivity, specifically for the lessstudied Asians and Hispanics in the United States. Researchers should consider the methodological challenges found in the studies when they plan studies that include considerations of racial/ethnic differences in pain sensitivity.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

Appendix A. Supplemental Digital Content

Supplemental Digital Content associated with this article can be found online at http://links.lww.com/PAIN/A351.

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