

Thermal and mechanical quantitative sensory testing values among healthy African American adults

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Keesha L Powell-Roach¹
Yingwei Yao²
Julienne N Rutherford³
Judith M Schlaeger³
Crystal L Patil³
Marie L Suarez⁴
David Shuey⁴
Veronica Angulo⁴
Jesus Carrasco⁴
Miriam O Ezenwa²
Roger B Fillingim¹
Zaijie J Wang⁵
Robert E Molokie⁵⁻⁷
Diana J Wilkie^{1,2}

¹Department of Community Dentistry and Behavioral Science, College of Dentistry, University of Florida, Gainesville, FL, USA;

²Department of Biobehavioral Nursing Science, College of Nursing, University of Florida, Gainesville, FL, USA; ³Department of Women, Children and Family Health Science, College of Nursing, University of Illinois at Chicago, Chicago, IL, USA;

⁴Department of Biobehavioral Health Science, College of Nursing, University of Illinois at Chicago, Chicago, IL, USA;

⁵Department of Biopharmaceutical Sciences, College of Pharmacy, Cancer Center, University of Illinois at Chicago, Chicago, IL, USA; ⁶Division of Hematology/Oncology, University of Illinois at Chicago College of Medicine, Chicago, IL, USA;

⁷Department of Hematology/Oncology, Jessie Brown Veteran's Administration Medical Center, Chicago, IL, USA

Correspondence: Keesha L Powell-Roach
Department of Community Dentistry and Behavioral Science, College of Dentistry, University of Florida, 2004 Mowry Drive, P.O. Box 100404, Gainesville, FL 32610, USA
Tel +1 312 952 1317
Email keesharoach@ufl.edu

Purpose: Only a few studies have reported quantitative sensory testing (QST) reference values for healthy African Americans, and those studies are limited in sample size and age of participants. The study purpose was to characterize QST values in healthy, pain-free African American adults and older adults whose prior pain experiences and psychological status were also measured. We examined the QST values for differences by sex, age, and body test site.

Patients and methods: A cross-sectional sample of 124 pain-free African American adults (age 18–69 years, 49% female) completed demographic and self-reported pain, fatigue and psychosocial measures. QST was performed to obtain thermal and mechanical responses and associated pain intensity levels.

Results: We found thermal detection values at the anterior forearm were (29.2 °C±1.6) for cool detection (CD) and (34.5 °C±1.2) for warm detection (WD). At that site the sample had cold pain threshold (CPT_h) (26.3 °C±5.0), heat pain threshold (HPT_h) (37.8 °C±3.6), and mechanical pain thresholds (MPT_h) (16.7±22.2 grams of force, gF). There was a significant between sex difference for WD, with women being more sensitive ($q=0.027$). Lower body sites were less sensitive than upper body sites across all thermal modalities ($q<0.003$), but not for the mechanical modality.

Conclusion: The QST values from this protocol at the anterior forearm indicate that the healthy African American adults had average thermal pain thresholds close to the temperature of adaptation and average MPT_h under 20 gF. Differences in responses to thermal and mechanical stimuli for upper versus lower body were consistent with prior research.

Keywords: quantitative sensory testing, QST, PROMIS, pain, healthy, African Americans

Introduction

Studies of quantitative sensory testing (QST) in sickle cell disease (SCD) showed that adequate reference values for patients' commonly reported pain sites are unavailable from healthy pain free African Americans, which limits interpretation of results.¹⁻⁵ Most studies of healthy African Americans include QST values for the anterior forearm, but patients with SCD report pain at sites all over their bodies. Furthermore, in contrast to the demographics of patients with SCD,⁶⁻⁹ most previous QST studies of healthy African American adults were based on relatively small samples¹⁰ of primarily young adults^{2,5,11} and their past pain experiences or psychological status were not reported. Although a few studies included older adults,^{5,12-14} none included sampling plans balanced by age and sex. The lack of sufficient QST data for healthy African American adults, especially older adults, is

a barrier to research needed to inform healthcare professionals who treat pain and other somatosensory disorders in this population. The purpose of our study was to address this gap by characterizing thermal and mechanical QST values in a sample of healthy African American adults whose prior pain experiences and psychological status were also documented.

Racial and ethnic disparities are pervasive in health care.¹⁵ Unrelieved pain among African Americans leads to unnecessary suffering, delayed healing, functional disability, increased length of hospital stays, and lost school and work days.^{16–18} Complicating the problem are the racial and ethnic differences in individual responses to pain.^{4,6,10,19–21} These differences are often misunderstood by health care providers because it is not known how healthy African American adults and older adults respond to standardized painful stimuli.^{15,17,22,23} To understand more fully the physiology of pain in African Americans and to develop personalized treatment plans, accurate QST values are needed from healthy African Americans whose past pain experiences and psychological status are documented.

QST values for healthy adults differ among race, ethnic groups, age, sex, body location and psychological status.^{3,4,24} African Americans are generally more sensitive to thermal heat than Non-Hispanic Whites (NHW) and Asians.^{3,5,6,19,25–27} Older adults typically show decreased sensitivity to brief, cutaneous pain stimuli but increased sensitivity to tonic, deep pain stimuli.^{9,19,28–30} Men generally have a higher pain threshold than women.^{26,31–33} Compared to lower body sites, upper sites are more sensitive to thermal and mechanical stimuli.^{33,34} Fatigue, anxiety and depression typically are associated with increased reports of pain.^{35–38} Most studies of healthy African Americans included college students and siblings of SCD patients with unknown trait status. **Table 1** shows that few were balanced by sex and age, and most tested only the anterior forearm. None of these studies included past pain experience or psychological status. Therefore, examination of these factors in a larger sample is needed to support QST research in pain conditions experienced by African Americans, such as SCD.

The intent of our study was to fill a gap in the literature regarding QST values for healthy African American adults that will contribute to understanding of pain and somatosensory function in African Americans. In a large cohort

of pain-free, healthy African American adults whose past pain experiences and current psychological status were known, our study aim was to determine thermal and mechanical QST values and compare those values at the anterior forearm by age and sex. We also determined the values for 5 other body sites and compared the values for differences by testing site location (upper body versus lower body).

Materials and methods

Design and participants

This cross-sectional study was approved by the Institutional Review Boards at the University of Illinois at Chicago (UIC) and University of Florida. All participants provided written informed consent. This study was conducted in accordance with the Declaration of Helsinki. This sample was intended to serve as the age-, sex- and site-matched controls for a QST study in a sample of individuals with SCD, whose proclivity for acute vaso-occlusive episodes necessitated a protocol focused on stimuli that a pilot study demonstrated was safe.⁷

Recruitment efforts focused on obtaining equal numbers of males and females and equal numbers of younger adults and older adults. Once the quota was filled for an age/sex group, recruitment for that group ended. The participants were healthy, pain-free adults who self-identified their race as Black/African American at a screening interview and via the demographic questionnaire. All participants verbally reported their race during initial screening. They also reported race and ethnicity in the demographic questionnaire. If they reported Black/African American during screening and in the questionnaire, their data were used in the analysis. Per NIH guidelines, we documented both race and ethnicity. Therefore, individuals who reported race as Black/African American and ethnicity as Hispanic were included. Other inclusion criteria were: English fluency in speaking and reading and age ≥ 18 years. Exclusion criteria included: diabetes mellitus, polyneuropathy, hypertension, SCD, cancer, history of chronic pain, being legally blind, inability to complete study measures, use of prescription pain medications or recreational drugs, and report of acute pain within the past 48 hrs.

Volunteers were recruited from the UIC campus, surrounding communities, churches, local sororities, fraternities, community organizations, by word of mouth, flyers, and social media. The study was conducted at the

Table 1 QST thermal threshold values for African Americans (AA) using the limits protocol on the medoc TSA

First Author/Reference/ Population/[U.S Latitude North/South]	Sample Size	Age: Mean (SD) [range] years	Modalities Mean (SD)	Comparisons by age or sex (multiplicity considered -Y/ NR)	Sites	Protocol (Baseline, Probe, Rise, Thermode overlap, mechanical measure)
Edwards et al, 1999 ⁵ Healthy [South]	48 students AA n=18 (56% Females)	[18-47]	WD 34.8° (0.3) HPTTh 44.8° (1.2)	Multiplicity NR	Left Anterior forearm	32° 30x30 mm 0.5°/s (heat) NR
Campbell et al, 2005 ³ Healthy [South]	AA n=62 (68% Female)	20.1 (2.6)	CPTTh (n=40) 9.8° (6.3) HPTTh (n=62) 42.3° (4.2)	Age Sex Multiplicity NR	Left Anterior forearm	32° 30x30 mm 0.5°/s (heat) NR
Mechlin et al, 2007 ⁶¹ Healthy [South]	AA n=45 (53% Female)	[18-47]	HPTTh F 42.7° (0.59) M 44.3° (0.64)	Sex Multiplicity NR	Left Anterior forearm	38° 1 cm diameter NR NR
Rahim - Williams et al, 2007 ¹³ Healthy [South]	AA n=63 (66% Female)	24.5 (7.4)	CPTTh 13.6° (1.0) HPTTh 42.0° (3.0) Female 42.3° (3.5) Male	Sex Multiplicity NR	Anterior forearm	NR NR 0.5°/s (heat) NR Pressure Algometer
Wang et al, 2010 ¹⁴ Healthy [South]	AA n=10 (50% Female)	[19-47]	WD 35.25° (0.80) HPTTh 44.99° (1.11)	Multiplicity NR	Anterior Forearm	32° 12 cm ² 0.4°/s (heat) NR
Hastie et al, 2012 ¹⁰ Healthy [South]	AA n=75	23.7 (7.1) [18- 54]	HPTTh 42.0° (3.1)	Age Multiplicity Y (0.025)	Anterior Forearm	32° 30x30 mm 0.5°/s (heat) No thermode overlap Pressure Algometer

(Continued)

Table 1 (Continued).

First Author/Reference/ Population/[U.S Latitude North/South]	Sample Size	Age: Mean (SD) [range] years	Modalities Mean (SD)	Comparisons by age or sex (multiplicity considered -Y/ NR)	Sites	Protocol (Baseline, Probe, Rise, Thermode overlap, mechanical measure)
Glover et al, 2012 ⁸ Knee OA [South]	AA n=45 (69% Females)	54.6 (5.4) [45– 68]	HPTH Forearm 40.9° (3.3) Knee 41.3° (3.0)	Age Multiplicity NR	Anterior Forearm (ipsilateral) Knee (index)	32° NR 0.5°/s (heat) No thermode overlap Pressure Algometer
Cruz-Almeida et al, 2014 ⁶ Knee OA [South]	n=147 (63% Females)	55.1 (6.5)	HPTH Forearm 40.9° (3.5) Knee 41.3° (3.5)	Age Multiplicity NR	Anterior Forearm (ipsilateral) Knee (index)	32° 16x16 mm 0.5°/s (heat) NR Pressure algometer
Ezenwa et al, 2016 ⁷ SCD [North]	AA n=25 (72% Females)	38.5 (12.5) [20– 58]	CD 28.7° (3.4) CPTH 19.9° (9.3) WD 35.9° (2.2) HPTH 41.1° (4.7)	Age Multiplicity NR	Anterior forearm Lower leg (lateral, medial, anterior)	32° 30x30 mm 0.5°/s (heat) NR Von Frey 0.6–60 g
Brandow et al, 2013 ¹ Healthy/SCD [North]	Healthy n=57 (56% Female) SCD n=55 (60% Females)	Healthy 16.3 [±10.2] 15.4 [±6.3] _{SCD}	Hand CD 28.6° _{Healthy} WD 35.5° _{Healthy} CPTH 14.8° _{Healthy} HPTH 45.2° _{Healthy}	Age Sex Multiplicity NR	Hand (thenar eminence) Foot (lateral dorsum)	32° NR 1.5°/s Th Threshold 1°/s Thermal detection NR Von Frey Filaments 0.026–110 g
O'Leary et al, 2013 ⁶² Healthy/SCD [North]	Healthy n=28 (36% Female) SCD n=27 (56% Females)	14.4±2.0 [10– 18] yrs _{Healthy} 14.8 (2.4) [10– 18] _{SCD}	CD 31° _{VF} WD 34.4° _{VF} CPTH 5.79° _{VF} HPTH 45.2° (3.91) _{VF} CD 30° _{TE} WD 35.9° _{TE} CPTH 8.26° (8.17) _{TE} HPTH 48.6° _{TE}	Pediatrics Multiplicity NR	Anterior Forearm Thenar Eminence	32° 9 cm ² _{AF} ; 2.56 cm ² _{TE} 0.5°/s Th Detection 1.0°/s Th Threshold NR

(Continued)

Table 1 (Continued).

First Author/Reference/ Population/[U.S Latitude North/South]	Sample Size	Age: Mean (SD) [range] years	Modalities Mean (SD)	Comparisons by age or sex (multiplicity considered -Y/ NR)	Sites	Protocol (Baseline, Probe, Rise, Thermode overlap, mechanical measure)
Riley et al, 2014 ⁹ Healthy and Knee OA [South]	Non-Hispanic Blacks n=53 (68% Female)	[45–76]	WD (forearm) 35.9° (2.2) HPTh (forearm) 41.8° (2.8) WD (knee) 37.0° (2.2) HPTh (knee) 41.9° (3.2)	Age Multiplicity NR	Anterior Forearm Knee	32° NR 0.5°/s NR Pressure Algometer
Campbell et al, 2015 ² Healthy/SCD [North]	Healthy n=27 (59% Female) SCD n=83 (69% Female)	35 (10) ^{Healthy} 38.9 (12.1) ^{SCD}	HPTh 41.8° (2.9) ^{Healthy} 40.7° (2.8) ^{SCD}	Multiplicity NR	Anterior forearm (dominant)	32° 30x30 mm 0.5 °C/s NR Pressure algometer

Abbreviations: Multiplicity considered: Y, Yes; NR, Not Reported; WD, Warm Detection; HPTh, Heat Pain Threshold; CD, Cool Detection; CPTTh, Cold pain Threshold; ° are reported in degrees Celsius SCD, sickle cell disease; OA, osteoarthritis.

UIC College of Nursing with 125 individuals who gave informed consent and completed the measures. One participant, who passed verbal screening criteria, was removed from the study because on the demographic questionnaire she electronically reported race as Asian and parents as being born in India.

Measures

Quantitative sensory testing

We used well-validated measures for the thermal and mechanical QST.³ The testing protocol was consistent with the EFNS (European Federation of Neurological Societies) recommendations for testing A β , A-delta, and C fiber function.³⁹ We included QST measures for 6 modalities: cool detection (CD), warm detection (WD), mechanical sensation detection, cold pain threshold (CPTTh), heat pain threshold (HPTh), and mechanical pain threshold (MPTh). The body sites, stimulus modalities, and QST measures used in this study were selected based upon common pain sites found in SCD samples and modalities that would, for ethical reasons, minimize risk of pain crisis.⁷ These values were intended to serve as comparators for studies with a similar protocol in pain conditions affecting African Americans such as SCD.

Thermal

The Medoc TSA-II sensory testing system is a precise, computer-controlled device capable of generating and documenting responses to highly repeatable thermal stimuli, such as cool detection, warm detection, cold-induced pain, and heat-induced pain. The TSA-II delivers quantitative assessment of small caliber sensory nerve function and was used to identify thermal detection and pain thresholds.^{40,41}

We conducted the study in a private temperature-controlled room. We used the TSA-II thermode (30 × 30 mm) that was placed on the skin to deliver standardized stimuli for determination of CD, CPTTh, WD, and HPTh.⁴⁰ To avoid tissue damage, we used the limits protocol, which had a predetermined cutoff temperature for all trials, 50 °C for heat and 0 °C for cold. For WD and HPTh, the temperature increased from a baseline of 32 °C (adaptation temperature) at a rate of 0.5 °C per second until the participants pressed a button to indicate when they first detected warmth or heat pain, respectively at which time the stimulus returned to 32 °C. CD and CPTTh were evaluated by decreasing the temperature from the baseline of 32 °C at a 0.5 °C per second rate until the participants

pressed a button to indicate when they first detected a cool sensation or cold pain, respectively.⁴⁰ There was a minimum of a 30-second inter-stimulus interval between test repetitions, which were conducted at non-overlapping sites. All tests included at least three repetitions, but additional trials were conducted if the initial three trials differed by more than 2 °C, up to a maximum of 5 trials.³ The value for a site was the average of the three closest readings. Participants verbally indicated the intensity of the pain they felt after the HPT_h trials and again after the CPT_h trials.

Mechanical

QST was conducted for mechanical detection and pain threshold using standardized calibrated von Frey monofilaments (Four D Rubber Co. Ltd). These filaments are measuring devices calibrated to bend at a set amount of force depending on the thickness of the filament. To ensure accurate testing of the detection threshold and pain threshold, the filament was placed perpendicular to the area being tested and pressure applied until the filament showed an “s-shaped” bending pattern.⁴⁰ The contact time to the surface of the skin was approximately one second. Seven filaments were used in sequence, from lightest to heaviest, starting with 3.84 (0.6 grams, g) and ending with 5.88 (60.0 g). These filaments were selected based on previous studies that provided non-painful sensations in all patients and a painful sensation in some patients as per the EFNS protocol.³⁹

Mechanical detection was defined as the lowest filament force at which the participant reported any sensation, and mechanical pain threshold was defined as the filament force at which the participant first reported pain. Three trials for each filament were conducted at non-overlapping sites, with the average of the three trials used for data analysis. The participants verbally indicated if they felt the filament and then reported if the sensation felt painful. If the participant reported pain as a result of a stimulus, the testing at that body site was stopped and the participants verbally indicated the intensity of the pain they felt.

Symptom and psychosocial measures PAINReportIt

PAINReportIt is a computerized version of the McGill Pain Questionnaire (MPQ) items. The MPQ is a valid and reliable measure of pain.⁴² Equivalence between the computerized and the paper and pencil versions of the MPQ have been reported.^{43–45} It includes items for

reporting previous pain experiences (eg, worst toothache, headache and stomachache). In this study we were examining the function of ascending neuronal pathways because findings from previous studies in patients with sickle cell disease (SCD) have shown that there may be a neuropathic component to SCD.⁴⁶ Throughout the lifespan, individuals may experience different types of common painful conditions, like a toothache, headache or stomachache and the relative magnitudes of common pain can be recalled when individuals are asked to report their worst common pain in comparison to an acute or chronic painful condition, like SCD or cancer pain.^{47,48} Therefore, previous pain experiences from worst toothache, headache and stomachache may be used as a guide to show that individuals recognize when pain is severe in comparison to reports of pain from QST testing. This self-report pain assessment tool is used to examine pain outcome measures without any additional subject burden.⁴⁹

Pain intensity number scale (PINS)

The PINS measure provides ratio level pain intensity data,^{50–52} scaled between 0 (“no pain”) and 10 (“pain as bad as it could be”), about the participant’s level of pain now and past common pain experiences (ie, worst toothache, headache, and stomachache).^{51,52} Concurrent and construct validity⁵³ have been reported for the PINS tool that has standardized instructions.⁵⁰

PROMIS fatigue, depression and anxiety

The Patient-Reported Outcomes Measurement Information Symptom Measures System (PROMIS) was designed to measure physical, mental and social health factors of individuals with chronic conditions.⁵⁴ The PROMIS Fatigue short form is a 7-item tool used to measure the impact of fatigue in the past seven days. The PROMIS Depression bank is comprised of 8 items and the PROMIS Anxiety bank is comprised of 7 items.⁵⁵ The Depression scale focuses on negative moods, views of self, social cognition, and somatic systems (rapid heartbeat, dizziness).⁵⁶ The Anxiety scale focuses on fear, anxious misery, heightened arousal, and somatic symptoms.⁵⁶ These tools have a 5-point Likert scale, where the responses range from 1= “never” to 5= “always”.⁵⁷ Scores are obtained by summing the items with the mean normalized at 50 and a standard deviation of 10.⁵⁷ Higher scores are consistent with increased fatigue, depression, or anxiety. Cronbach’s alphas for depression, anxiety, and fatigue were 0.96, 0.95, and 0.83, respectively.⁵⁸

Demographics

Demographics were collected to provide sample characteristic information. Specifically, we captured the participant's age, race, ethnicity, and sex.

Procedures

Using the TSA-II and von Frey filaments, an internationally recognized QST expert trained all staff members in the QST procedures. Staff members practiced the protocol until they performed it with high fidelity, and the project director observed them periodically for adherence to the study protocol.

Data collection was scheduled at times convenient to participants, including occasional evening and weekend appointments, and occurred in a temperature-controlled room, adequate for the QST protocol. After written consent was obtained, participants used PAINReportIt to provide demographic information, complete self-report pain questionnaires to verify that they did not have pain and report their previous pain experiences (worst toothache, headache, and stomachache). In addition, they completed the PROMIS measures (fatigue, depression, and anxiety). Then QST procedures occurred with the participant seated on a comfortable leather recliner, the seat back positioned at approximately 45°, for easy access to the anterior forearm.

Prior to QST procedures, each participant was trained on QST testing procedures at a practice site (anterior forearm). We emphasized to them that pain scale was from 0 to 10, where 0 is "no pain" and 10 was "pain as bad as it could be", and could be described as any number in between (therefore, on a continuum). During training, we instructed them to give their responses when they "FIRST" detected the sensation. They were instructed to press the button when the thermal sensation "FIRST" felt warm/cool, and press the button when the cold/hot sensation "FIRST" felt painful. They had visual cues for each response task with written instructions to maintain their focus on the specific task. They also indicated if they felt the von Frey filament and if the sensation was painful. We asked patients not only to verbalize and demonstrate understanding of the study procedures since their behavior was important to study validity.

Once the training and practice were completed, QST testing began at the other sites. QST values were obtained across the entire sample from a combination of six sites total: three upper extremity (left or right: anterior forearm, posterior forearm, and upper arm lateral) and three lower

extremity lower leg sites (left or right: lateral, medial, posterior) (Figure 1). To reduce participant burden, each participant was tested at only three sites, no more than one site per limb. All participants were tested at the anterior forearm site and two other sites as determined by a random sampling list that was stratified by age, gender and included at least one lower extremity site. Thermal testing was completed first followed by mechanical testing. The same protocol was used for all participants.

Using the von Frey filament, starting at 0.6 g of force, the participant was asked to report when they first felt a sensation and the strength of the filament was recorded. As with the EFNS protocol, each test site was tested with three repetitions for each filament. We tested the filaments in increasing order of force and testing stopped when the participant reported a force as being painful for any one of the repetitions.

After each QST thermal or mechanical pain threshold test, the participant used the PINS to rate the intensity of the perceived pain. Participants were compensated \$50 to cover the cost of transportation, travel, and subjects' time to complete the study measures. Payment was rendered once all testing was completed.

Statistical analysis

Relevant descriptive statistics for various measures, including mean, standard deviation, range, frequency, and percentage, were obtained. The data for the six modalities were examined by age groups 18–39 years (ie, younger adult) and ≥ 40 years (ie, older adult), sex, test site, and upper vs lower body sites. Independent *t*-tests were used to compare the means for each modality by age group and sex. We used paired *t*-tests to examine the means of upper compared to lower body values. Analysis was performed with the R statistical package. Benjamini-Hochberg procedure was used to adjust the *p*-values to account for multiple testing.⁵⁹ Statistical significance was set at $q < 0.05$, where *q* is the adjusted *p*-value.

Results

A total of 124 participants were included in the study analysis. Table 2 shows the sample demographic information. Participants ranged in age from 18 to 69 years, mean age was 38.6 ± 12.5 years; 64 (52%) were 18–39 years and 60 (48%) were ≥ 40 years of age. The sample included 61 (49%) women. The 124 participants identified their race as Black/African American, including those who also reported being Hispanic/Latino ($n=5$) or multi-ethnic

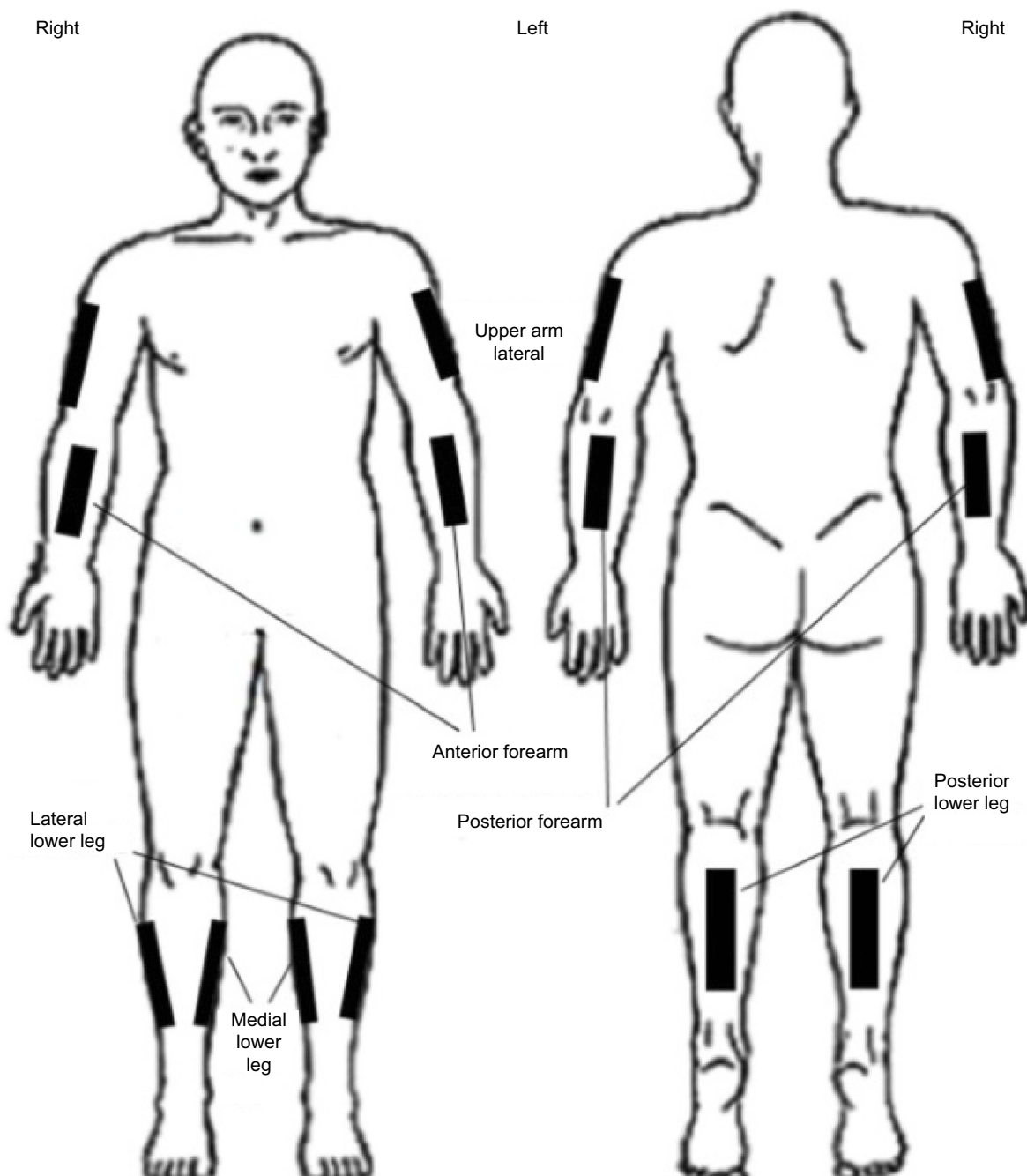


Figure 1 Body sites used for QST testing: three upper extremity (left or right: anterior forearm, posterior forearm, and upper arm lateral) and three lower extremity lower leg sites (left or right: lateral, medial, posterior).

($n=4$). Fifty participants (40%) had an associate degree or higher degree.

Descriptive statistics for QST values are reported in Table 3 and Figure 2. All participants were sensate to the thermal stimuli and to mechanical stimuli above 10 g. There were 124 participants providing QST data for the anterior forearm, and 48–53 participants providing QST data for the other five site subgroups and 22–30

participants for the site/age or site/sex subgroups (Table 3). The QST values for each modality showed variability across sites, especially for pain threshold.

Sex and age

At the anterior forearm, differences in CD values were not significantly different by sex, but mean WD values were significantly lower for females ($34.3\text{ }^{\circ}\text{C} \pm 1.1$) than males

Table 2 Sample demographic information, intensity of previous pain experiences, and current fatigue, depression and anxiety

Characteristic	Mean (SD)	Frequency	Percent
Sex			
Female		61	49
Male		63	51
Age group (18–69)	39 (13)		
18–39 years		64	52
≥40 years Psychosocial Status		60	48
PROMIS Fatigue	41.5 (7.6)		
PROMIS Depression	42.1 (7.0)		
PROMIS Anxiety	42.8 (7.5)		
Current and previous pain experiences			
Current pain	0 (0)		
Worst toothache (range 0–10)	5.2 (3.8)		
Worst headache (range 0–10)	5.7 (3.4)		
Worst Stomachache (range 0–10)	4.9 (3.5)		

(34.8 °C ±1.2, $p=0.009$, $q=0.027$). (Table 3). Differences in mean CD, CPT_h, HPT_h, and MPT_h values were not statistically significant by sex at the anterior forearm. Also, in Table 3, differences in CD, WD, CPT_h, HPT_h, MPT_h values were not statistically significant by age at the anterior forearm.

Upper and lower body sites

The differences in QST values between upper and lower body sites were statistically significant across all thermal modalities but not for the mechanical modality (Table 4 and Figure 3). Thermal detection (CD, WD) and pain threshold (CPT_h, HPT_h) occurred closer to the temperature of adaptation in the upper body sites compared to the lower body sites.

Symptoms and psychosocial measures

As shown in Table 5, mean pain intensity scores rated immediately after the CPT_h and HPT_h were 1.9±1.3–2.2 ±1.2 on the 0–10 PINS. Similarly, after the MPT_h tests the mean PINS scores were 0.5±0.5–0.8±0.6. These scores did not differ significantly by sex or age group and clearly indicate that the participants reported pain threshold at an appropriately low perceptual intensity and consistent with the instructions to report when they FIRST felt pain.

As shown in Table 2, the mean scores for worst toothache, headache, and stomachache are close to the middle of the scale with wide standard deviations (3.4–3.8). These findings indicate that participants chose the whole range of

scores (0–10) to describe their pain experiences. Furthermore, these findings indicate that the sample of healthy, pain-free individuals had prior experiences with pain.

We also considered participants' psychosocial status as another potential factor that may have affected their performance on the QST procedures. As shown in Table 2, the mean fatigue, depression and anxiety scores were lower than the population mean, indicating that the burden of fatigue, depression or anxiety status was low among these healthy volunteers.

Discussion

This study provides QST values for six modalities (CD, WD, CPT_h, HPT_h, MD, MPT_h) among healthy, pain-free African American adults across multiple body sites in a sample characterized by a wide age range and equal distribution by sex. All participants were able to feel sensations for all modalities. Overall, our QST values showed that this sample of healthy African American adults indicated the stimuli were mildly painful on average at 5.7 °C above the temperature of adaptation for HPT_h, 5.8 °C below the temperature of adaptation for CPT_h, and on average below 20 gF for MPT_h. At the anterior forearm, none of the QST pain threshold temperatures were different by sex or age, but women detected the warm stimulus at a significantly lower temperature than men. Thermal responses were significantly closer to the temperature of adaption for upper

Table 3 QST values for cool detection (CD), warm detection (WD), cold pain threshold (CPT_h), heat pain threshold (HPT_h), and Mechanical detection at six test sites for the entire sample and by sex and age group. Thermal QST is reported in degrees Celsius (C) and mechanical QST is reported in grams of force

	Entire Sample			Female			Male			p [q]	19–39 years			≥40 years			p [q]
	Mean (SD)	Min-Max	n	Mean (SD)	Min-Max	n	Mean (SD)	Min-Max	n		Mean (SD)	Min-Max	n	Mean (SD)	Min-Max	n	
Anterior Forearm	29.2 (1.6)	18.4–31.5	n=124	29.4 (1.2)	24.9–31.4	n=61	29.1 (1.8)	18.4–31.5	n=63	0.35 [0.38]	29.0 (1.9)	18.4–31.3	n=64	29.5 (1.1)	26.3–31.5	n=60	0.05 [0.088]
CD	34.5 (1.2)	32.3–38.9		34.3 (1.1)	32.5–37.3		34.8 (1.2)	32.3–38.9		0.01 [0.027]	34.7 (1.3)	32.3–38.9		34.4 (1.1)	32.6–36.6		0.26 [0.30]
WD	26.3 (5.0)	0.0–31.0		27.2 (3.6)	10.1–31.0		25.4 (5.9)	0.0–30.9		0.04 [0.081]	26.1 (4.5)	0–30.9		26.5 (5.5)	0–31		0.64 [0.64]
CPT _h	37.8 (3.6)	33.1–48.5		37.1 (3.4)	33.1–45.3		38.5 (3.7)	33.5–48.5		0.04 [0.081]	38.5 (3.4)	33.1–48.5		37.5 (3.7)	33.1–46.8		0.02 [0.053]
HPT _h	16.7 (22.2)	0.6–60		14.1 (21.2)	0.6–60		19.2 (23.2)	0.6–60.0		0.21 [0.26]	19.9 (23.6)	0.6–60		13.2 (20.4)	0.6–60		0.09 [0.14]
Mechanical	n=48			n=22			n=26				n=23			n=25			
Posterior Forearm	29.6 (1.1)	26.8–31.5		29.6 (1.2)	26.8–31.2		29.6 (0.91)	28.2–31.5			29.5 (1.1)	26.8–30.9		29.6 (1)	27.7–31.5		
CD	34.5 (1.5)	32.5–41.7		34.3 (1.1)	32.5–37.2		34.6 (1.8)	32.6–41.7			34.2 (1)	32.5–36.6		34.7 (1.9)	32.6–41.7		
WD	25.8 (6.6)	0.0–31.0		26.5 (6.4)	1.2–31.0		25.6 (6.8)	0–30.4			27.4 (2.1)	22.9–30.7		24.2 (8.7)	0–31		
CPT _h	37.8 (4.1)	33.0–47.9		36.9 (3.6)	33.0–45.5		38.6 (4.4)	33.8–47.9			37.2 (3.6)	33–45.7		38.3 (4.5)	33.7–47.9		
HPT _h	17.4 (22.8)	0.6–60		14.9 (21.9)	1.4–60		19.5 (23.8)	0.6–60			19.8 (1.6)	1.4–60		15.2 (21)	0.6–60		
Mechanical	n=53			n=27			n=26				n=30			n=23			
Lateral Upper Arm	28.9 (1.3)	26.0–3.9		29.0 (1.1)	26.5–30.9		28.7 (1.4)	26–46.9			28.6 (1.2)	26–30.5		29.2 (1.2)	26.1–30.9		
CD	34.9 (2.7)	32.7–46.9		34.1 (1)	32.7–36.4		35.8 (3.7)	32.7–46.9			35.5 (3.4)	32.7–46.9		34.2 (1.2)	32.7–37.5		
WD	25.2 (6.3)	0.0–30.7		26.6 (2.8)	16.6–30.6		23.7 (8.3)	0–30.7			23.4 (7.6)	0.0–28.7		27.6 (2.5)	19.1–30.7		
CPT _h	39.1 (4)	33.2–49.6		38.1 (3.3)	33.7–46.3		40.2 (4.5)	33.2–49.6			40.6 (4.0)	35.4–49.6		37.2 (3.3)	33.2–46.3		
HPT _h	23.0 (26.2)	0.6–60		17.4 (25.7)	0.6–60		28.9 (26)	0.6–60			26.2 (26.8)	0.6–60		18.9 (25.5)	0.6–60		
Mechanical	n=48			n=25			n=23				n=25			n=23			
Lateral Leg	29.0 (1.4)	26–31.8		29.3 (1.6)	26.2–31.8		28.7 (1.3)	26–31.5			28.7 (1.3)	26.2–31.8		29.3 (1.6)	26–31.5		
CD	35.1 (1.5)	32.9–39.9		35.2 (1.6)	33–39.9		35.1 (1.3)	32.9–38.1			35 (1.2)	33–38.1		35.2 (1.8)	32.9–39.9		
WD	25.3 (5.7)	5.2–31.3		26.1 (4.7)	11.8–31.3		24.4 (6.6)	5.2–30.7			24.8 (5.5)	5.8–31.3		25.7 (6)	5.2–31.1		
CPT _h																	

(Continued)

Table 3 (Continued).

	Entire Sample			Female		Male		p [q]	19-39 years		≥40 years		p [q]
	Mean (SD)	Min-Max	n	Mean (SD)	Min-Max	Mean (SD)	Min-Max		Mean (SD)	Min-Max	Mean (SD)	Min-Max	
HPT _h	39.1 (4.2)	33.2-48.2	n=50	38.0 (3.9)	33.2-46.2	40.3 (4.2)	33.4-48.2		39.6 (3.7)	34.5-45.2	38.5 (4.6)	33.2-48.2	
Mechanical	23.9 (22.7)	0.6-60		19.9 (21.8)	0.6-60	28.2 (23.3)	0.6-60		26.9 (2.1)	4.0-60	20.7 (24.4)	0.6-60	
Medial Leg	n=50		n=25			n=25			n=25		n=25		
CD	28.2 (1.5)	25.2-31.3		28.2 (1.5)	25.7-31	28.3 (1.6)	25.2-31.3		28 (1.4)	25.2-31	28.4 (1.7)	25.9-31.3	
WVD	35.4 (2.1)	32.9-46.5		34.8 (1.4)	33.2-39.4	35.9 (2.5)	32.9-46.5		35.6 (2.6)	33.4-46.5	35 (1.6)	32.9-39.4	
CPT _h	24.4 (7.5)	0.0-30.1		24.9 (7)	2.1-29	23.8 (8.2)	0-30.1		23.5 (7.6)	0.0-28.6	25.2 (7.5)	0.2-30.1	
HPT _h	39.0 (4.2)	33.6-48.4		38.2 (3.4)	33.9-46.7	39.8 (4.8)	33.6-48.4		39.8 (4.2)	34.5-48.4	38.2 (4)	33.6-46.9	
Mechanical	17.9 (23.1)	0.6-60		17.6 (22.5)	1.4-60	18.2 (24.1)	0.6-60		20.7 (23.3)	1.4-60	15.2 (23)	0.6-60	
Posterior Leg	n=49		n=23			n=26			n=25		n=24		
CD	28.7 (1.9)	20.8-31.4		29.1 (1.2)	26-31.4	28.3 (2.3)	20.8-31.2		28.8 (1.3)	26-30.7	28.6 (2.4)	20.8-31.4	
WVD	35.3 (1.8)	32.7-43.5		34.8 (1.1)	32.7-37.9	35.7 (2.2)	33.7-43.5		35.4 (1.5)	33.5-39.8	35.2 (2.1)	32.7-43.5	
CPT _h	25.0 (4.7)	6.7-30.6		25.7 (4.8)	7.2-30.6	24.5 (4.7)	6.7-29.3		25.7 (2.5)	19.3-29.9	24.3 (6.3)	6.7-30.6	
HPT _h	38.7 (3.4)	33.2-45.7		37.5 (3.2)	33.2-44.1	39.7 (3.3)	34.8-45.7		38.6 (3)	33.8-44.1	38.8 (3.8)	33.2-45.7	
Mechanical	18.8 (22.1)	0.6-60		11.7 (16.5)	0.6-60	25.1 (24.7)	0.6-60		19.3 (22.2)	0.6-60	18.2 (22.4)	0.6-60	

Note: The bolded values represent statistically significant raw p-values and adjusted (false discovery rate) q values for paired t-tests.

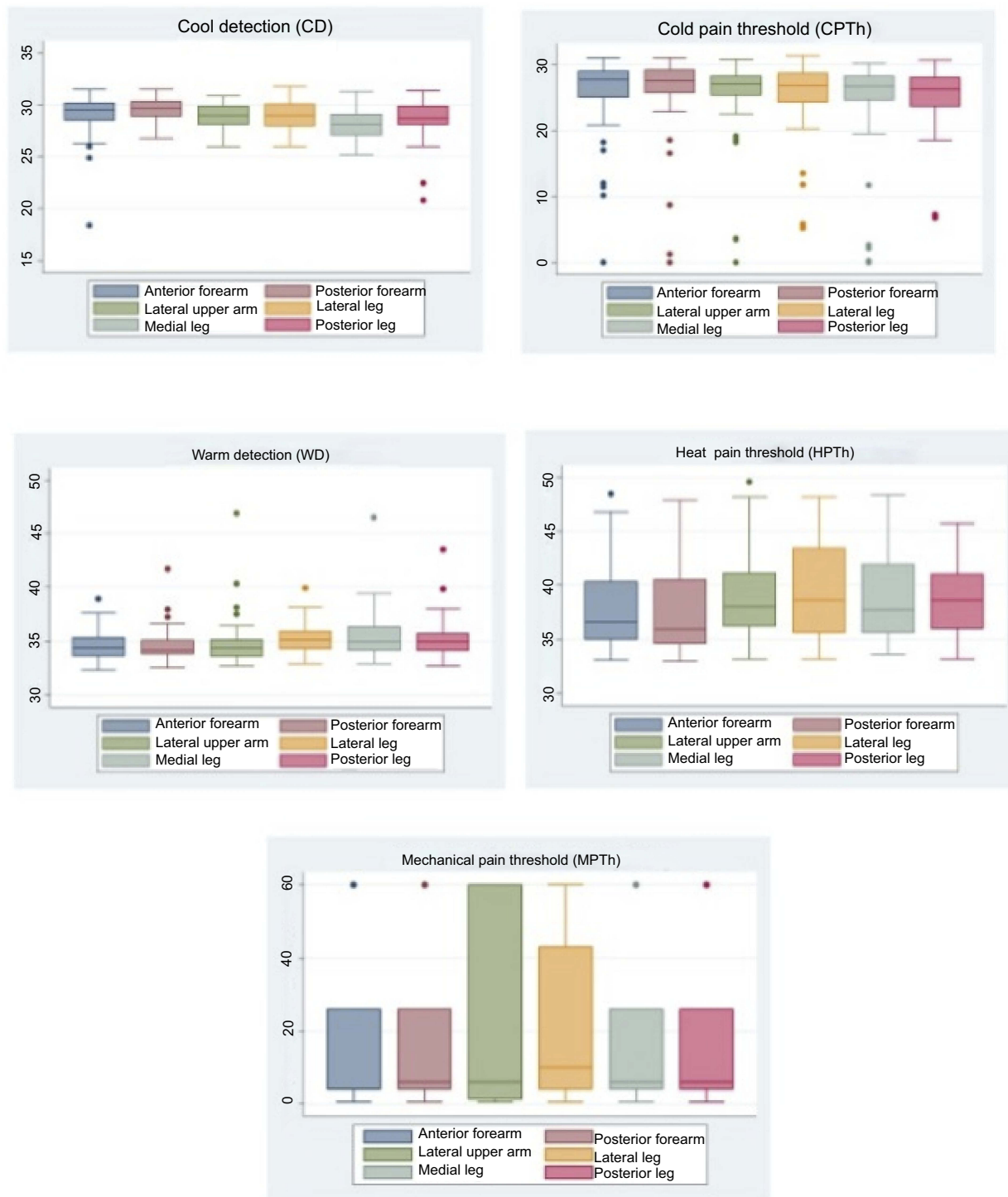


Figure 2 Box plots for thermal and mechanical modalities (CD, CPTTh, WD, HPTH, and MPTh) at six test sites.

Abbreviations: CD, cold detection; CPTTh, cold pain threshold; WD, warm detection; HPTH, heat pain threshold; MPTh, mechanical pain threshold.

body sites compared to lower body sites. None of the mechanical responses differed significantly by sex, age, or upper vs lower body sites. Pain intensity values for current and past pain experiences showed that participants had an understanding of pain and the use of the tool for reporting pain intensity. In addition, their low

ratings for fatigue, depression and anxiety indicated that these factors were unlikely contributors to their pain threshold reports.

In studies with similar testing methods, protocols, anatomic test sites and probe size, our QST values were similar to other African Americans,⁷ Asians²⁷ and Hispanics,^{20,60}

Table 4 Comparison of thermal and mechanical quantitative sensory testing in upper body verses lower body sites (N=124*)

Modality	Upper Body Mean (SD)	Lower Body Mean (SD)	Mean (SD) of differences	p	q
CD	29.2 (1.3)	28.6 (1.7)	0.66 (1.4)	<0.001	0.003
WD	34.6 (1.5)	35.2 (1.7)	-0.64 (1.5)	<0.001	0.003
CPTH	25.9 (5.4)	24.8 (6.1)	4.44 (5.7)	<0.001	0.003
HPTh	38.1 (3.7)	39.0 (3.8)	-0.88 (2.3)	<0.001	0.003
MPTH	18.4 (22.4)	20.3 (22.5)	-1.96 (13.7)	0.12	0.17

Notes: Raw p-values and adjusted (false discovery rate) q values for paired t-tests; *All participants were sensate to touch.

Abbreviations: °C: CD, cool detection; WD, warm detection; CPTH, cold threshold; HPTh, heat threshold; MPTh, Mechanical Pain Threshold. (grams of force)

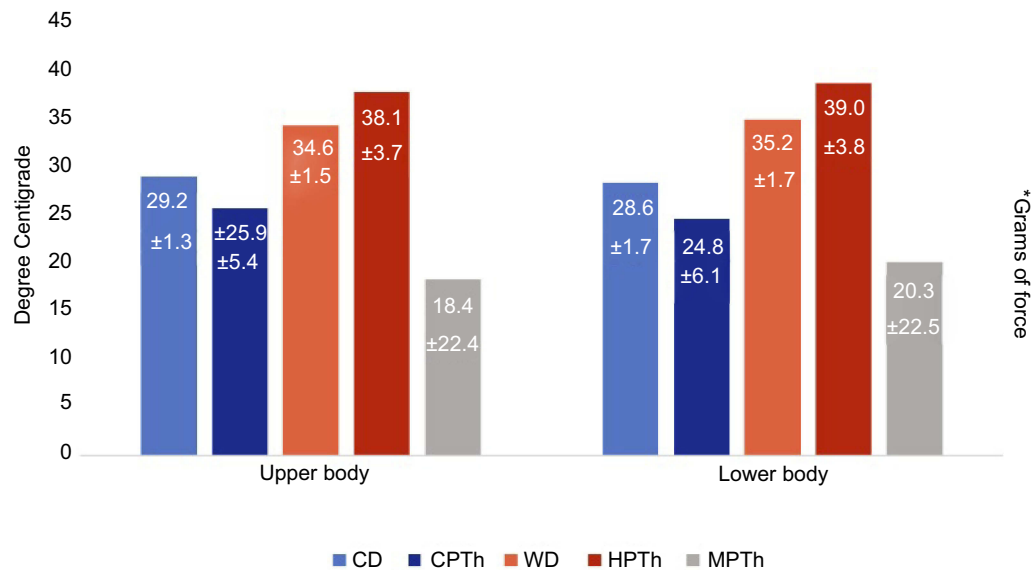


Figure 3 Comparison of upper body and lower body QST values by thermal and mechanical modalities.

Note: *Mechanical pain threshold (MPTh) is reported in grams of force.

Table 5 Pain intensity ratings (0–10 scale) for cold pain threshold (CPTH), heat pain threshold (HPTh), and mechanical pain threshold (MPTh) by sex and age group

	Female (n=61) Mean (SD) Min/Max	Male (n=63) Mean (SD) Min/Max	p
Cold pain	2.0 (1.2), 0.1–5.7	1.9 (1.3), 0.0–7.0	0.50
Heat pain	2.1 (1.3), 0.1–6.3	2.1 (1.4), 0.3–8.0	0.96
Mechanical pain	0.7 (0.5), 0.0–3.0	0.7 (0.7), 0.0–2.7	0.76
	Younger (n=64) Mean (SD) Min/Max	Older (n=60) Mean (SD) Min/Max	p
Cold pain	1.9 (1.2), 0.0–5.3	2.0 (1.3), 0.0–7.0	0.48
Heat pain	2.1 (1.3), 0.3–6.3	2.2 (1.4), 0.1–8.0	0.59
Mechanical pain	0.5 (0.5), 0.0–2.7	0.8 (0.6), 0.0–3.0	0.01

Note: p for independent t-test.

but Whites were further from the temperature of adaptation.^{3,5,14,61} Across the racial groups with reference to the temperature of adaptation, CD occurred at an average of 2.8 °C and WD at 2.5 °C.^{5,7,9,14,20,62} In our study, average HPTh and CPTH was reported within 6 °C from the temperature of adaptation. In contrast, the average CPTH

in other studies was 22.2 °C from the temperature of adaptation and the average HPTh was 10.3 °C from the temperature of adaptation.^{2,3,5–10,13,14,20,27,62} Overall, our QST pain threshold values were much closer to the temperature of adaptation than published values for other African Americans and other ethnic/racial groups.^{2,3,5–10,13,14,20,27,62}

Reasons for the discrepancy between our pain threshold values and those from other studies could be related to the protocol or the participants' past pain experiences or psychological status. As a part of our protocol implementation, the participants were trained to indicate their pain threshold when they first felt pain, and we emphasized to them that pain scale was from 0 to 10, where 0 is "no pain" and 10 was "pain as bad as it could be", and pain could be described as any number in between (on a continuum). They had used this tool to report their current and past pain experiences. It may be that these instructions and recall of their previous pain experiences influenced our findings since we taught the participants to see pain on a continuum. Participants did not wait until the pain was moderate to severe to indicate they felt the stimulus as pain. As a result, pain intensity ratings reported after they indicated their pain threshold were quite low compared to other studies. Notably, a previous study in healthy adults from age 18–60 had substantially higher mean pain intensity ratings for CPT_h (2.9–3.8, median 3.3) and HPT_h (4.6–5.5, median 5.0) when they indicated their thermal pain thresholds.⁶³ Thus, the lower perceptual intensity criterion of our sample is consistent with their pain thresholds being closer to the temperature of adaptation.

Sex and age

Our results showed a significant between sex difference only for WD at the anterior forearm, with women being more sensitive. Interestingly, this is the site where women commonly test milk temperature before feeding their babies. Previous investigators explored sex differences in QST responses using multiple modalities and test sites.^{26,29,31,32,64} Many investigators found that men and women differed significantly in their response to thermal stimuli, with women being more sensitive than men,^{27,33,64,65} but most studies did not include adjusted *p*-values for multiple testing. Results from previous studies have shown a consistent pattern of lower heat pain thresholds in females, but the magnitude of these differences has been quite variable.^{11,29,31,33,34,65,66} We adjusted for multiplicity and found that only WD differed.

In healthy individuals, age dependency for sensory pain thresholds has been observed. As age increases, CPT_h decreases and HPT_h increases,⁴⁰ likely due to age-related declines in both pain detection and reaction times.¹⁹ The association of age with thermal sensation appears to be variable, but not all of the studies with multiple comparisons included adjusted *p*-values.^{12,13,67–70} Controlling for multiplicity, however, we did not see age differences. We

grouped age with 40 years as the cut off between younger and older adults because this age grouping is highly relevant in the sickle cell population given their short life expectancy.⁷

In our study we examined A β , A δ , and C fiber input using von Frey filaments. We found one study that included von Frey filaments in healthy African Americans with results only reported for the hand and foot instead of the anterior forearm as in our study.⁶⁷ In other studies of healthy African Americans, investigators used the pressure algometer, which limits interpretation with our findings. MPTh values were not significantly different by sex, age, or upper and lower body sites, which is consistent with previous findings for sex,^{27,31,64,71} age,^{67,70,72} and upper and lower body sites.^{33,34}

Although many body sites have been used in QST studies, upper versus lower body site comparisons have been consistent across studies and over time. Some investigators have reported no significant difference in thermal threshold differences between upper extremity and lower extremities after controlling for multiplicity.³⁴ In our study, we adjusted for multiplicity and found thermal values for upper body sites that were closer to the adaptation temperature for all thermal modalities than the lower body sites, but the mechanical modality did not show a difference between upper and lower sites. Reasons for differences in thermal responses between the upper and lower body may be related to variations in skin characteristics, epidermal nerve fiber density or axonal length.^{11,27} Our findings that the QST values for the upper body sites were closer to the temperature of adaptation than lower body sites are robust, valid, and consistent with what other researchers have found.^{11,20,34,69}

Symptoms and psychosocial measures

Since thermal pain thresholds for QST stimuli were close to the temperature of adaptation in our sample, we considered participant characteristics that could have influenced their pain threshold responses. To verify that the participants understood what was meant by "pain", we examined their reports of worst toothache, headache and stomachache. Their pain intensity values were similar to those in previous studies.^{57,58} In addition, Findings from previous studies have shown that as pain increases, fatigue, anxiety and depression also increase.^{54,57,58} Our results for fatigue, anxiety, and depression show that the participants were less than one SD lower than the average for the general population. Therefore, our findings demonstrate that the participants

understood what pain is, and that their fatigue, depression, and anxiety levels were not likely contributors to the findings of this study. These results give us confidence that the QST pain intensity values for the pain thresholds were not a reporting problem.

Lack of random sample selection is a study limitation. Also, all participants were from the same region of the country and were obtained via advertisement and word of mouth. It is unknown if regional climate, seasonal, genetic, or epigenetic factors impact responses to the QST stimuli. All but two of the prior QST studies of healthy, pain-free African Americans were conducted with samples located in the Southern latitudes in the US, but ours was located in the Northern latitudes in the US and the impact of this difference on our findings is unknown. Also, we did not use biological measures (pain related genetic, epigenetic, inflammatory markers), that might help explain our pattern of results. Future studies should incorporate these biological measures to further characterize the determinants of QST responses in African American samples. Additionally, future studies should include replication of this study in the Southern region using the same protocol.

Study strengths include QST values for six test sites that were obtained from a relatively large sample of younger and older African American adults with balanced distribution by age and sex. In addition, we included current and previous pain, fatigue and psychological context of the sample to help interpret the results. In addition, we applied the Benjamini-Hochberg procedure⁵⁹ to adjust the *p*-values to account for the multiple tests. The aim of the present study was to characterize QST values for healthy African American adults, thus, we did not attempt to compare thresholds between ethnic/racial groups. The study protocol was consistent with the EFNS protocol for testing A β , A δ , and C fiber function.⁶⁶ These QST values may be used for comparisons in studies where the same protocol is utilized.

Conclusion

Overall, this sample of healthy African American adults had average thermal pain thresholds within 6 °C of the temperature of adaptation that were not significantly different by age or sex. Differences in responses to thermal and mechanical stimuli for upper verses lower body sites were consistent with previous research. We believe that participant training established a low perceptual intensity criterion for pain threshold, which is a plausible explanation for our findings. Regardless of the cause for the thresholds being closer to the temperature of adaptation, these results can be used as

controls for African Americans with SCD and tested with the same protocol. Additional research is needed to resolve differences in QST values observed with different protocols and to establish normative QST values for healthy, pain-free African Americans with consideration of geographic region within the US and genetic admixtures of the participants.

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Disclosure

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