Published in final edited form as:
Psychosom Med. 2014 May ; 76(4): 302–310. doi:10.1097/PSY.0000000000000058.

Temporal summation of pain as a prospective predictor of clinical pain severity in adults aged 45 years and above with knee osteoarthritis: ethnic differences

Burel R. Goodin, Ph.D.[1,*], **Hailey W. Bulls, B.S**[1], **Matthew S. Herbert, M.A.**[1], **Jessica Schmidt, B.A.**[1], **Christopher D. King, Ph.D.**[2,3], **Toni L. Glover, M.S.N., A.R.N.P., Ph.D.**[2,3,4], **Adriana Sotolongo, M.P.H.**[5], **Kimberly T. Sibille, Ph.D.**[2,3], **Yenisel Cruz-Almeida, M.S.P.H., Ph.D.**[2,3], **Roland Staud, M.D.**[3,6], **Barri J. Fessler, M.S.P.H., M.D.**[5], **David T. Redden, Ph.D.**[7], **Laurence A. Bradley, Ph.D.**[5], and **Roger B. Fillingim, Ph.D.**[2,3]

[1]University of Alabama at Birmingham, Department of Psychology, Birmingham AL 35294, USA

[2]University of Florida, College of Dentistry, Gainesville FL 32610, USA

[3]University of Florida, Pain Research and Intervention Center of Excellence (PRICE), Gainesville FL, 32610, USA

[4]University of Florida, College of Nursing, Gainesville FL 32610, USA

[5]University of Alabama at Birmingham, School of Medicine, Division of Clinical Immunology and Rheumatology, Birmingham AL 35294, USA

[6]University of Florida, College of Medicine, Gainesville FL 32610, USA

[7]University of Alabama at Birmingham, School of Public Health, Department of Biostatistics, Birmingham AL 35294, USA

Abstract

Objective—Enhanced pain facilitation is reportedly an important contributor to the clinical pain experiences of individuals with knee osteoarthritis (OA). Ethnic differences in the prevalence and severity of knee OA in addition to associated pain are also well documented. Temporal summation (TS) of pain is a widely applicable quantitative sensory testing method that invokes neural mechanisms related to pain facilitatory processes. This study tested whether TS of pain, an index of pain facilitation, differentially predicts the clinical pain experiences of African Americans and non-Hispanic Whites with symptomatic knee OA.

Methods—A total of 225 study participants underwent assessment of TS of mechanical and heat pain stimuli applied to their most symptomatic knee and their ipsilateral hand (mechanical) or forearm (heat). Using telephone-based surveys, participants subsequently reported their average and worst clinical pain severity across four consecutive weeks following assessment of TS.

Results—In predicting future clinical pain, ethnicity interacted with TS of mechanical pain (but not heat pain), such that TS of mechanical pain at the knee significantly predicted greater clinical

[*]Corresponding author: Tel.: +1-205-934-8743; fax: +1-205-975-6110. bgoodin1@uab.edu. Address for corresponding author: B.Goodin, University of Alabama at Birmingham, 1300 University Boulevard, Campbell Hall, Room 328, Birmingham, AL 35294..

ratings of average (b = .02, p = .016) and worst (b = .02, p = .044) clinical pain for non-Hispanic Whites but not African Americans (p's > .30).

Conclusions—These results reveal the importance of considering ethnicity when examining pain facilitation and the clinical pain of individuals with symptomatic knee OA. The results of this study are discussed in terms of ethnic differences in the predictors of clinical pain experiences among African Americans and non-Hispanic Whites with knee OA.

Keywords

Pain; Knee Osteoarthritis (OA); Ethnicity; Pain Facilitation; Temporal Summation (TS)

Introduction

Historically, knee osteoarthritis (OA) was considered a peripheral disease, with nociceptive damage at the joint presumed to account primarily for the experience of pain. Recently, it has been suggested that altered central processing of nociceptive information is also an important contributor to painful knee OA (1). Specifically, knee OA appears to be characterized by an altered pain modulatory balance reflecting an enhancement of pain facilitation (1-3). Evidence of enhanced pain facilitation in knee OA has emerged from laboratory research using quantitative sensory testing to assess central pain processes (3). Temporal summation (TS) of pain is a quantitative sensory testing method that is widely incorporated in experimental studies to invoke neural mechanisms related to pain facilitation (4-7). Studies from our group and others have shown greater TS of pain among individuals with knee OA compared to matched controls without knee OA, particularly for those who report severe clinical pain (8,9). Further support for the role of pain facilitation in painful knee OA comes from pre-clinical research showing that continuous and intense input from afferent nociceptive pathways originating in the OA-damaged knee joint potentiates central sensitization processes (10,11). Enhanced pain facilitation may also help explain the known discordance between radiographic changes and clinical pain associated with knee OA (12-14). Support for this hypothesis comes from previous studies which have shown that TS of pain correlates with knee OA-related clinical pain reports (2); however, much of this evidence has been cross-sectional, making it difficult to ascertain the directionality of the relationships. Whether quantitative sensory tests of pain facilitation such as TS of pain might be useful for prospectively predicting future reports of knee OA clinical pain severity has received less attention.

When examining predictors of knee OA clinical pain in human studies, it is important to consider the ethnicity of study participants. This is because previous research has noted significant ethnic differences in the presence of knee OA and its symptoms, particularly pain (15-17). These differences include findings of greater knee OA prevalence and associated pain severity for African Americans compared to non-Hispanic Whites (18). African Americans also tend to describe the qualities of their painful experiences differently than do non-Hispanic Whites, with a greater emphasis on the affective—motivational dimension of pain relative to the sensory—discriminative dimension (19-24). Moreover, among healthy adults and individuals with painful conditions like knee OA, African Americans demonstrate greater TS of pain (21) and generally exhibit greater sensitivity to suprathreshold measures

of experimentally-induced pain compared to their non-Hispanic White counterparts (22-24). Taken together, these findings suggest the possibility of greater pain facilitatory processes among both healthy African Americans and those with chronically painful conditions. Although it has not been empirically tested to date, it seems plausible that the relationship between pain facilitation and clinical pain severity in knee OA could differ according to individuals' ethnic background. This is consistent with the biopsychosocial model, which suggests that the experience of pain is shaped by interactions among biological, psychological, and social variables (25), all of which can vary according to individuals' ethnicity.

This study included a sample of community-dwelling African American and non-Hispanic White adults aged 45 years and above with symptomatic knee OA. The goal was to determine whether TS of pain, an experimental index of pain facilitation, prospectively predicted clinical ratings of knee OA-related pain severity, and whether the strength of any such prediction varied across ethnic groups. TS of pain was examined using mechanical and heat stimuli applied to the most symptomatic knee and the ipsilateral hand (mechanical) or forearm (heat). The following hypotheses were tested: 1) African Americans and non-Hispanic Whites will differ in TS of pain and ratings of clinical pain severity, and 2) the ability of TS of pain to significantly predict clinical pain severity ratings will vary between African Americans and non-Hispanic Whites.

Methods

Participants

This study is part of a larger ongoing project that aims to enhance the understanding of ethnic differences in pain and limitations among individuals with knee OA (Understanding Pain and Limitations in Osteoarthritic Disease, UPLOAD) (26,27). The UPLOAD project is a multi-site investigation that recruits participants at the University of Florida and the University of Alabama at Birmingham. The participants described in this study were recruited at both study sites between January, 2010 and January, 2013. The measures and procedures described below are limited to those involved in this study. Participants were recruited via posted fliers, radio and print media advertisements, orthopedic clinic recruitment, and word-of-mouth referral. All procedures were reviewed and approved by the University of Florida and University of Alabama-Birmingham Institutional Review Boards.

Only those participants who identified their ethnic background as African American or non-Hispanic White were included in this study. This included 225 community-dwelling adults aged 45 years and above with knee OA, who met inclusion criteria and were enrolled in the UPLOAD study as of January, 2013. The majority of the sample was comprised of women (68%), and participants' sex was coded as 0 = women and 1 = men. Of these participants, 54% self-identified as African American, while the remaining 46% self-identified as non-Hispanic White. Ethnicity was coded as 0 = non-Hispanic white and 1 = African American. All participants provided informed consent and were compensated for their participation.

Procedures

Individuals with symptomatic knee OA who were interested in being part of this study were screened for eligibility during an initial telephone screening and a subsequent health assessment session. Those individuals who were eligible to continue in the study then completed a quantitative sensory testing battery which included TS of mechanical and heat pain assessment. Following quantitative sensory testing, study participants completed weekly phone surveys addressing their experiences of clinical pain severity related to their knee OA.

Telephone Screening

All of the current study's participants completed study screening via telephone to determine eligibility for study inclusion. The following demographic and physical health data were obtained as part of the screening: self-reported sex, age, and ethnicity, as well as a health history pertaining to painful experiences related to knee OA. Individuals who endorsed knee pain and met initial study inclusion criteria presented approximately one to two weeks later for a health assessment session. Criteria for full inclusion into the current study can be found elsewhere in recent publications written by our group using data derived from the UPLOAD project (26,27).

Health Assessment Session

During the health assessment session, additional health history information was collected to confirm study eligibility. Additionally, all participants underwent a bilateral knee joint evaluation by an experienced examiner (i.e., the study rheumatologist or nurse practitioner) to confirm their diagnosis of osteoarthritis using the American College of Rheumatology clinical criteria for knee OA (28). Based on the physical exam and the participant's self-report, the affected knee was used for participants with unilateral knee OA and the most symptomatic knee was chosen for those with bilateral knee OA. The chosen knee was designated as the index knee. Height and weight were measured for the calculation of body mass index (BMI). The Center for Epidemiological Studies-Depression Scale (CES-D; described below) was completed to assess for depressive symptoms. Also as part of the health assessment session, participants reported their annual household income and number of current occupants residing in the household. As an indicator of socioeconomic status, it was determined whether a participant fell above or below the poverty line based upon reported annual household income and number of household occupants using the 2012 Health and Human Services poverty guidelines (29). Poverty status was coded as 0 = below the poverty line and 1 = above the poverty line.

Quantitative Sensory Testing Session

Between one and four weeks following the health assessment session, participants completed the quantitative sensory testing session. On the day of the quantitative sensory testing session, all participants underwent a series of controlled sensory stimulation procedures to assess TS of mechanical and heat pain, respectively. The order of presentation of mechanical and heat stimulation was randomly counterbalanced. Prior to commencing the QST session, participants were provided with audio recorded instructions regarding how to

rate the intensity of the pain produced by the mechanical and heat TS procedures on a "0-100" numeric rating scale, such that 0 = no pain and 100 = the most intense pain imaginable. Following these instructions, all participants were asked to use the 0-100 numeric rating scale to rate any current clinical pain they might be experiencing in their index knee.

TS of mechanical pain was assessed using a nylon monofilament (Touchtest Sensory Evaluator 6.65) that was calibrated to bend at 300g of pressure. Testing sites included the patella of the index knee and the back of the ipsilateral hand, in randomized order. To assess TS of mechanical pain at each site, participants were instructed to provide a verbal 0-100 rating of pain following a single contact of the monofilament. Then, participants were instructed to provide another 0-100 rating of their greatest pain intensity experienced following a series of 10 contacts, which were provided at a rate of one contact per second. This procedure was repeated twice at each anatomical location. Pain ratings for the single and multiple contacts performed at each anatomical location were averaged across the two trials.

TS of heat pain was assessed using a Medoc Pathway Neurosensory Analyzer (Medoc, Ltd., Ramat Yishai, Israel) with a 27 mm diameter thermode. All participants underwent six separate trials to assess TS of heat pain (three at the index knee, three at the ipsilateral volar forearm) in ascending order using heat stimulus intensities of 44°C, 46°C, and 48°C as target temperatures with 32°C as the inter-pulse temperature. For each heat TS trial, sequences of 5 consecutive heat pulses of 700 millisecond durations were delivered with inter-pulse intervals of 2.5 seconds. The position of the thermode was altered slightly between temperatures to minimize local peripheral sensitization (though it remained on the index knee and forearm).The inter-trial interval (i.e., time between each testing temperature) was 30 seconds. The assessment of heat TS at the forearm always preceded assessment at the index knee. For each TS procedure, the participants were asked to rate the intensity of the pain produced by each heat pulse on a 0-100 numeric rating scale.

Weekly telephone surveys of clinical pain severity

Starting one week following the quantitative sensory testing session, all study participants were phoned once per week for four weeks and asked to report their knee OA clinical pain severity over the course of that particular week. Specifically, participants were asked to answer the following two questions: "please rate your pain on average in the last week" and "please rate your pain at its worst in the last week". Participants rated their average and worst clinical pain using a 0 (no pain) to 10 (worst pain imaginable) scale.

Measures

Center for Epidemiological Studies Depression Scale (CES-D)—The CES-D is a 20-item self-report tool that measures symptoms of depression in the past week including depressed mood, guilt/worthlessness, helplessness/hopelessness, psychomotor retardation, loss of appetite and sleep disturbance (30). The CES-D has previously been used in research involving psychiatric and non-psychiatric samples, as well as clinical samples with medical illness (31). The total score ranges from 0 to 60, and this single total score was used in this

study as an estimate of the degree of individuals' depressive symptomatology. The validity and internal consistency of the CES-D has been reported to be acceptable when used specifically for people with knee OA (15).

Data analysis—All data were analyzed using SPSS, version 21 (IBM; Chicago, IL). All participants provided complete demographic data (e.g., sex, age, and ethnicity); however, a small portion of missing data existed for TS of mechanical pain (< 5% for each stimulus modality) as well as the weekly telephone surveys (< 10% for each of the four weeks). Data were deemed to be missing at random, and missing data did not systematically vary between African Americans and non-Hispanic Whites. For missing data, a simple data imputation method was completed using the macro for Hot Deck imputation (32). This data imputation method is well validated and accepted in the statistical community and resulted in complete study data for each of the 225 study participants. Descriptive data for the sample are reported overall and separately for African Americans and non-Hispanic Whites as either percentages or as means and standard deviations as indicated. Ethnic differences on categorical variables were assessed using Chi-square tests, while ethnic differences on continuous variables were assessed using analysis of variance (ANOVA). Ethnic differences in TS of pain as well as ratings of clinical pain over the four weeks were assessed using repeated measures ANOVA with Greenhouse-Geisser corrections. Zero-order relationships among study variables were assessed using Pearson correlations as indicated. Lastly, a series of hierarchical moderated regression analyses were performed to examine whether the ability of TS of pain to predict clinical ratings of weekly average and worst pain ratings significantly differs according to participants' ethnic background. In order to account for multicollinearity due to high correlations among interaction (i.e., cross-product) and main effect terms, residualized cross-product terms were saved and used to predict clinical pain ratings of knee OA (33). The residuals can be considered the unique portions of the cross-product terms that do not correlate with the main effect terms.

Results

Participant characteristics

Table 1 presents descriptive characteristics for the entire study sample as well as separately for African Americans and non-Hispanic Whites. The proportion of women to men in this study did not significantly differ across ethnic groups ($\chi^2 = .17$, $p = .68$). A significantly greater proportion of African Americans fell below the poverty line relative to non-Hispanic Whites ($\chi^2 = 32.36$, $p < .001$). On average, the African Americans were significantly younger than non-Hispanic Whites ($F_{1,223} = 15.57$, $p < .001$). Furthermore, African Americans had significantly greater BMI ($F_{1,223} = 4.19$, $p = .041$) and reported more depressive symptoms ($F_{1,223} = 4.61$, $p = .033$) than their non-Hispanic White counterparts. On the day of the quantitative sensory testing session, African Americans reported significantly greater clinical pain in their index knees compared to non-Hispanic Whites ($F_{1,223} = 5.15$, $p = .024$).

Selected Covariates

Poverty status, age, BMI, depressive symptoms, and reported knee OA clinical pain severity immediately prior to the quantitative sensory testing session were each included as control

variables in data analysis examining ethnic differences and hierarchical moderated regression models.

Ethnic differences in TS of mechanical and heat pain

The African Americans were significantly more sensitive to the painful mechanical stimuli following both a single contact and 10 contacts compared to non-Hispanic Whites (Table 2). Findings revealed that ethnicity significantly interacted with contacts (1 vs. 10 contacts) to influence ratings of the mechanical stimuli at both the index knee ($F_{1,218} = 15.87$, $p < .001$) and hand ($F_{1,218} = 33.37$, $p < .001$). These findings indicate that African Americans demonstrated significantly greater TS of mechanical pain compared to non-Hispanic Whites (Figure 1A and 1B).

For TS of heat pain, the pain rating elicited by the first heat pulse was compared to the maximum pain rating obtained across all five heat pulses for each of the stimulus intensities (44°C, 46°C, 48°C) assessed at the index knee and ipsilateral forearm. Ethnicity was found to interact with heat pulses for each of the stimulus intensities at the index knee: 44°C ($F_{1,218} = 11.32$, $p = .001$), 46°C ($F_{1,218} = 7.04$, $p = .009$), 48°C ($F_{1,218} = 8.89$, $p = .003$). Furthermore, ethnicity was found to also interact with heat pulses for each of the stimulus intensities assessed at the forearm: 44°C ($F_{1,218} = 8.53$, $p = .004$), 46°C ($F_{1,218} = 9.38$, $p = .003$), 48°C ($F_{1,218} = 8.89$, $p = .003$). These results indicate that African Americans consistently demonstrated significantly greater TS of heat pain compared to non-Hispanic Whites (Figure 2A through 2F).

Ethnic differences in weekly survey ratings of clinical pain

The African Americans rated their average ($F_{1,218} = 6.82$, $p = .011$) and worst ($F_{1,218} = 5.39$, $p = .021$) weekly pain significantly higher than non-Hispanic Whites across the entire four week time span (Figure 3A and 3B). Pairwise differences in clinical pain ratings between African Americans and non-Hispanic Whites are presented for each week in Table 2. Clinical ratings of pain did not significantly change over the course of the four week time span (p's > .10), which suggests that average and worst pain ratings were relatively stable for both African Americans and non-Hispanic Whites.

Data transformation

TS indices for mechanical pain were obtained by subtracting the pain rating following a single contact with the mechanical stimulus from the pain rating following 10 mechanical stimulus contacts for the index knee and hand. For the TS of heat pain indices at the index knee and forearm, first pain ratings were subtracted from the maximum pain ratings for each of the heat stimulus intensities. These indices reflect the Δ change scores for TS of pain obtained from the mechanical and heat stimulation procedures. The TS indices were subsequently included in the correlation analysis and considered for inclusion as primary predictor variables in the hierarchical moderated regression models. Furthermore, weekly ratings of average and worst pain were collapsed (i.e., averaged) across weeks in order to derive overall composites of average and worst pain ratings. These overall composites of average and worst pain ratings were also included in the correlation analysis and used as criterion variables in the hierarchical moderated regression models.

Correlations

Zero-order relationships among study variables are presented in Table 3. The control variables (poverty status, age, BMI, depressive symptoms, and reported knee OA clinical pain severity immediately prior to the quantitative sensory testing session) were all significantly correlated with the composite scores for the weekly clinical ratings of average as well as worst pain. Participants' sex was not significantly correlated with weekly ratings of average or worst clinical pain, and therefore, it was not included as a control variable in any of the data analysis. Interestingly, all of the zero-order relationships among TS of mechanical pain and the composite scores for the weekly ratings of average as well as worst clinical pain were significant; however, the overwhelming majority of the relationships among TS of heat pain and clinical pain ratings were not. Given the lack of significant correlations among TS of heat pain and clinical pain ratings, TS of heat pain was excluded from further analyses. Instead, hierarchical moderated regression models were limited to testing whether TS of mechanical pain was a significant prospective predictor of clinical pain ratings, and whether this prediction significantly differed as a function of ethnicity.

Hierarchical moderated regression models predicting clinical ratings of average and worst pain

There was a significant interaction between ethnicity and TS of mechanical pain at the index knee in relation to clinical ratings of average pain (b = −.28, p = .018) and worst pain (b = −.29, p = .046). Specifically, TS of mechanical pain at the index knee was found to significantly predict greater clinical ratings of average pain (b = .02, p = .016) and worst pain (b = .02, p = .044) for non-Hispanic Whites but not African Americans (p's > .30; see Figure 4A and 4B, respectively). The interaction between ethnicity and TS of mechanical pain at the hand did not significantly predict average clinical pain ratings (b = −.19, p = .084) or ratings of worst pain (b = −.23, p = .092).

In addition to TS of mechanical pain, results demonstrated that ethnicity also interacted with BMI in relation to clinical ratings of average pain (b = .28, p = .019) and worst pain (b = .39, p = .015). BMI significantly predicted greater clinical ratings of average pain (b = .07, p = .002) and worst pain (b = .09, p = .001) for African Americans but not non-Hispanic Whites (p's > .90).

Discussion

This study examined relationships among ethnicity, TS of pain (as an index of pain facilitation), and clinical pain severity in a sample of adults aged 45 years and above with symptomatic knee OA. Specifically, we examined whether African Americans and non-Hispanic Whites demonstrated significant differences in TS of mechanical and heat pain as well as ratings of clinical pain severity surveyed across four consecutive weeks. This study further tested whether TS of mechanical pain differentially predicts clinical pain severity ratings for African Americans and non-Hispanic Whites. In support of our first hypothesis, the overall magnitude of TS of pain for mechanical and heat stimuli assessed at the index knee and distal sites was significantly greater for African Americans compared to non-Hispanic Whites, suggesting the possibility for greater levels of pain facilitation for African

Americans. Ethnic differences in pain were not limited to the quantitative sensory testing methods; African Americans reported significantly greater levels of average and worst clinical pain on weekly surveys compared to non-Hispanic Whites, which also supports our first study hypothesis. Perhaps the most novel and interesting finding was that TS of mechanical pain at the index knee significantly predicted greater ratings of average and worst clinical pain (collapsed across the four week period) for non-Hispanic Whites but not African Americans. Alternatively, BMI was found to be a significant predictor of clinical pain severity for African Americans only. These findings lend support to our second study hypothesis, and further highlight the importance of considering ethnicity when examining predictors of clinical pain severity in individuals with knee OA.

Ethnic differences in clinical and experimental pain

An increasing literature addressing ethnic group differences in knee OA-related clinical pain and experimentally-induced pain has emerged, with the most frequent comparisons involving African Americans and non-Hispanic Whites. While not unanimous, on balance the evidence indicates that knee OA is more prevalent and associated with higher levels of pain and disability among African Americans than non-Hispanic Whites (15-18). Further, considerable experimental evidence from healthy and clinical samples demonstrates greater basal pain sensitivity among African Americans compared to non-Hispanic Whites, especially for suprathreshold measures (22-24). Recent findings from our group also suggest diminished pain inhibition among healthy African Americans compared to non-Hispanic Whites (34).

Despite the evidence supporting ethnic differences in clinical and experimental pain, relatively little research has examined experimental and clinical pain responses as part of a single study involving individuals with a chronic pain condition. A particular strength of this study is that all participants completed quantitative sensory testing prior to completing surveys regarding their average and worst clinical pain across a four week time span. Our findings showed that African Americans demonstrated greater TS of mechanical and heat pain compared to non-Hispanic Whites, while also reporting greater severity of average and worst clinical pain. These results are consistent with preliminary findings previously reported by our group demonstrating significant ethnic differences in TS of pain (21). Based upon this study's findings related to TS of pain, it appears that African Americans with knee OA may possess a greater propensity for pain facilitation compared to their non-Hispanic White counterparts.

Predicting clinical pain from experimental pain measures

Given our hypothesis that TS of pain would differentially predict clinical pain severity according to individuals' ethnic background, it is important to first address the overall clinical relevance of experimental pain measures. While experimentally-induced pain does not fully replicate the experience of clinical pain, increasing evidence supports the clinical relevance of experimental pain measures (35-37). Studies indicate that knee OA is characterized by enhanced perceptual responses to experimental pain suggestive of pain facilitation (3,8,13). This is because individuals with knee OA demonstrate hyperalgesia not only when noxious stimuli are applied to the painful joint (38-41), but also when tested at

unaffected sites (39,40,42). TS of pain is a sensitive experimental measure of pain facilitation (2), and as such, TS of pain has previously been correlated with the severity of clinical pain in cross-sectional studies of chronic pain populations (4,7,43,44) including individuals with knee OA (8). This study further demonstrated that TS of mechanical pain at the index knee remained a significant prospective predictor of future ratings of average and worst clinical pain severity for non-Hispanic Whites, even after controlling for important factors such as poverty status, age, BMI, depressive symptoms, and clinical knee OA pain severity at the time of the quantitative sensory testing session.

That TS of mechanical pain, but not TS of heat pain, significantly predicted future clinical pain severity among non-Hispanic Whites is an interesting finding, which may be related to differences in clinical relevance between painful mechanical and heat stimuli. Given the pathophysiology of knee OA, the accompanying clinical pain is typically mechanically evoked (e.g., walking, stair climbing); therefore, mechanical stimuli may be more clinically relevant than other modalities of painful stimulation such as heat. Indeed, previous research showed that cutaneous mechanical pain sensitivity was significantly related to the pain elicited from movement and manipulation of an osteoarthritic joint, whereas cutaneous heat pain sensitivity was not (45). Unlike the assessment of heat TS, which requires costly equipment and methodologies that are technically elaborate and time consuming, the assessment of mechanical TS with a nylon monofilament (Touchtest Sensory Evaluator) is relatively brief, inexpensive, and requires minimal technical expertise (46). Whether the simple experimental pain measure for mechanical TS used in this study could be included in clinical practice and clinical trials is worthy of additional consideration.

Ethnic differences in predictors of clinical pain

African Americans demonstrated greater TS of mechanical pain as well as greater BMI compared to non-Hispanic Whites. Further, these factors were found to differentially predict their reported clinical pain severity. TS of mechanical pain, as our index of pain facilitation, did not predict the clinical pain severity of African Americans, whereas BMI was a significant predictor. This is not to say that processes associated with pain facilitation are unimportant for African Americans with knee OA, but rather that BMI was simply a more potent contributor to the overall clinical pain experiences of African Americans in this study. The difference in BMI between African Americans and non-Hispanic Whites was statistically significant; however, their respective means were both in the obese range (i.e., BMI > 30). This finding presents a challenge for future research to better understand why obesity appears to be a powerful predictor of clinical pain severity for African Americans with knee OA but not non-Hispanic Whites. In previous research, the prevalence of obesity was reportedly higher for African Americans (particularly women) compared to non-Hispanic Whites (47), and therefore, obesity may be more relevant to knee OA for the ethnic group with the highest prevalence. Among overweight and obese women with knee OA, African Americans have been shown to be at greater risk than non-Hispanic Whites for worsening pain and function across a 4-year observation period (48). Taken together, results from this study and others provide new and important information regarding differential predictors of knee OA-related clinical pain according to individuals' ethnic background.

Limitations

Several limitations of this study deserve mention. First, although it is one of the first to prospectively examine the relationship of TS of pain (as an index of pain facilitation) with knee OA clinical pain severity, the time period for the assessment of clinical pain was relatively short. It remains to be determined whether pain facilitation predicts longer-term clinical pain outcomes among individuals with knee OA. Second, evidence of pain facilitation was detected by significant TS of mechanical pain; however, TS is not the only means of characterizing pain facilitation. Whether other aspects of pain facilitation such as allodynia, secondary hyperalgesia, and referred pain also predict future knee OA-related pain occurrences and severity remains unclear. Third, no determination can be made from this study about whether pain facilitation negatively impacts objective functional outcomes related to knee OA. Fourth, although this study statistically adjusted for the influence of poverty status when examining ethnic differences in knee OA-related clinical pain, it is unclear to what extent other socioeconomic factors that were not assessed (e.g., adequate access to healthcare) may have acted to confound our findings. Lastly, this study highlights a limited number of explanatory factors (e.g., TS of mechanical pain and BMI) that differentially predict the clinical pain severity of African Americans and non-Hispanic Whites with knee OA. Additional research is still needed to better understand other potentially important factors that may be related to ethnic differences in knee OA such as use of pain treatments, lifestyle differences, and physical as well as social environments.

Conclusion

Despite the limitations, this study's findings provide novel support for the ability of pain facilitation, assessed via mechanical TS, to predict future reports of knee OA clinical pain severity, particularly among non-Hispanic Whites. Findings also demonstrate the ability of BMI to predict future reports of knee OA clinical pain severity among African Americans. This study contributes to the literature by helping to elucidate ethnic group differences in important factors that differentially predict knee OA-related clinical pain severity.

Acknowledgments

Conflicts of Interest and Source of Funding: This work was supported in part by NIH/NIA Grant R01AG033906-10 (R.B.F., L.A.B.); NIH/NCATS Clinical and Translational Science Award to the University of Florida, UL1 TR000064; NIH/NCATS and NCRR Clinical and Translational Science Award to the University of Alabama at Birmingham, UL1TR000165. The contents are solely the views of the authors and do not necessarily represent the official views of the NIH. All authors declare that there are no conflicts of interest with this study.

Dr. Fillingim has received received grant support from Pfizer and he owns stock or stock options in Algynomics. Dr. Staud has received consulting fees, speaking fees, and/or honoraria from Pfizer (less than $10,000). All other authors report no conflicts of interest.

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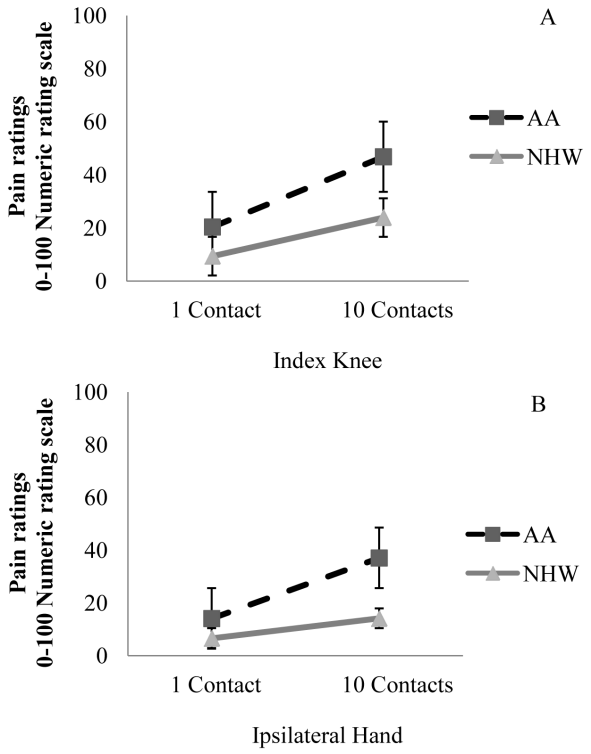

Figure 1.

Ethnic differences in TS of mechanical pain assessed at the **index knee** (1A) and **ipsilateral hand** (1B). Error bars = standard error.

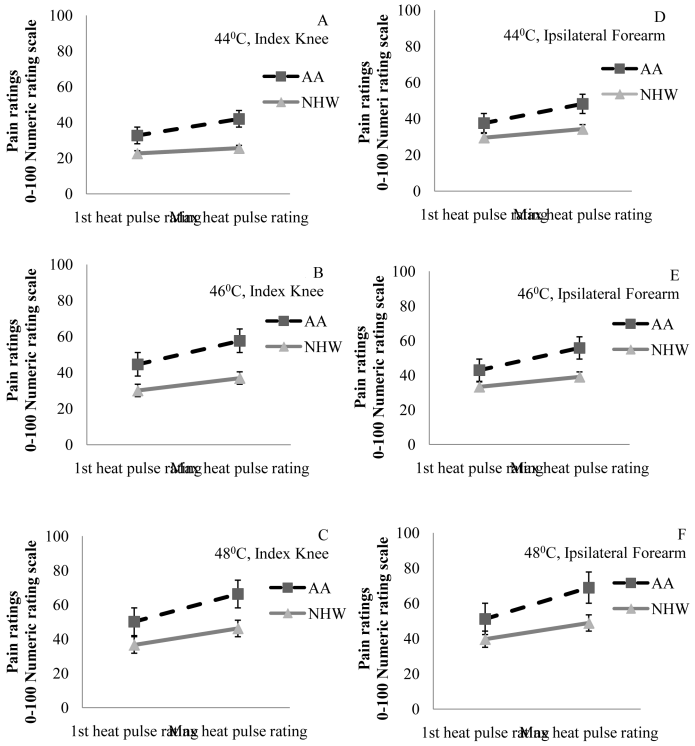

Figure 2.

Ethnic differences in TS of heat pain assessed at the **index knee**: 44°C (2A), 46°C (2B), 48°C (2C) and at the **ipsilateral forearm**: 44°C (2D), 46°C (2E), 48°C (2F). Error bars = standard error.

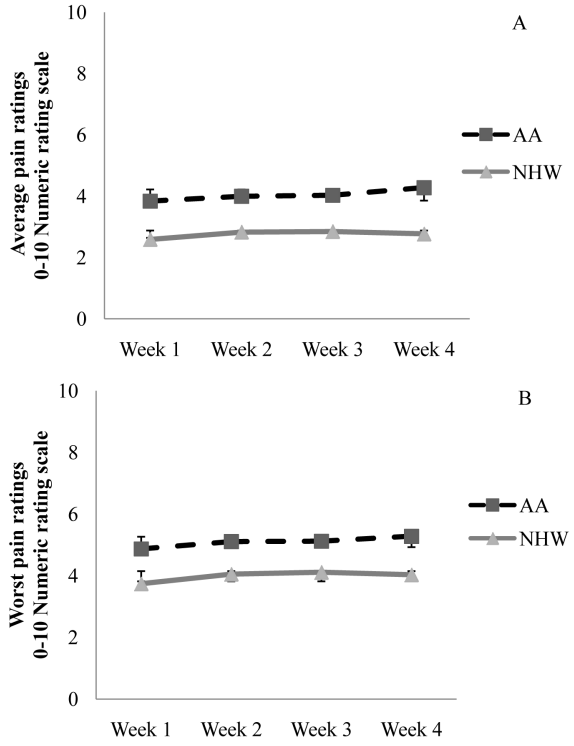

Figure 3.
Ethnic differences in weekly survey ratings of **average** pain (3A) and **worst** pain (3B). Error bars = standard error.

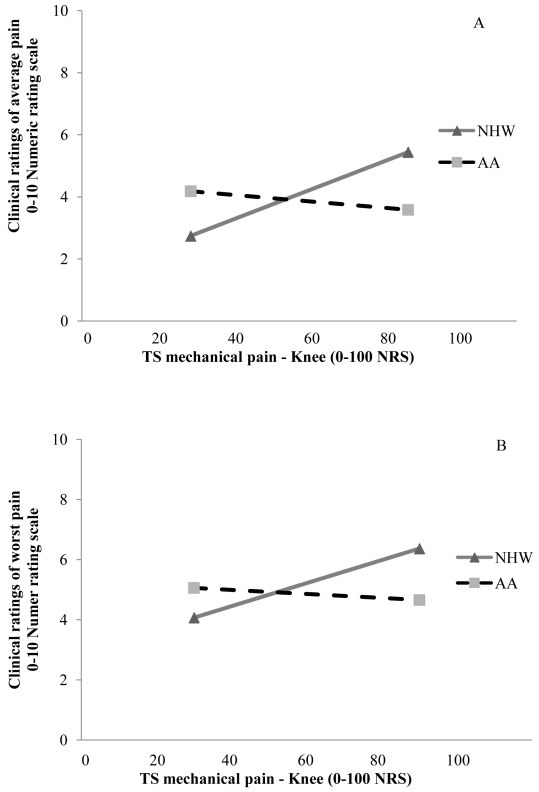

Figure 4.
Ethnic differences in the ability of TS of mechanical pain to predict clinical ratings of **average** (4A) and **worst** (4B) pain.

Table 1

Descriptive characteristics

	Overall N = 225			African Americans N = 122			non-Hispanic Whites N = 103		
Variable	**Mean**	**SD**	**%**	**Mean**	**SD**	**%**	**Mean**	**SD**	**%**
Sex									
Men			32.2			33.3			30.8
Women			67.8			66.7			69.2
Poverty status									
Above poverty line			71.2			55.4			90.1
Below poverty line			28.8			44.6			9.9
Age	57.1	7.7		55.2	6.3		59.2	8.7	
BMI	31.6	8.4		32.6	7.8		30.4	8.6	
CES-D	9.5	7.5		10.5	7.5		8.4	7.3	
Knee OA clinical pain-(QST)	11.9	19.5		14.5	21.5		8.7	16.4	

Note: BMI = body mass index; CES-D = Center for Epidemiological Studies Depression Scale; knee OA clinical pain-(QST) = reported clinical pain severity on the day of quantitative sensory testing session prior to pain testing (0-100 numeric rating scale).

Table 2

Ethnic differences in mechanical pain stimuli and ratings of clinical pain severity

	African Americans N = 122		non-Hispanic Whites N = 103	
Variable	**Mean**	**SD**	**Mean**	**SD**
1 contact - knee	20.4	21.3	9.4	13.4
10 contacts - knee	46.8	29.5	23.9	26.8
TS mechanical pain – knee*	26.3	18.8	14.4	17.6
1 contact - hand	14.1	16.6	6.6	13.3
10 contacts - hand	37.1	28.1	14.2	20.9
TS mechanical pain – hand*	22.5	20.5	7.8	12.5
44^0 first rating - knee	32.7	27.7	22.6	21.5
44^0 max rating - knee	41.9	27.7	25.6	22.9
44^0 TS heat pain – knee*	9.3	17.6	3.0	7.1
46^0 first rating - knee	44.6	26.8	30.1	25.0
46^0 max rating - knee	57.6	28.9	37.0	28.7
46^0 TS heat pain – knee*	13.1	15.6	6.9	14.3
48^0 first rating - knee	50.1	28.4	36.6	28.5
48^0 max rating - knee	66.3	28.0	46.2	31.4
48^0 TS heat pain – knee*	16.2	16.9	9.6	14.7
44^0 first rating - forearm	37.6	26.6	29.5	25.3
44^0 max rating - forearm	48.4	28.3	34.3	27.1
44^0 TS heat pain – forearm *	10.5	17.1	4.8	8.8
46^0 first rating - forearm	42.9	27.2	33.3	25.7
46^0 max rating - forearm	55.8	28.6	39.0	27.9
46^0 TS heat pain – forearm *	12.9	15.7	5.7	11.0
48^0 first rating - forearm	51.1	28.1	39.6	27.9
48^0 max rating - forearm	68.9	27.8	48.8	30.1
48^0 TS heat pain – forearm *	17.8	19.5	9.2	12.0
Average clinical pain^	4.2	2.2	2.7	1.8
Worst clinical pain^	5.1	2.6	4.1	2.1

Note: Mechanical and heat pain rated on the 0-100 numeric rating scale;

* = Δ change scores for TS;

^ = pain ratings collapsed across four weeks.

Table 3

Zero-order correlations across the entire sample.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Sex	—														
2. Poverty status	−.07	—													
3. Age	−.04	.09	—												
4. BMI	−.01	.04	−.16*	—											
5. CES-D	.02	−.21**	−.30**	.04	—										
6. Knee OA clinical pain-(QST)	.12	−.15*	−.18*	.15*	.22**	—									
7. TS mechanical - knee	−.20**	−.14*	−.01	.05	.11	.14*	—								
8. TS mechanical - hand	−.04	− 23**	−.03	.15*	.17*	.11	.65**	—							
9. TS heat 44^{0}C - knee	−.08	−.08	.07	.10	.09	.15*	.10	.15*	—						
10. TS heat 46^{0}C - knee	−.08	−.08	−.03	.02	.10	−.01	19**	.16*	.48**	—					
11. TS heat 48^{0}C - knee	−.08	−.06	−.01	−.02	.07	−.03	.20**	.25**	.38**	64**	—				
12. TS heat 44^{0}C - forearm	−.11	−.10	.04	.03	.02	−.03	.09	.10	.36**	.47**	.32**	—			
13. TS heat 46^{0}C - forearm	−.08	−.09	−.04	.01	.08	.07	.20**	.18**	.51**	.63**	.53**	64**	—		
14. TS heat 48^{0}C - forearm	−.10	−.06	−.06	.02	.09	.03	.17*	.14*	.30**	.55**	.55**	.43**	.66**	—	
15. Average clinical pain	.03	−.33**	−.22**	.23**	.33**	.50**	.21**	.22**	.08	.10	.03	.11	.16*	.08	—
16. Worst clinical pain	.02	−.25**	−.14*	.23**	.26**	44**	.17*	.14*	.11	.07	.08	.10	.08	.05	.84**

* Note: = p < .05,

** = p < .01;

Sex coded 0 = women, 1 = men; poverty status coded 0 = below poverty line, 1 = above poverty line; BMI = body mass index; CES-D = Center for Epidemiological Studies-Depression Scale; Knee OA clinical pain-(QST) = reported clinical pain severity on the day of quantitative sensory testing session prior to pain testing (0-100 numeric rating scale); TS = change scores for temporal summation of pain.