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Demographic Predictors of Pain Sensitivity: Results from the OPPERA Study

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Abstract

The demographic factors of sex, age, and race/ethnicity are well recognized as relevant to pain sensitivity and clinical pain expression. Of these, sex differences have been the most frequently studied, and most of the literature describes greater pain sensitivity for women. The other two factors have been less frequently evaluated, and current literature is not definitive. Taking advantage of the large OPPERA study cohort, we evaluated the association of sex, age, and self-reported race with 34 measures of pressure, mechanical, and thermal pain sensitivity encompassing both threshold and suprathreshold perception. Women were significantly more pain sensitive than men for 29/34 measures. Age effects were small, and only significant for 7/34 measures, however the age range was limited (18–44 y.o.). Race/ethnicity differences varied across groups and pain assessment type. Non-Hispanic whites (NHW) were less pain sensitive than African-Americans (for 21/34 measures), Hispanics (19/34), and Asians (6/34). No pain threshold measure showed significant racial differences, while several suprathreshold pain measures did. This suggests that racial differences are not related to tissue characteristics or inherent nociceptor sensitivity. Rather, the differences observed for suprathreshold pain ratings or tolerance are more

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likely related to differences in central nociceptive processing, including modulation imposed by cognitive, psychological, and/or affective factors.

Keywords

quantitative sensory testing; sex differences; racial differences; ethnic differences; pain sensitivity; heat pain; pressure pain

Introduction

Multiple factors are recognized to influence an individual's pain sensitivity; among these are the major demographic variables of sex, age, and race/ethnicity. A large literature addresses the issues of sex and gender differences in pain sensitivity, clinical pain expression, and mechanisms underlying such differences[5,11,20]. The majority of these studies report greater pain sensitivity for women vs. men, but several studies fail to find significant sex differences. The conditions leading to the expression of sex differences in pain sensitivity are not clear and do not appear to be distinctly related to types of stimulation or the perceptual metrics. However, sample size issues have been proposed as a reason for at least some of the studies reporting no significant sex differences[11].

Considerably less work has been done evaluating age and racial/ethnic factors as related to pain sensitivity. Regarding age differences, a recent meta-analytic review reported that pain thresholds increased with age across several stimulus modalities[14]. In contrast, findings for measures of pain tolerance revealed no age differences in response to thermal and electrical stimuli, while pressure pain tolerance decreased with age. Racial/ethnic group differences in pain threshold and tolerance have also been the topic of two recent meta-analyses [13,21]. The studies revealed that, on average, African Americans reported lower pain thresholds and tolerances across multiple stimulus modalities, with small to moderate effects sizes for threshold and moderate to large effects sizes for tolerance. Notably, most studies of racial/ethnic group differences have compared African Americans and non-Hispanic whites, but infrequently include other racial/ethnic groups in sufficient numbers to permit comparisons.

This paper investigates the demographic predictors of pain sensitivity among a large cohort of volunteers, recruited for the OPPERA study (Orofacial Pain: Prospective Evaluation and Risk Assessment). Specifically, sex, age (years), and race (Non-Hispanic White [NHW], African American [AA], Hispanic, Asian) are used as predictors for 34 quantitative pain sensitivity measures. The sensory domains evaluated include heat pain, cutaneous mechanical (pricking) pain, and muscle/joint pressure pain.

Methods

Study Design and Participant Recruitment

Four sites recruited 3431 study participants: 1) The University of North Carolina at Chapel Hill, NC, 2) The University of Maryland, Baltimore, MD, 3) The University at Buffalo, NY, and 4) The University of Florida at Gainesville, FL. Inclusion criteria permitted either sex, any racial or ethnic group, and ages 18–44. Recruitment targeted individuals who were

either 1) of general good health or 2) identified as having temporomandibular disorder (TMD). Demographic statistics are provided in Tables 1 and 2. Detailed descriptions of the study design and recruitment protocols are provided elsewhere[25].

The OPPERA study was approved by IRBs at all four sites and at the data coordinating center, Battelle Memorial Institute. All participants provided informed consent for all procedures.

Demographic Data and Psychophysical Protocols

Demographic data were collected on individuals at baseline, including sex (male/female), age (in years), and race/ethnicity. The demographic questionnaire provided the following self-identifying racial/ethnic categories: White, Black/African American, Hispanic, Asian, Native Hawaiian/Pacific Islander, American Indian/Alaskan Native, and Other. (For simplicity, these will be referred to as racial categories throughout the paper.) Due to the low sample size for the latter three racial categories (Table 1), they were not included in any analyses.

Quantitative sensory testing (QST) was conducted in three sensory domains: 1) pressure pain, 2) mechanical cutaneous (pricking) pain, and 3) heat pain. Protocols are outlined below; more detailed information can be found elsewhere[10]. Pressure pain thresholds (PPT) were measured using a pressure algometer (Somedic; Horby, Sweden). Five facial and upper body sites were tested bilaterally: 1) overlying the temporalis muscle, 2) overlying the masseter muscle, 3) overlying the temporomandibular joint (TMJ), 4) overlying the upper trapezius muscle, and 5) overlying a proximal portion of the flexor carpi ulnaris muscle. The examiner manually applied the algometer to these sites using $1cm^2$ tip at 30 kPa/s increase in pressure until the participant indicated first feeling a pain sensation by pressing a button. If no pain indication was given by 600 kPa, 600 kPa was used as the threshold value. This procedure was repeated until two values were recorded within 20 kPa or until five trials were conducted. The mean of the two closest values was used as the PPT outcome variable for each body site.

Mechanical cutaneous pain (MCP) was assessed using weighted probes matching those used by the German Neuropathic Pain Network[24]. Probes exerted forces between 8 and 512 mN and stimuli were applied to the dorsal surface of the middle phalanx of digits two to four. MCP threshold was calculated as the geometric mean of five series of ascending and descending intensities, using a classical Method of Limits protocol. However, if a participant gave two consecutive “no” responses to the most intense stimulus (512mN), the process was stopped and a threshold value of 512 was recorded. After threshold was determined, single stimulus MCP ratings were determined using suprathreshold stimuli. Participants were instructed to provide a numerical rating of pain intensity when asked, using “0” for no pain and “100” for the most intense pain imaginable. Participants reported pain intensity on this 0–100 scale after a single stimulus was applied for 0.6 – 1.0 seconds. Additionally, participants were asked to provide pain intensity ratings once immediately after a series of ten stimuli was applied at a rate of 1Hz (to calculate temporal summation), and then once again at 15 and 30 seconds after this series (as measures of after-sensation). This testing series was conducted four times each with two different stimulus intensities: 256 and 512

mN. Temporal summation (TS) was calculated as the difference between the series of ten stimuli and the single stimulus ratings. If a participant reported a rating of 100, the procedure was stopped. Participants were informed that they could stop the test at any time by request.

Heat pain (HP) sensitivity was assessed using a commercially available thermal stimulator (Pathway; MEDOC; Ramat Yishai, Israel). Stimuli were applied to the ventral forearm. HP threshold was determined by placing the thermode in contact with the skin at 32°C and the temperature increased by 0.5°C per second until the participant pressed a button to indicate the first perception of pain. This final temperature was recorded as HP threshold. HP tolerance was conducted in the same manner, but the participant indicated when s/he could no longer tolerate the pain sensation. A temperature of 52°C was set as the upper limit for both these procedures. One study site used a different starting temperature (38°C rather than 32°C) for the threshold and tolerance protocols. These data were evaluated and there was no distributional difference among study sites for tolerance measurements; however, there was a noticeable distributional difference between this site and the other three in regards to threshold. Thus, for all statistical analyses of threshold, the HP threshold data collected at the higher starting temperature (809 participants) were omitted from analysis.

Following HP threshold and tolerance measures, ratings of suprathreshold heat stimuli and after-sensation were collected using the same verbal 0–100 rating scale. For this protocol, the thermode was placed on the skin at a temperature of 38°C, then ten pulses were given at 2.5 second intervals with a ramp rate of 20°C per second. The participant was instructed to report his/her peak pain intensity, and was cued to do so by the experimenter when the temperature reached its peak temperature, just before it began to return to the starting temperature. This test was conducted three times, using peak temperatures of 46°C, 48°C, and 50°C. If a participant reported a rating of 100 or requested to stop the stimulus series, the procedure was stopped. Four HP measures were derived for each temperature series: 1) the rating of the first stimulus of the series, 2) the sum of all 10 ratings in a series (area under the pain rating curve), 3) the highest pain rating minus the first stimulus pain rating, and 4) the slope of the first three pain ratings. The last two derived measures were considered indices of TS of pain.

Additionally, after-sensation ratings were collected at 15 and 30 sec after each series of ten heat pulses.

Statistical Methods

Missing data in the pain sensitivity variables were imputed using an expectation maximization (EM) method as described previously[10]. Inverse probability weighting[23] was used to adjust for over-representation of TMD cases in the cohort due to the casecontrol study design. The prevalence of TMD in the general population was assumed to be 5%, which is a conservative estimate of population prevalence. In this case-control study design, TMD cases are overrepresented. Thus, we performed weighted regression where TMD-free controls received a weight of 1 and chronic TMD cases received a weight of $(0.05N_0)/(0.95N_1)$, where N_0 denotes the number of controls in the cohort and N_1 represents the number of cases. Under this weighting scheme, the total weight of TMD cases in the

regression models is 5%, which would be the proportion of cases we would expect to observe had we sampled from the general population rather than using a case-control study design.

The association between the pain sensitivity variables and the demographic variables was evaluated using a series of regression models. The demographic variables were treated either as categorical (sex, race) or continuous (age). The outcome in each model was the pain sensitivity variable of interest. A separate model was performed for each variable of interest. The covariates in each model included age and dummy variables for study site, sex, and race (NHW, AA, Asian, Hispanic, or other). A second set of models was also calculated that included all possible interactions between age, sex, and race. The variance of the resulting regression coefficients was estimated using generalized estimating equations to compute the sandwich estimator of the variance[17].

For each regression model, the coefficients for each demographic variable of interest were computed, and the null hypothesis that a given regression coefficient is equal to 0 (corresponding to the null hypothesis of no association between a demographic variable and a pain sensitivity variable) was evaluated using Wald tests. In order to compare the relative strengths of the associations between a given demographic variable and the different measures of pain sensitivity, the adjusted effect size of each association was calculated by dividing each regression coefficient by its standard deviation. Confidence intervals for these adjusted effect sizes were computed using bootstrapping[4]. Statistical analysis was performed using SAS version 9.3 and R version 3.0.1.

Results

Sex Differences in Pain Sensitivity

Women showed greater sensitivity than men for 29 of 34 measures of pain sensitivity (Figures 1–2 and Tables 3–4). This included all of the PPT measures, all of the mechanical cutaneous pain measures, and most of the HP measures. Several measures of HP TS did not meet the Bonferroni-adjusted threshold for significance. The largest sex differences were observed in measures of pressure pain threshold and HP tolerance. Most measures of HP sensitivity showed large sex differences, while measures of HP aftersensations and mechanical pain sensitivity showed smaller (although still robust) differences.

Age Effects in Pain Sensitivity

In general pain sensitivity tended to decrease with age, although only seven of 34 variables showed an association that was significant at the Bonferroni-adjusted threshold (Figures 3–4 and Tables 3–4). Specifically, the TMJ and trapezius PPT's, the MCP single stimulus ratings, and HP aftersensations following more intense stimuli met the Bonferroni-adjusted threshold for significance. Most other measures of pressure pain and mechanical cutaneous pain sensitivity, while not showing statistically significant effects at the Bonferroni-adjusted threshold, showed the same trend of a decrease in pain sensitivity with increasing age. Only a very weak trend in the same direction was observed for age and the measures of HP sensitivity, other than the HP aftersensation measures noted above.

Race Differences in Pain Sensitivity

No significant associations were observed between race and any of the pressure pain thresholds (Tables 5 and 7; Fig. 5). AAs and Hispanics showed greater sensitivity than NHWs for nearly all measures of mechanical cutaneous pain, except for threshold. Asians showed slightly greater sensitivity to mechanical pain compared to NHWs, although the differences were small and generally not statistically significant (Tables 5 and 7; Fig. 6). AAs, Asians, and Hispanics all showed greater HP sensitivity than NHWs, with AAs and Hispanics showing the largest differences. These results were consistent across most measures of HP sensitivity and HP aftersensations (Tables 6 and 8; Figs. 7–8). However, no racial differences were observed with respect to measures of HP threshold, and significant differences in HP TS were observed for AAs, but only with 50°C stimuli (Table 6). Unexpectedly, that difference was in the direction of AAs showing less TS than NHWs.

Interactions among Demographic Variables

A series of separate regression analyses were performed to identify any statistically significant interactions among the three major demographic variables examined. Evaluating each QST measure separately, and all possible combinations of demographic variables, we found only two of 306 analyses to be significant at $p<0.001$. These two were 1) a sex by race interaction for MCP TS with the 512mN probe, and 2) an age by race interaction for HP tolerance. Based on these few effects, showing no apparent pattern, no further analysis of interaction effects were performed.

Discussion

Pain sensitivity measures varied significantly according to sex, age, and self-reported race across multiple pain domains: pressure, mechanical cutaneous, and heat pain. However, not all of the pain sensitivity measures showed the same profile of significant effects, reflecting underlying differences in the neurophysiological basis for the separate pain measures. Sex differences produced the largest effect sizes in this study, with women showing greater pain sensitivity than men in nearly all measures (29/34). Pain sensitivity decreased with age, however this effect was only statistically significant for 7/34 measures, and of very weak magnitude. Racial differences were observed for many of the pain sensitivity measures, largely in the direction of NHW showing the least pain sensitivity and AAs showing the greatest pain sensitivity. However, patterns of racial differences in pain sensitivity varied according to the individual pain measures, and were not found for any threshold measures.

Sex Differences in Pain Sensitivity

Uniformly, women had significantly lower pain thresholds across all three domains, and higher pain ratings for most MCP and HP measures compared to men. Women also showed greater HP TS, although significant differences for HP TS were only observed for the lowest temperature. Despite these statistically significant effects, the magnitude of the effects varied across measures. The sex differences for PPTs and HP tolerance were the largest (ES: 0.3–0.4), followed by those for ratings of individual HP stimuli (0.2–0.3), all of which are likely clinically meaningful. However, the sex differences for other measures, while statistically

significant, were of smaller effect sizes (all < 0.20), and could easily have failed to achieve statistical significance with a smaller sample size.

Many studies have evaluated sex differences in human pain sensitivity, and a majority finds women to be more sensitive than men. Nearly all other studies failed to find a significant sex difference, while only rarely does a study report greater pain sensitivity for men [5,11,20]. It is not clear what factors determine the expression of sex differences in experimental pain sensitivity, since significant sex differences can be observed (or not) for different stimulus modalities and different types of pain measures. The power of any given study is certainly critical to its ability to identify a significant sex difference. However, the literature reviews on this topic reveal that weaker statistical power, while certainly relevant, does not explain all the failures to observe significant sex differences. Sex differences clearly exist on the basis of both physiological and psychological features, and many factors from both domains can influence pain perception and reporting[9]. Thus, “sex differences” reflects a constellation of factors that have a role in determining one’s pain sensitivity, the influence of which can vary according to situational variables. Accordingly, it has been shown that the testing environment can influence whether or not significant sex differences in pain sensitivity are found. For instance, some studies have demonstrated a significant effect of experimenter gender upon subjects’ experimental pain sensitivity, particularly with respect to male study participants[1,7,15]. Yet, the failure to find such effects in other reports[2,18,19] supports the idea that multiple factors play a role in determining the expression of sex differences in pain sensitivity, with any one of them having greater of lesser prominence in any particular situation.

Age-Related Effects upon Pain Sensitivity

Despite a consistent trend of reduced pain sensitivity with age across many measures in this study, few variables showed significant age effects. Furthermore, the magnitude of the significant age effects was very small (all effect sizes < 0.1). The variables that did show significant age effects were scattered among the different stimulus modalities and the different types of pain measures, thus not showing any pattern with respect to these factors.

The literature on age-related effects upon experimental pain sensitivity has produced variable results. One systematic review characterized the literature as showing “consistent, although not invariable, age differences” in experimental pain. The most common differences were less sensitivity with age for weakly painful stimuli (higher thresholds and lower ratings for weaker suprathreshold stimuli), but greater sensitivity to stronger stimuli (higher pain ratings for more intense stimuli and reduced tolerance).[6] However, nearly every study compares a “younger” and “older” age group, and the cohort of the present study encompasses an age range that did not represent an “older” age group. Thus, this report is the first, to our knowledge, to explore age effects upon multiple measures of pain sensitivity within a more restricted 18–44 year old age range. The modest reduction in pain sensitivity observed within this age range likely reflects the more significant age effects observed in other studies which include an older age group.

Racial Differences in Pain Sensitivity

There were varying patterns of racial differences observed, depending upon the groups compared and the particular pain sensitivity variable evaluated. Contrasts of NHWs and AAs showed the largest number of significant racial differences, including 1) nearly all of the MCP tests, and 2) many of the HP tests, including suprathreshold ratings and aftersensations. These contrasts uniformly indicated greater pain sensitivity for AAs compared to NHW. Unexpectedly, HP TS showed no significant AA-NHW racial difference with lower temperatures, while the significant difference seen at 50°C was in the direction of less TS for AAs. This contrasts with several reports of greater HP TS for AAs[13,16]. This data set did show significant TS overall, with rating increases averaging 20–25 points on a 0–100 VAS[10]. One possible factor affecting these 50°C TS results is that the initial ratings for AAs were higher than for NHWs, leaving less room for ratings increases compared to NHWs. Of note, none of the threshold measures indicated a significant racial difference.

These results are generally congruent with previous literature. According to recent meta-analyses, AAs show greater pain sensitivity than NHWs in multiple studies evaluating HP intensity ratings, and tolerance, with small or no differences in HP threshold[13,21]. The only study evaluating AA-NHW differences in PPTs, reported no statistically significant differences, when tested on two of the same body sites as in the current study[22].

Hispanics showed greater pain sensitivity than NHW in all MCP measures (except threshold), and several measures of HP sensitivity. No difference was seen for any threshold or HP TS measure. Furthermore, there were no significant differences recognized between AAs and Hispanics, with the exception of HP aftersensation measures for 50°C stimuli (based on the absence of overlap of 95% CIs; Figure 8). Few comparable studies exist. Similar to our results, one study found significant HP tolerance differences between Hispanic and NHW groups, but no significant HP or pressure pain threshold differences[22].

Asians were more similar to NHW than AAs or Hispanics with respect to nearly all pain sensitivity measures. Compared to NHWs, Asians provided significantly higher HP ratings for suprathreshold stimuli, but showed no differences for HP aftersensation or TS measures. There were also no significant differences between Asians and NHWs for PPTs or any MCP measure. While some previous work has compared NHWs with specific Asian groups (i.e., Japanese, Indian, and others reviewed by Rahim-Williams et al.[21]), these are not sufficiently comparable to our sample of mixed Asian participants to warrant comparison.

The fact that pain thresholds from all types of stimuli failed to show significant racial differences, while other measures did show such differences, suggests that the basis for any racial differences is not related to tissue characteristics or inherent sensitivity of nociceptors. Rather, any differences observed for suprathreshold pain ratings or tolerance are more likely related to differences in central nociceptive processing, including the modulation of such processing imposed by cognitive, psychological, and/or affective differences[21].

Despite the many significant racial differences noted above, effect sizes were modest. The largest effect sizes observed - HP ratings and tolerance comparing NHW and AA – were between 0.14–0.20. For these same measures comparing NHW and Hispanics, the effect

sizes were between 0.10–0.15. For all the statistically significant mechanical cutaneous pain measures and HP aftersensation measures, effect sizes were under 0.15. Thus, even with the consistency of racial differences observed across multiple pain measures in the current study and parallel results from previous studies, quantitative differences among the races are small.

Limitations

The size of the study cohort and the wide array of pain sensitivity measures are very strong features of this study. However, the limited age range (18–44) in the study sample did not allow for a full evaluation of pain sensitivity across the life span. This prevented any meaningful comparisons with existing literature on age effects upon pain. Another limitation, relevant to sex differences, is the absence of control for menstrual cycle variation. While the literature contains reports of pain sensitivity fluctuations across the menstrual cycle of healthy women, a comparable number of studies report finding no cycle effects[11]. A recent review of this topic concluded: "… the majority of the more recent, well-controlled studies show that menstrual cycle phase has no effect on the perception of pain in healthy, pain-free women" (Iacovides et al., p. 1398).[12]

Conclusions

This large-scale study allowed for a powerful analysis of sex, age, and racial/ethnic effects upon a wide range of pain sensitivity measures. Greater pain sensitivity for women was robustly found for nearly all pain measures, however, only some of the effect sizes could be considered clinically significant. Age effects were weak or nonexistent, but interpretations are limited given the restricted age range evaluated. While significant racial/ethnic differences were observed for several pain measures, no differences were found for pain thresholds. With respect to suprathreshold pain, sensitivity generally followed the following pattern: AA>Hispanic>Asian>NHW, although few significant differences were observed between AA and Hispanic, or between Asian and NHW. These demographic differences in experimental pain sensitivity are likely to have relevance to clinical pain expression[3], as was recently demonstrated in the context of racial differences in OA knee pain[8].

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Disclosures

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This work was done at: University of North Carolina at Chapel Hill, NC; University at Buffalo, NY; University of Maryland-Baltimore, MD; University of Florida, FL; and Battelle Memorial Institute, NC.

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Highlights

- Greater female pain sensitivity is seen across many domains and measures.
- Non-Hispanic whites are often less pain sensitive than other racial/ethnic groups.
- Racial/ethnic differences are seen with suprathreshold, but not threshold pain.
- While many racial/ethnic differences are significant, they are of small effect size.
- Only a weak trend of decreased pain sensitivity with age is seen among 18–44 y.o.

Perspective

The influence of sex, age, and race/ethnicity upon various aspects of pain sensitivity, encompassing threshold and suprathreshold measures and multiple stimulus modalities, allows for a more complete evaluation of the relevance of these demographic factors to acute pain perception.

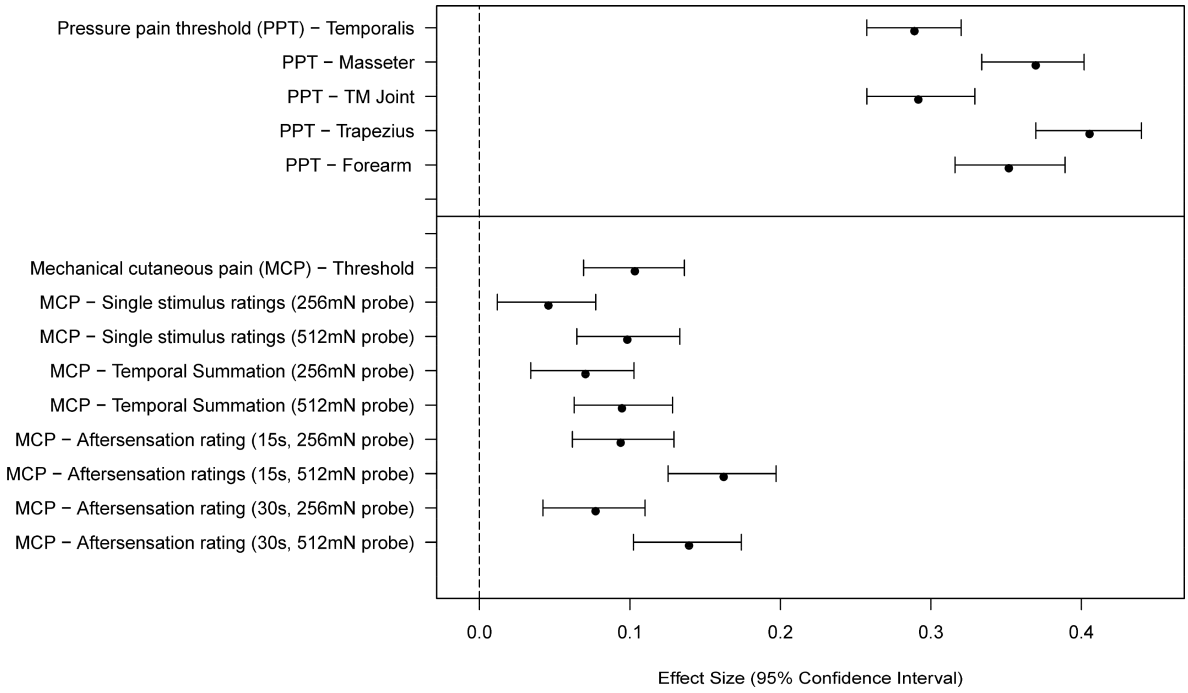

Figure 1.

Effect sizes (and 95% confidence intervals) for sex differences are shown for each of the mechanical pain sensitivity measures. Values are shown for each measure such that positive values denote a greater pain sensitivity (lower threshold or higher ratings) for women vs. men.

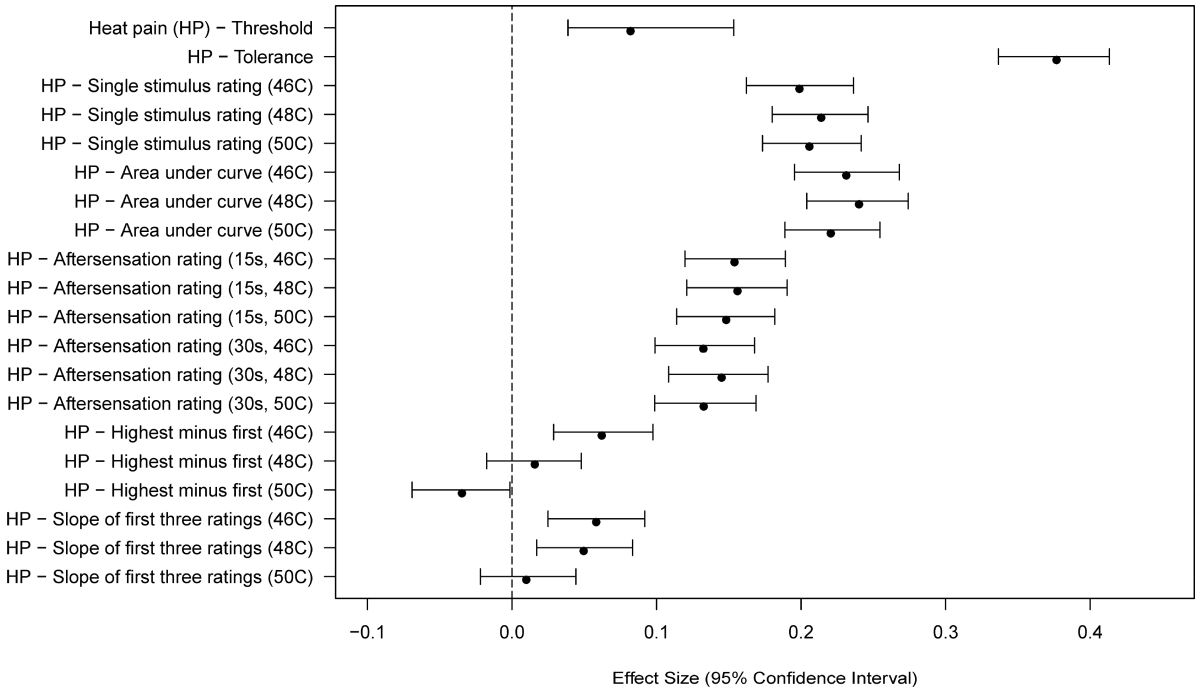

Figure 2.

Effect sizes (and 95% confidence intervals) for sex differences are shown for each of the heat pain sensitivity measures. Values are shown for each measure such that positive values denote a greater pain sensitivity (lower threshold or higher ratings) for women vs. men.

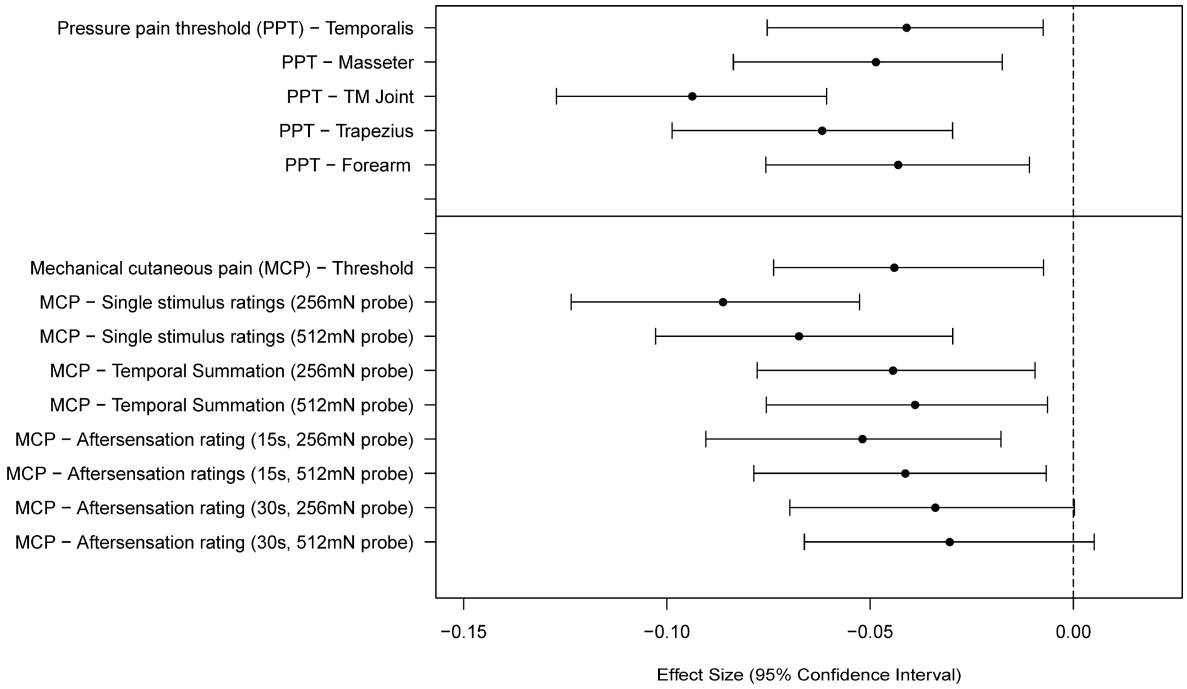

Figure 3.

Effect sizes (and 95% confidence intervals) for age effects are shown for each of the mechanical pain sensitivity measures. Values are shown for each measure such that negative values denote a decreased pain sensitivity (higher threshold or lower ratings).

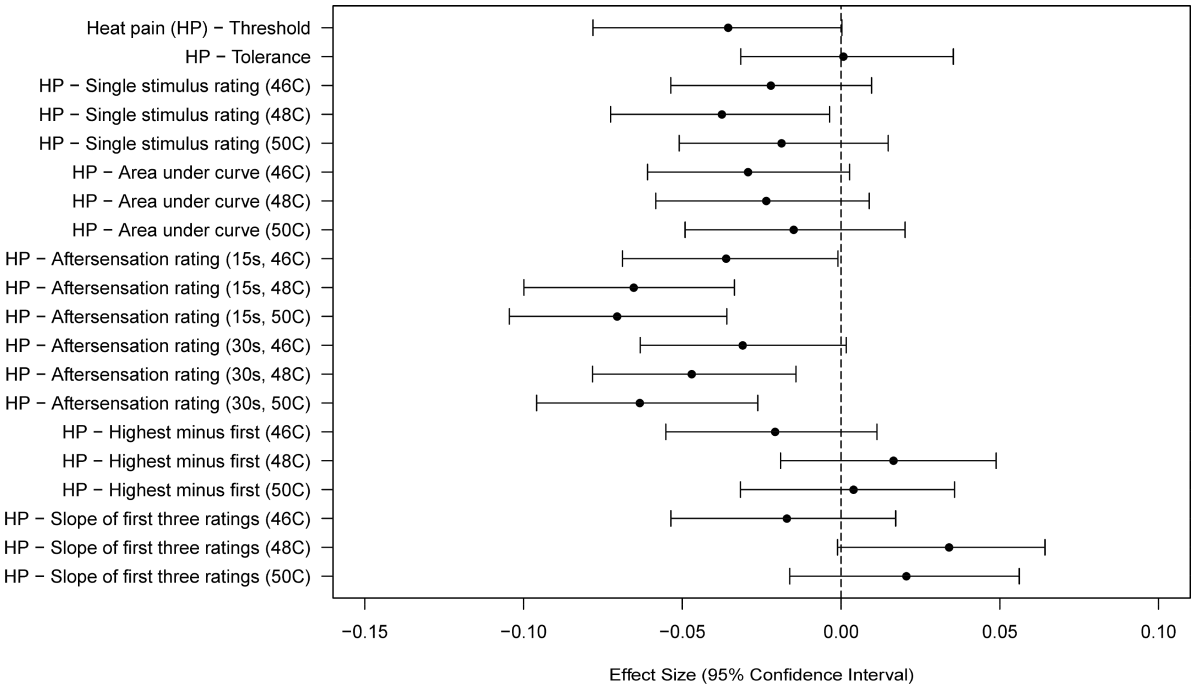

Figure 4.

Effect sizes (and 95% confidence intervals) for age effects are shown for each of the heat pain sensitivity measures. Values are shown for each measure such that negative values denote a decreased pain sensitivity (higher threshold or lower ratings).

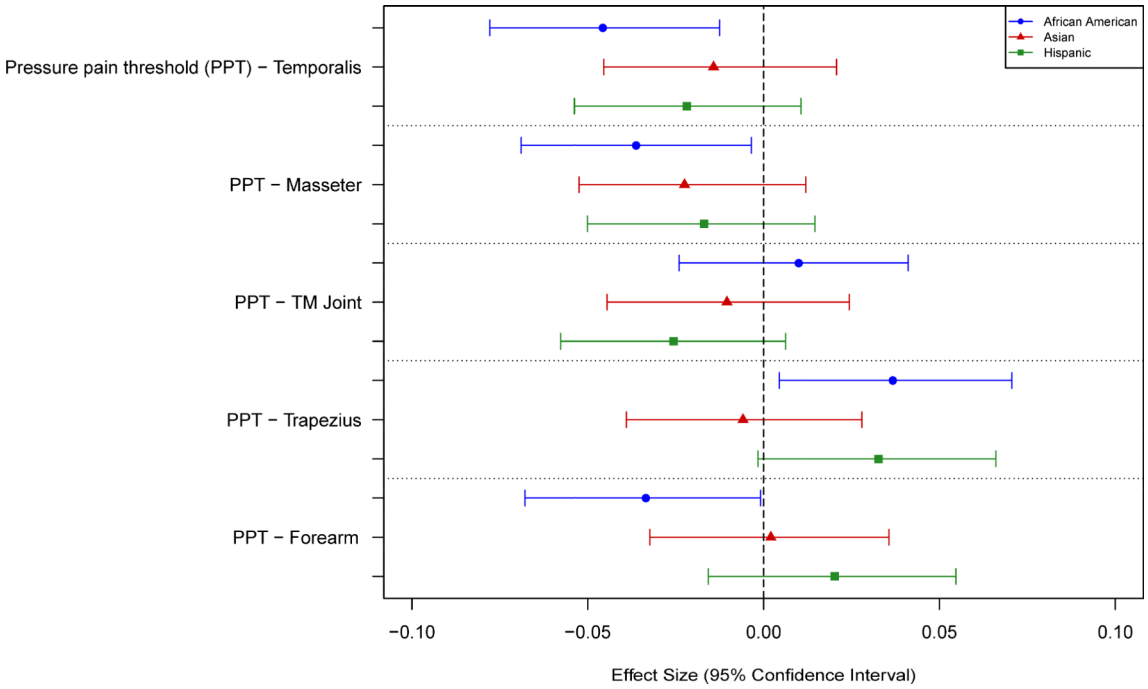

Figure 5.

Effect sizes (and 95% confidence intervals) for race/ethnicity differences are shown for the pressure pain threshold measures. Values are shown for each measure such that positive values denote a greater pain sensitivity (lower threshold) for a given race/ethnicity vs non-Hispanic whites.

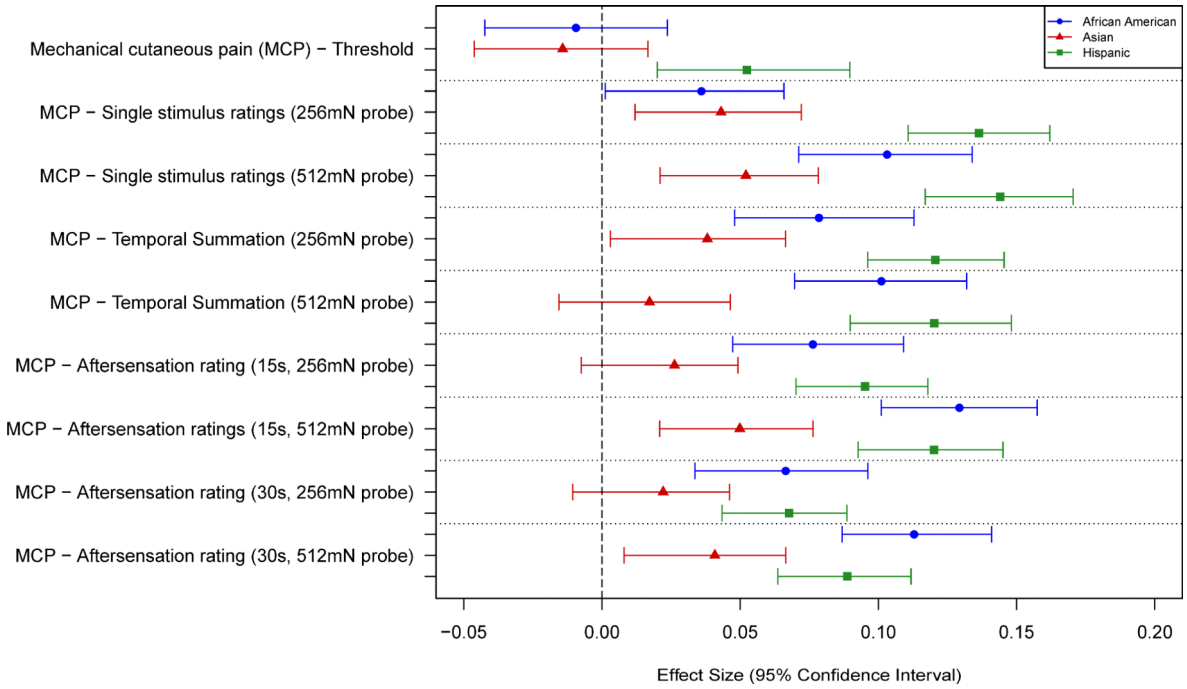

Figure 6.

Effect sizes (and 95% confidence intervals) for race/ethnicity differences are shown for the mechanical cutaneous pain measures. Values are shown for each measure such that positive values denote a greater pain sensitivity (lower threshold or higher ratings) for a given race/ethnicity vs non-Hispanic whites.

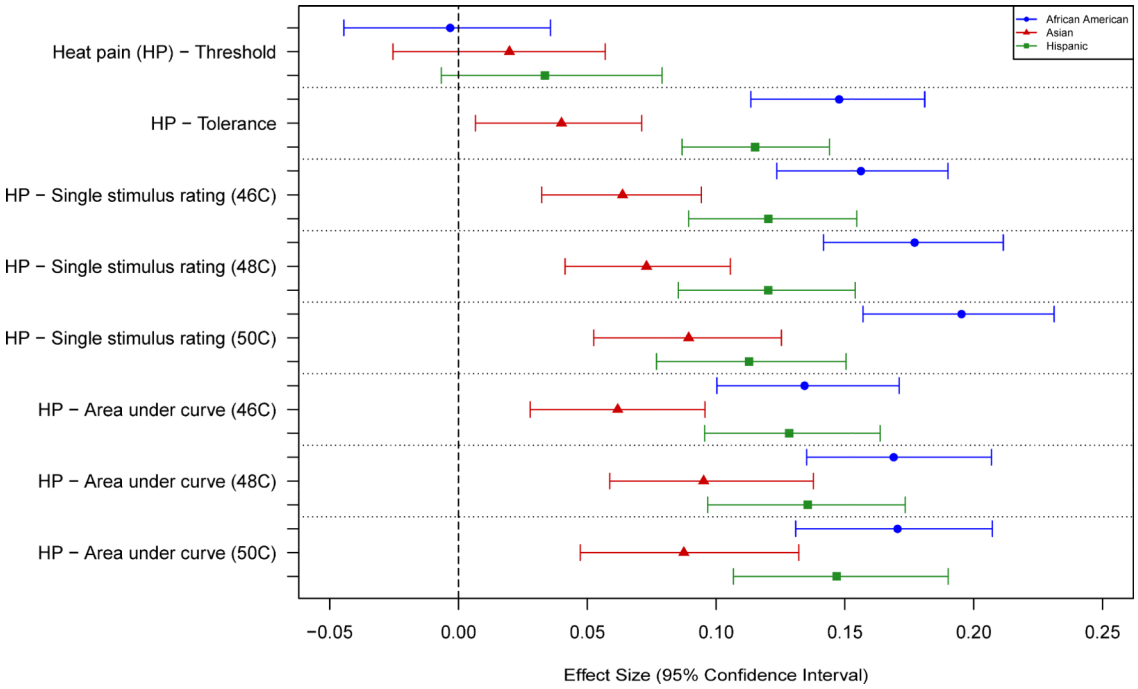

Figure 7.

Effect sizes (and 95% confidence intervals) for race/ethnicity differences are shown for several heat pain measures. Values are shown for each measure such that positive values denote a greater pain sensitivity (lower threshold or higher ratings) for a given race/ethnicity vs non-Hispanic whites.

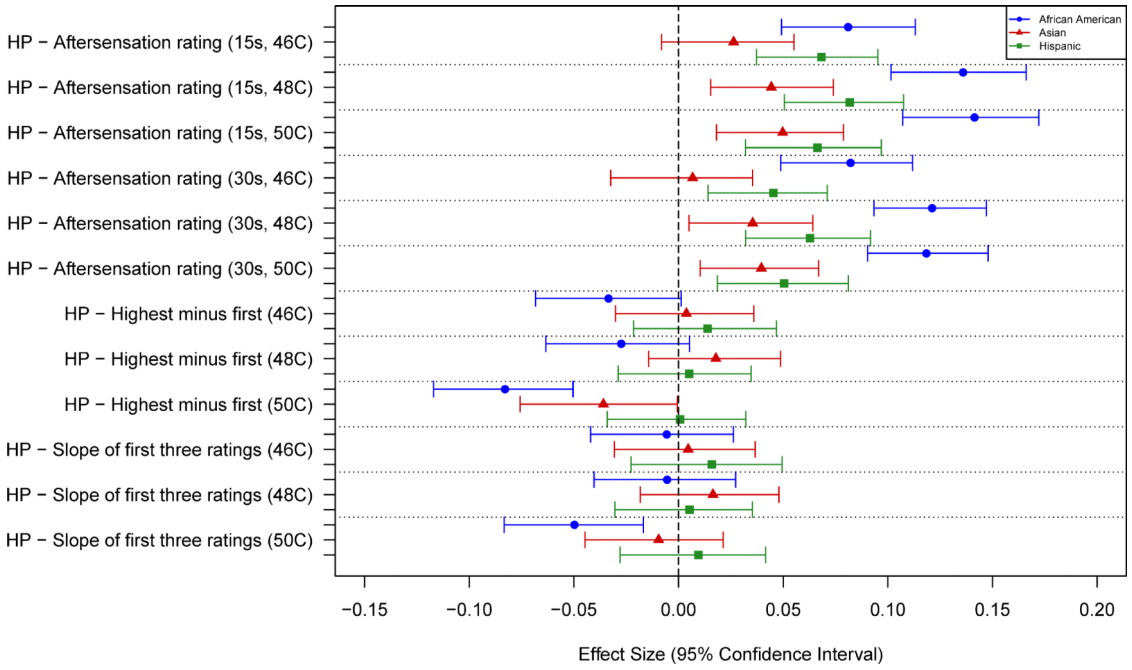

Figure 8.

Effect sizes (and 95% confidence intervals) for race/ethnicity differences are shown for heat pain measures related to aftersensation and temporal summation. Values are shown for each measure such that positive values denote a greater pain sensitivity (higher ratings) for a given race/ethnicity vs non-Hispanic whites.

Table 1:

Participant numbers by sex and race/ethnicity

	NHW	AA	Asian	Hispanic	Other	Total (%)
Male	752	432	74	144	21	1423 (41.5)
Female	1077	616	112	183	20	2008 (58.5)
Total (%)	1829 (53.3)	1048 (30.5)	186 (5.4)	327 (9.5)	41 (1.2)	

Table 2:

Ages for Different Participant Groups

	Male		Female	
	Mean	SE	Mean	SE
NHW	25.0	0.2	26.1	0.2
AA	32.3	0.4	30.2	0.3
Asian	23.0	0.6	24.2	0.5
Hispanic	25.1	0.4	24.3	0.4

Table 3:

Model Estimates and Significance for Sex and Age Covariates for Pressure Pain Threshold and Mechanical Cutaneous Pain Outcomes

	---Sex---				---Age---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate[2]**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Pressure Pain Threshold								
Temporalis	−48.30	167.07	−16.901	**<.0001**	4.75	115.81	2.399	0.0165
Masseter	−55.79	150.92	−21.613	**<.0001**	5.16	106.12	2.841	0.0045
TMJ	−38.48	131.95	−17.047	**<.0001**	8.72	93.01	5.481	**<.0001**
Trapezius	−111.04	273.94	−23.699	**<.0001**	12.09	195.55	3.614	**0.0003**
Epicondyle	−91.60	260.38	−20.566	**<.0001**	8.14	188.93	2.520	0.0117
Mechanical Cutaneous Pain								
Threshold	−35.74	346.27	−6.035	**<.0001**	10.91	247.72	2.575	0.0100
Single Stimulus Rating - 256mN Probe	1.14	24.83	2.678	0.0074	−1.43	16.58	−5.040	**<.0001**
Single Stimulus Rating - 512mN Probe	3.76	38.30	5.743	**<.0001**	−1.83	27.18	−3.945	**<.0001**
Temporal Summation - 256mN Probe	1.67	23.71	4.116	**<.0001**	−0.75	16.82	−2.594	0.0095
Temporal Summation - 512mN Probe	3.08	32.50	5.532	**<.0001**	−0.93	23.76	−2.277	0.0228
Aftersensation Rating (15s) - 256mN Probe	1.37	14.57	5.487	**<.0001**	−0.53	10.23	−3.032	0.0024
Aftersensation Rating (15s) - 512mN Probe	4.58	28.22	9.487	**<.0001**	−0.86	20.84	−2.417	0.0157
Aftersensation Rating (30s) - 256mN Probe	0.73	9.49	4.510	**<.0001**	−0.23	6.71	−1.986	0.0470
Aftersensation Rating (30s) - 512mN Probe	2.89	20.75	8.144	**<.0001**	−0.45	14.66	−1.778	0.0754

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

1. Significance evaluated at Bonferroni corrected level of 0.001

2. Estimate value for age effects represents difference per decade

Table 4:

Model Estimates and Significance for Sex and Age Covariates for Heat Pain Outcomes

	---Sex---				---Age (Decades)---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Heat Pain								
Threshold	−1.31	16.04	−3.907	**<.0001**	0.42	11.87	1.694	0.0902
Tolerance	−1.66	4.407	−22.023	**<.0001**	−0.00	2.95	−0.044	0.9652
Single Stimulus Rating - 46C	11.40	57.33	11.626	**<.0001**	−0.96	43.57	−1.295	0.1955
Single Stimulus Rating - 48C	12.81	59.90	12.503	**<.0001**	−1.67	44.38	−2.195	0.0281
Single Stimulus Rating - 50C	12.78	62.13	12.024	**<.0001**	−0.85	45.25	−1.096	0.2731
Area Under Curve - 46C	123.61	534.50	13.520	**<.0001**	−11.65	397.39	−1.714	0.0866
Area Under Curve - 48C	126.40	526.49	14.036	**<.0001**	−9.01	382.32	−1.378	0.1683
Area Under Curve - 50C	110.71	502.20	12.888	**<.0001**	−5.37	360.03	−0.872	0.3830
Aftersensation Rating (15s) - 46C	4.48	29.13	9.001	**<.0001**	−0.79	21.87	−2.117	0.0343
Aftersensation Rating (15s) - 48C	5.59	35.82	9.117	**<.0001**	−1.77	27.06	−3.819	**0.0001**
Aftersensation Rating (15s) - 50C	5.76	38.89	8.660	**<.0001**	−2.03	28.78	−4.124	**<.0001**
Aftersensation Rating (30s) - 46C	2.78	21.03	7.740	**<.0001**	−0.50	16.00	−1.812	0.0699
Aftersensation Rating (30s) - 48C	4.08	28.13	8.473	**<.0001**	−1.02	21.68	−2.751	0.0059
Aftersensation Rating (30s) - 50C	3.95	29.80	7.753	**<.0001**	−1.41	22.16	−3.707	**0.0002**
Highest Rating Minus First - 46C	2.66	42.91	3.626	**0.0003**	−0.70	33.50	−1.215	0.2245
Highest Rating Minus First - 48C	0.72	45.68	0.923	0.3558	0.60	36.13	0.965	0.3343
Highest Rating Minus First - 50C	−1.55	44.60	−2.028	0.0426	0.13	33.40	0.228	0.8196
Slope of First Three Ratings - 46C	0.90	15.36	3.408	**0.0007**	−0.20	11.76	−0.998	0.3182
Slope of First Three Ratings - 48C	0.82	16.53	2.900	0.0037	0.46	13.39	1.990	0.0466

	---Sex---				---Age (Decades)---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value**[1]	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value**[1]
Slope of First Three Ratings - 50C	0.17	16.93	0.580	0.5617	0.28	13.57	1.203	0.2290

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

1. Significance evaluated at Bonferroni corrected level of 0.0015

2. Estimate value for age effects represents difference per decade

Table 5:

Model Estimates and Significance for Self-Identified Race (NHW vs. African American or Asian) for Pressure Pain Threshold and Mechanical Cutaneous Pain Outcomes

	---African American---				---Asian---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Pressure Pain Threshold								
Temporalis	10.05	219.50	2.676	0.0075	4.73	332.63	0.832	0.4056
Masseter	7.17	197.43	2.122	0.0338	7.03	312.74	1.315	0.1887
TMJ	−1.64	164.64	−0.583	0.5602	2.89	277.62	0.609	0.5422
Trapezius	−12.86	350.15	−2.148	0.0317	3.33	570.43	0.342	0.7327
Epicondyle	11.38	339.41	1.960	0.0500	−1.16	557.92	−0.121	0.9033
Mechanical Cutaneous Pain								
Threshold	4.13	439.06	0.549	0.5827	11.18	785.62	0.832	0.4055
Single Stimulus Rating - 256mN Probe	1.19	33.12	2.104	0.0354	2.62	60.85	2.520	0.0117
Single Stimulus Rating - 512mN Probe	5.48	53.15	6.030	**<.0001**	4.92	94.54	3.044	0.0023
Temporal Summation - 256mN Probe	2.58	32.88	4.591	**<.0001**	2.27	59.63	2.229	0.0258
Temporal Summation - 512mN Probe	4.51	44.64	5.909	**<.0001**	1.29	75.00	1.006	0.3146
Aftersensation Rating (15s) - 256mN Probe	1.56	20.43	4.460	**<.0001**	1.19	45.46	1.534	0.1251
Aftersensation Rating (15s) - 512mN Probe	5.42	41.91	7.559	**<.0001**	3.89	77.92	2.916	0.0035
Aftersensation Rating (30s) - 256mN Probe	0.89	13.45	3.885	**0.0001**	0.68	30.95	1.294	0.1956
Aftersensation Rating (30s) - 512mN Probe	3.61	32.00	6.601	**<.0001**	2.40	58.76	2.388	0.0169

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

[1] Significance evaluated at Bonferroni corrected level of 0.0015

Table 6:

Model Estimates and Significance for Self-Identified Race (NHW vs. African American or Asian) for Heat Pain Outcomes

	---African American---				---Asian---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Heat Pain								
Threshold	0.07	20.71	0.153	0.8782	−0.41	20.72	−0.942	0.3461
Tolerance	−0.81	5.47	−8.639	**<.0001**	−0.38	9.53	−2.337	0.0194
Single Stimulus Rating - 46C	12.26	78.47	9.131	**<.0001**	8.23	129.20	3.724	**0.0002**
Single Stimulus Rating - 48C	14.21	80.30	10.349	**<.0001**	9.96	136.35	4.268	**<.0001**
Single Stimulus Rating - 50C	15.65	80.14	11.415	**<.0001**	12.45	139.35	5.223	**<.0001**
Area Under Curve - 46C	95.24	708.93	7.854	**<.0001**	75.11	1215.19	3.614	**0.0003**
Area Under Curve - 48C	114.21	676.25	9.873	**<.0001**	107.97	1134.57	5.563	**<.0001**
Area Under Curve - 50C	104.53	613.43	9.962	**<.0001**	95.49	1091.84	5.113	**<.0001**
Aftersensation Rating (15s) - 46C	3.41	42.14	4.737	**<.0001**	1.85	70.22	1.540	0.1236
Aftersensation Rating (15s) - 48C	6.93	50.99	7.948	**<.0001**	3.84	86.54	2.592	0.0095
Aftersensation Rating (15s) - 50C	7.74	54.71	8.268	**<.0001**	4.79	96.18	2.909	0.0036
Aftersensation Rating (30s) - 46C	2.61	31.81	4.802	**<.0001**	0.31	46.59	0.395	0.6927
Aftersensation Rating (30s) - 48C	5.04	41.56	7.084	**<.0001**	2.28	64.30	2.070	0.0384
Aftersensation Rating (30s) - 50C	5.10	43.08	6.925	**<.0001**	3.02	76.26	2.314	0.0207
Highest Rating Minus First - 46C	−1.89	56.62	−1.954	0.0507	0.35	93.50	0.221	0.8254
Highest Rating Minus First - 48C	−1.64	59.81	−1.600	0.1096	1.92	107.48	1.045	0.2960
Highest Rating Minus First - 50C	−4.84	58.42	−4.845	**<.0001**	−3.33	92.78	−2.097	0.0360
Slope of First Three Ratings - 46C	−0.12	21.06	−0.330	0.7416	0.16	33.59	0.271	0.7868

	---African American---				---Asian---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Slope of First Three Ratings - 48C	−0.13	22.97	−0.321	0.7479	0.63	37.94	0.964	0.3352
Slope of First Three Ratings - 50C	−1.15	23.07	−2.906	0.0037	−0.37	39.20	−0.555	0.5786

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

1. Significance evaluated at Bonferroni corrected level of 0.0015

Table 7:

Model Estimates and Significance for Self-Identified Race (NHW vs. Hispanic or Other) for Pressure Pain Threshold and Mechanical Cutaneous Pain Outcomes

	---Hispanic---				---Other---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Pressure Pain Threshold								
Temporalis	6.47	296.22	1.276	0.2019	3.48	628.98	0.324	0.7461
Masseter	4.33	256.10	0.988	0.3229	4.35	581.74	0.437	0.6619
TMJ	5.83	227.52	1.497	0.1343	2.48	459.50	0.315	0.7528
Trapezius	−15.09	462.08	−1.910	0.0562	11.21	1184.93	0.553	0.5803
Epicondyle	−9.34	462.16	−1.182	0.2374	18.35	1192.83	0.900	0.3684
Mechanical Cutaneous Pain								
Threshold	−29.60	564.55	−3.065	0.0022	15.21	1458.37	0.610	0.5421
Single Stimulus Rating - 256mN Probe	8.79	64.44	7.975	**<.0001**	0.73	76.51	0.554	0.5794
Single Stimulus Rating - 512mN Probe	12.08	83.87	8.423	**<.0001**	3.39	159.31	1.243	0.2138
Temporal Summation - 256mN Probe	6.18	51.28	7.050	**<.0001**	3.94	154.12	1.496	0.1347
Temporal Summation - 512mN Probe	7.44	61.90	7.031	**<.0001**	4.20	191.62	1.281	0.2003
Aftersensation Rating (15s) - 256mN Probe	3.60	37.78	5.564	**<.0001**	−0.02	28.22	−0.051	0.9593
Aftersensation Rating (15s) - 512mN Probe	7.47	62.12	7.025	**<.0001**	6.30	189.94	1.939	0.0525
Aftersensation Rating (30s) - 256mN Probe	1.66	24.46	3.956	**<.0001**	0.22	18.97	0.681	0.4957
Aftersensation Rating (30s) - 512mN Probe	3.85	43.36	5.192	**<.0001**	4.69	153.74	1.785	0.0742

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

1. Significance evaluated at Bonferroni corrected level of 0.0015

Table 8:

Model Estimates and Significance for Self-Identified Race (NHW vs. Hispanic or Other) for Heat Pain Outcomes

	---Hispanic---				---Other---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value[1]**
Heat Pain								
Threshold	−0.67	19.99	−1.599	0.1097	−0.58	26.07	−1.052	0.2928
Tolerance	−0.95	8.23	−6.733	<.0001	−0.65	22.57	−1.690	0.0910
Single Stimulus Rating - 46C	12.27	101.98	7.031	**<.0001**	8.65	278.18	1.818	0.0691
Single Stimulus Rating - 48C	12.74	105.98	7.029	**<.0001**	10.59	295.48	2.095	0.0361
Single Stimulus Rating - 50C	12.11	107.40	6.592	**<.0001**	10.33	290.08	2.082	0.0373
Area Under Curve - 46C	117.88	918.41	7.504	**<.0001**	55.85	2531.39	1.290	0.1971
Area Under Curve - 48C	118.99	877.59	7.927	**<.0001**	67.82	2440.65	1.625	0.1043
Area Under Curve - 50C	115.16	784.44	8.582	**<.0001**	71.59	2131.18	1.964	0.0495
Aftersensation Rating (15s) - 46C	3.81	55.75	3.991	**<.0001**	4.77	186.33	1.498	0.1342
Aftersensation Rating (15s) - 48C	5.41	66.04	4.787	**<.0001**	5.52	204.56	1.579	0.1144
Aftersensation Rating (15s) - 50C	4.46	67.23	3.880	**0.0001**	4.00	201.32	1.163	0.2449
Aftersensation Rating (30s) - 46C	1.82	40.15	2.652	0.0080	4.18	165.66	1.477	0.1398
Aftersensation Rating (30s) - 48C	3.22	51.27	3.674	**0.0002**	5.00	181.56	1.611	0.1071
Aftersensation Rating (30s) - 50C	2.57	50.95	2.949	0.0032	3.85	168.16	1.338	0.1810
Highest Rating Minus First - 46C	1.01	72.77	0.814	0.4156	−2.47	191.23	−0.756	0.4499
Highest Rating Minus First - 48C	0.41	79.41	0.299	0.7646	−4.04	200.46	−1.179	0.2383
Highest Rating Minus First - 50C	0.06	81.50	0.043	0.9657	−3.42	222.36	−0.895	0.3709
Slope of First Three Ratings - 46C	0.39	24.55	0.931	0.3517	0.19	80.96	0.138	0.8902

	---Hispanic---				---Other---			
	Estimate	**Standard Deviation**	**Wald t-Statistic**	**p-value**[1]	**Estimate**	**Standard Deviation**	**Wald t-Statistic**	**p-value**[1]
Slope of First Three Ratings - 48C	0.13	25.10	0.310	0.7567	−0.60	79.92	−0.440	0.6602
Slope of First Three Ratings - 50C	0.28	29.36	0.555	0.5791	−1.10	91.95	−0.702	0.4825

All estimates are compared to a referent White non-Hispanic male, controlling for site and TMD status

1. Significance evaluated at Bonferroni corrected level of 0.0015