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Enhanced pain sensitivity among individuals with symptomatic knee osteoarthritis: Potential sex differences in central sensitization

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Abstract

Objective—Symptomatic knee osteoarthritis (OA) is a condition commonly associated with increased pain, disability, and functional limitations. Given the poor correspondence between radiographic evidence and clinical pain, central sensitization has been implicated as a potential mechanism underlying pain facilitation in knee OA. Sex may be a moderator of centrally-mediated changes in knee OA pain; however, few studies have systematically assessed this. Therefore, the aim of this study was to examine differences in peripheral and central sensitization in men and women with symptomatic knee OA, as well as to determine whether these differences vary across age (middle-age vs. older-age).

Methods—Participants ($N=288$) between the ages of 45 and 85 completed a battery of quantitative sensory pain procedures assessing sensitivity to contact heat, cold pressor, mechanical pressure, and punctate stimuli. Differences in temporal summation (TS) were examined, as well as measures of clinical pain and functional performance.

Results—When compared to men, women exhibited greater sensitivity to multiple pain modalities (i.e., lower heat, cold, pressure thresholds/tolerances, greater TS of pain); however,

there were no sex differences in clinical pain with the exception of greater widespread pain observed in women. Although there were select age-related differences in pain sensitivity, sex differences in pain varied minimally across age cohort.

Conclusion—Overall, these findings provide evidence for greater overall sensitivity to experimental pain in women with symptomatic knee osteoarthritis (OA), compared to men, suggesting that enhanced central sensitivity may be an important contributor to pain in this group.

Keywords

knee osteoarthritis; central sensitization; sex differences; experimental pain sensitivity; clinical pain

Osteoarthritis (OA) is the most common form of arthritis, with characteristic symptoms of joint pain, stiffness, and decreased functional mobility. OA drives significant healthcare utilization, psychosocial and physical impairment, and disability (1, 2). Age represents a significant risk factor for increased incidence and prevalence of OA (3), as older adults often present with greater pain complaints, more persistent pain, and greater pain-related disability than younger adults (4–6). Although OA can affect multiple joints in the body, the knee is one of the most commonly affected sites (7), with approximately 45% of older adults in the United States population estimated to be at risk for developing knee OA (8, 9).

Traditionally, knee OA has been characterized as a condition of peripheral pathology. However, given that radiological findings of joint damage do not impressively correlate with the degree of clinical symptoms, other centrally-mediated factors have been suggested to influence its pathology (10–12). While localized pain and hyperalgesia at the affected joint suggest a strong peripheral component to knee OA, more widespread pain and hyperalgesia indicate that central sensitization may contribute to pain-related symptomatology (12). Supporting this, persons with knee OA (relative to healthy individuals) exhibit greater sensitivity to mechanical pressure (13–15) and heat (14, 15) stimuli across multiple body sites, signifying potential disturbances in central pain processing.

Female sex appears to be a contributor to pain and disability in knee OA, regardless of radiographic severity of OA (16). In fact, women are at greater risk of developing knee OA, and they often experience greater pain, disability, and more advanced stages of the condition, relative to men (17, 18). Further, sex may be an important contributor to central changes in osteoarthritic pain. This is supported by several studies suggesting women have a higher propensity to develop chronic pain due to central sensitization (16, 19). Although less is known about sex differences in experimental pain processing in OA (20, 21), one study by Tonelli and colleagues (22) observed increased sensitivity to pressure and heat pain stimuli in women compared to men with knee OA. However, these authors examined a population with advanced knee OA immediately prior to joint replacement surgery; therefore, generalization may be restricted to individuals with more severe, late stage OA. Additionally, experimental pain assessment occurred at the operative knee site which limits assessment of both localized and widespread, somatosensory changes in pain.

The primary aim of the current study was to examine sex-related differences in pain responses in community-dwelling adults with symptomatic knee OA using quantitative sensory testing as a method to examine somatosensory dysfunction (23). We hypothesized that women would experience enhanced pain sensitivity (i.e., lower pain thresholds and tolerances) and temporal summation of pain, as well as greater clinical pain, disability, and decreased functional performance relative to men. Interestingly, the influence of sex on pain has also been shown to vary as a function of age (17, 24–27); therefore, age may mediate sex differences in pain. Notably, while sex-related differences have been well-established in younger adults, the degree to which these disparities exist across older populations has not been well characterized. Hence, a secondary aim of the study was to examine whether sex differences in experimental and clinical pain varied across participant age (middle-aged vs. older-aged adults).

Materials and Methods

Participants

Individuals ($N=288$) between the ages of 45 to 85 with symptomatic knee OA (based upon American College of Rheumatology criteria (28)) were recruited from the community through flyers and radio/newspaper advertisement. Participants self-identified as “black/African-American” or “white/Caucasian/European” and were recruited as part of a larger, multi-site (University of Florida; University of Alabama at Birmingham) study examining ethnic differences in knee osteoarthritis. Participants were excluded for: uncontrolled hypertension ($>150/95$); history of myocardial infarction; systemic rheumatic disorders; peripheral neuropathy; psychiatric hospitalization during previous year; cognitive impairment (MMSE score <22); excessive anxiety regarding study procedures; or daily opioid use.

Procedures

All procedures were fully approved by the University of Florida and University of Alabama-Birmingham Institutional Review Boards. Participants were initially evaluated for exclusion criteria via a phone screen. Those deemed eligible were asked to attend a health assessment session (HAS) during which a more thorough evaluation of eligibility criteria was conducted, health history and socio-demographic information was obtained, questionnaires were completed, and participants underwent a Short Physical Performance Battery (SPPB) test. All participants provided written informed consent prior to enrollment and were scheduled for their quantitative sensory testing (QST) session within 4 weeks of the HAS.

During the QST session, participants were given a brief overview of study procedures and health status was reviewed to confirm eligibility requirements. The session included the following sensory testing procedures: heat pain, mechanical and punctate pressure pain, cold pressor pain. To control for potential order and carry-over effects, heat and pressure pain procedures were counterbalanced across participants and mandatory rest breaks were provided prior to cold pressor tasks. Standardized instructions were delivered via a recording prior to the commencement of each procedure. Sensory testing occurred on the participant’s index (most affected) knee and sites ipsilateral to the index knee. The index knee was

chosen based upon self-report of pain in the designated knee. If participants reported bilateral knee pain, they were asked to identify their most painful knee (selected as the “index” site for testing).

Questionnaires

Pain Intensity/Unpleasantness Rating Scales—Participants verbally rated pain intensity and unpleasantness using two separate 0–100 numerical rating scales (NRS) where 0 indicated “no pain/unpleasantness” and 100 indicated the “most intense pain/unpleasantness imaginable.”

Western Ontario and McMaster Universities Index of Osteoarthritis (WOMAC)—The WOMAC (29) is a 24-item scale assessing symptoms of knee OA over the past 48 hours. Items are scored on a 5-point scale ranging from 0–4 with higher scores indicating greater symptom severity. Three subscales comprise the WOMAC: 1) pain during activities (5 items); 2) daytime stiffness (2 items); and 3) impairments in physical function (17 items). The WOMAC demonstrates good construct validity and reliability (30).

Graded Chronic Pain Scale (GCPS)—The GCPS (31) is a 7-item scale asking about pain severity and disability over the past 6 months. Using a 0–10 scale, participants rated the intensity of their current knee pain and the worst and average pain during the past 6 months (Characteristic Pain Intensity score). Participants also rated the degree to which their knee pain interfered with daily activities during the past 6 months (Disability score). All items were averaged and multiplied by 10 to generate index scores for pain intensity and disability, with higher scores indicating greater symptomatology. High internal consistency and reliability has been reported for the GCPS (32).

Pain Sites—The number of pain sites was assessed by having participants indicate the number of regions in which they experienced pain on “more days than not over the past three months.” From a list of twelve body areas (i.e., hands, arms, shoulders, neck, head or face, chest, stomach, upper back, lower back, knees, legs, feet and ankles), participants reported areas in which they currently have pain (reported bilaterally). Items were summed to create a total score ranging from 0–24.

Short Physical Performance Battery (SPPB)—The SPPB (33) assesses limitation in functional movement, including standing balance, 4-meter gait speed, and chair rising tasks. A single summary performance score is calculated, ranging from 0–12, with lower scores indicating greater functional limitation.

Experimental Pain Outcomes

Mechanical Pain—Pressure pain threshold (PPT_h) was assessed through three trials of pressure pain stimuli delivered to the medial and lateral joint line of the index knee, and the ipsilateral trapezius muscle, dorsal forearm, and quadriceps muscle (order counterbalanced). Stimuli were delivered at a constant rate of 30 kilopascals (kPa) per second to each site, with the participant indicating their pain threshold by pressing a button. PPT_h (in kPa) was calculated by averaging the three trials for each site.

Punctate mechanical stimuli were delivered to the patella and the dorsal surface of the hand (order counterbalanced) using a 300g nylon monofilament. First, a single stimulus was delivered and the participant provided a rating of pain intensity. Then, 10 consecutive stimuli (1 second inter-trial interval) were delivered and the participant provided a rating of the peak pain intensity experienced during the series of 10 stimuli (i.e., TS of punctate pressure). Pain ratings for the two trials of single stimuli and for the series of 10 contacts were averaged for each site.

Heat Pain—Thermal stimuli were delivered using a computer-controlled device (Medoc Pathway Thermal Sensory Analyzer; Ramat Yishai, Israel). Thermal stimuli were delivered to the ventral forearm and the medial aspect of the index knee. Using an ascending method of limits and starting at 32 °C, heat temperature was increased at a rate of 0.5 °C/s (max 52 °C) until participants first felt warmth (WTh), first felt pain (HPTh), or could no longer tolerate the pain (HPTo). Participants provided their response by pressing a computer mouse button. Three trials each of WTh, HPTh, and HPTo were collected at each area (forearm, knee), with the average of these responses being recorded. Pain ratings (0–100) were obtained after each HPTh and HPTo trial.

For temporal summation of heat pain, participants verbally rated the intensity of pain evoked by each of 5 brief, repetitive suprathreshold heat pulses on the 0 to 100 scale. Three target temperatures (44 °C, 46 °C, and 48 °C) were delivered by a Contact Heat-Evoked Potential Stimulator thermode for less than 1 second, with a 2.5-second inter-pulse interval during which the temperature of the contactor returned to baseline (32 °C).

Cold Pain—A modified cold pressor procedure was conducted during which participants were asked to immerse their right hand up to the wrist in 1-minute water immersions (Neslab refrigeration unit; Portsmouth, NH), with temperatures set at 12 °C and 8 °C (in descending order). The time until participants first reported pain (CPT_h) and withdrew their hand (CPT_o) was recorded. Participants also provided pain intensity and pain unpleasantness ratings at 60 seconds after immersion (or upon hand withdrawal). A 5-minute rest break was provided between each cold pressor trial.

Data Analysis

Statistical analyses were conducted using 2 (Sex) × 2 (Age) ANCOVAs with SPSS 22.0 (SPSS Inc., Chicago, IL) software. An age cut-point of 56 years was employed to discriminate between the middle-aged (45–56 years) and older-aged (57–85 years) groups, and is consistent with previous research (34–37). Since race and BMI have been associated with clinical and experimental pain in prior research, these variables were included as covariates in all analyses. Due to differences amongst sex and age groups in education, marital status, and employment, these variables were also included as covariates. MANCOVA models were used when families of dependents were highly correlated ($r > .50$), while repeated measures ANCOVAs were conducted when time/trial was involved (i.e., TS of heat and punctate stimuli). If sphericity was violated, Greenhouse-Geisser corrections were used. To obtain effect size estimates associated with *F*-tests, partial eta-squared (η_p^2)

was calculated from GLM analyses (small=.01, medium=.06, large=.14). Significance was set at $p < 0.05$ (two-tailed).

Results

Participants

Table 1 presents demographic and clinical data for the sample. Women had higher educational attainment and were more likely to be employed. The older age group had a higher proportion of whites, were more highly educated and married, less likely to be employed, and had a lower BMI and chronic pain grade.

Experimental Pain Outcomes

Mechanical and Punctate Pressure—The main effect of sex was significant for all mechanical pressure pain outcomes (Table 2), signifying that relative to men, thresholds were lower for women at all sites ($p < .001$). The main effect of age was significant for pressure pain thresholds at the quadriceps and epicondyle, with older adults exhibiting lower thresholds at both sites ($p < .05$). The Sex \times Age interaction for all mechanical pressure pain outcomes was non-significant ($p > .05$).

Figure 1 and Supplementary Figure 1 present results for punctate pressure outcomes. For punctate pain at the hand, the main effects of sex [$F(1, 276)=2.81, p=.10, \eta_p^2=.01$] and age [$F(1, 276)=2.34, p=.13, \eta_p^2=.01$] were both non-significant for the single stimulus. Additionally, there were no differences in TS of punctate pressure pain at the hand across sex [$F(1, 275)=.24, p=.63, \eta_p^2=.00$] or age [$F(1, 275)=.53, p=.47, \eta_p^2=.00$]. For punctate pain at the knee, there was a significant main effect of sex [$F(1, 276)=3.81, p=.05, \eta_p^2=.01$] for the single stimulus pain rating; however, no significant effects occurred for age [$F(1, 276)=3.31, p=.07, \eta_p^2=.01$]. Specifically, women ($d=.24$) provided higher pain ratings for the single stimulus compared to men. Women also exhibited greater TS of punctate pressure at the knee, relative to men [$F(1, 275)=12.61, p<.001, \eta_p^2=.04, d=.35$], whereas there were no significant differences across age groups for TS [$F(1, 275)=.15, p=.70, \eta_p^2=.00$]. The Sex \times Age interaction for all punctate pressure outcomes was non-significant (all $p > .05$).

Heat Pain—The main effect of sex was significant for all heat pain outcomes (Table 3) indicating that women exhibited lower thresholds and tolerances at both the arm and knee ($p < .05$). Further, intensity ratings at the arm and knee for tolerance were lower in women ($p < .01$). The main effect of age and the Sex \times Age interaction for all heat pain outcomes were non-significant (all $p > .05$).

For TS of heat pain, the main effect of sex was significant for all temperatures and sites, indicating that women produced overall higher heat pain ratings than men (44 °C Arm: $F(1,260)=8.03, p=.005, \eta_p^2=.03$; 46 °C Arm: $F(1,265)=12.43, p<.001, \eta_p^2=.05$; 48 °C Arm: $F(1,269)=8.91, p=.003, \eta_p^2=.03$; 44 °C Knee: $F(1,255)=13.19, p<.001, \eta_p^2=.05$; 46 °C Knee: $F(1,266)=7.70, p=.006, \eta_p^2=.03$; 48 °C Knee: $F(1,270)=13.32, p<.001, \eta_p^2=.05$). There was also a significant Sex \times Trial interaction for TS at the arm for 48 °C ($F(1.65,443.11)=3.21, p=.05, \eta_p^2=.01$), as well as at the knee for 46 °C

($F(1.53,407.65)=4.49, p=.02, \eta_p^2=.02$) and 48 °C ($F(1.47,397.73)=3.95, p=.04, \eta_p^2=.01$), indicating that the sex difference (women>men) for TS was greater across subsequent trials. All other main effects and interactions for sex (Figure 2), age (Supplementary Figure 2), and trial were non-significant (all p 's>.05).

Cold Pain—The main effect of sex was significant for cold pain outcomes (Table 3) at 8 °C, with women demonstrating lower tolerances and greater pain intensity ratings than men (p 's<.05). The main effect of age was non-significant for all outcomes (p 's>.05). There were also significant Sex \times Age interactions for CPT_h, CP intensity ratings, and CP unpleasantness ratings at 8 °C, suggesting that women exhibited lower pain thresholds, as well as higher pain intensity and unpleasantness ratings than males, but only in the older-aged group (p 's<.05).

Clinical Pain—Table 4 presents descriptive and inferential statistics, as well as internal consistency estimates (range .83 to .97) for clinical pain outcomes. The main effect of sex was non-significant for all outcomes, with the exception of women having a greater number of pain sites relative to men ($p=.001$). The main effect of age was significant for clinical pain intensity and disability on the GCPS, with middle-aged adults reporting greater pain intensity and disability (p 's<.05). The Sex \times Age interaction for all clinical pain outcomes was non-significant (p 's>.05).

Discussion

The aim of the current study was to examine sex and age differences in experimental and clinical pain, in addition to functional and physical performance in adults with symptomatic knee OA. Several notable findings were observed: 1) clear sex differences existed in experimental pain, with women exhibiting greater pain sensitivity to multiple pain modalities, compared to men; 2) clinical pain did not differ across sex; and 3) sex differences in experimental and clinical pain varied minimally across age cohorts (middle-age vs. older-age).

As expected, women with knee OA, compared to their male counterparts, exhibited greater sensitivity to a number of stimuli, including lower pain thresholds and tolerances to heat, cold, and pressure stimuli, greater mechanical pressure pain, and higher mechanical and heat temporal summation of pain. In contrast to the consistent sex differences found in responses to experimental noxious stimuli (20, 21, 26), men and women did not differ on measures of clinical pain, with the exception of greater widespread pain reported by women. Although it is unclear why women did not exhibit enhanced clinical pain as has been observed in other studies (20, 21), it is possible that sex differences in pain processing in older adults with knee OA are more easily detected using evoked pain measures rather than retrospective report of clinical symptoms.

It is well-known that sex differences in pain exist in healthy adults, yet little research has examined these effects among older adults, particularly among clinical samples. To our knowledge, only one study has examined sex differences in both experimental and clinical pain sensitivity in individuals with knee OA. Specifically, in 208 older adults with late-stage

OA, Tonelli and colleagues (22) found that women, relative to men, exhibited greater sensitivity to heat and mechanical pressure stimuli at the operative knee, as well as lower functional performance and greater clinical pain. However, Tonelli and colleagues recruited a sample of individuals with severe OA requiring total joint replacement; therefore, sample characteristics may have led to variability across studies. Our study, which included a community-dwelling sample with less severe knee OA, extends these findings by also revealing that women demonstrate enhanced hyperalgesia (i.e., greater experimental and widespread pain, greater temporal summation) both locally and distally relative to the affected joint.

Regarding age differences, older participants, compared to the middle-aged group, displayed lower mechanical pain thresholds in the quadriceps and epicondyle. These results are somewhat surprising, since previous evidence suggests that older adults show increased pain thresholds relative to their younger counterparts (38). However, most previous comparisons have examined healthy samples, and the presence of OA pain could alter the pattern of age-related differences in pain perception. Also, age-related effects in pain sensitivity may be dependent upon pain modality (36), such that older adults may exhibit dysregulation in the processing of sustained C-fiber mediated pressure pain, and in particular, among sites distal to the affected joint. Interestingly, the middle-aged group reported greater clinical pain intensity and disability relative to older-aged adults. While factors such as pain-related beliefs (i.e., believing pain is a normal part of aging) and stoicism among older adults may have influenced results, differences among groups in physical activity could also account for findings. That is, older adults often decrease their physical activity (39), which could lead to lower pain and disability since pain may be more commonly evoked upon movement in knee OA, while decreased physical activity is also associated with increased pain sensitivity (40). Further, it is important to note that a higher proportion of our middle-aged sample reported being employed, and with the increase in physical activity that often coincides with employment, this could potentially augment pain and subsequent pain-related disability. Hence, middle-aged adults may represent a cohort at greater risk for adverse pain-related functional outcomes (4). These findings are speculative, however, and warrant further exploration.

We found little evidence that sex differences vary with age, as the only effects observed were in cold pressor pain. In particular, women exhibited lower cold pain thresholds, as well as higher pain intensity and unpleasantness ratings relative to men, but only in older-aged adults. Notably, there have been few studies examining the interactive roles of sex and age in relation to pain sensitivity. Riley and Gilbert (27) reported that among adults between the ages of 45–64, females with orofacial pain reported greater clinical pain than males; however, no sex differences emerged in the older age group (ages 65+). Further, Pickering and colleagues (41) found that although healthy females, compared to men, showed lower thermal pain threshold levels, these differences were attenuated in the older adult group (ages 75+), relative to the younger-aged cohort (ages 18–25). Although we did not employ a younger-aged sample to examine whether similar effects would be found in younger adults, our results are in accordance with others suggesting that sex differences in pain may vary minimally in older adults (27, 41) and more specifically, in older individuals with knee osteoarthritis.

There are some limitations of the current study that warrant acknowledgement. First, this sample was restricted to middle-aged and older adults from the community who generally had mild to moderate knee OA symptoms; therefore, results may not generalize to clinic-based samples with more severe symptoms. Second, participants had to be willing to undergo two laboratory sessions, as well as an extensive battery of experimental pain testing. Thus, our sample may have been more resilient (e.g., less functionally limited; greater functional abilities) than other samples with symptomatic knee OA. Third, although there were clear sex differences observed in experimental pain, we did not detect any differences across men and women in measures of clinical pain, a finding that differs from those of many previous studies. It is unclear whether these findings are due to our study methodology (e.g., type of clinical measures) or to our sample, or perhaps reflective of some other unmeasured factor.

Despite these limitations, there are several strengths that are worth noting. First, whereas most studies have focused mainly on investigating sex differences in younger individuals, we attempted to expand previous research by examining these differences in a large sample of middle-aged and older adults with knee OA. Second, we utilized a multi-modal battery of quantitative sensory and clinical measures to examine pain sensitivity in our sample. And third, limited research has examined sex differences in both clinical and experimental pain among persons with symptomatic knee OA. Therefore, our study highlights the role that sex differences may have on pain sensitivity in individuals with knee OA.

Conclusions and Future Directions

Overall, study findings suggest that central sensitization may contribute to pain in women with knee OA, as observed from the pattern of findings in this group (i.e., greater temporal summation, heightened sensitivity to multiple pain modalities, greater number of pain sites, pain in areas distal to the knee joint). This may have important treatment implications as centrally-acting therapies (e.g., tricyclics, SSRI's) targeting central nervous system hyperexcitability may be more effective in women with knee OA rather than peripherally-targeted treatments (e.g., topicals, NSAID's). To a large extent, these differences did not vary significantly across age groups. Given the limited research examining pain sensitivity in older adults, further investigation is warranted to clarify whether sex-related differences in pain exist in other aging clinical populations. Continued research is also needed to elucidate the underlying biological and psychosocial mechanisms that not only increase vulnerability for enhanced pain sensitivity in women with knee OA, but that also identify why men may be particularly resilient toward augmented pain sensitivity in this population. Identification of these factors may facilitate the development of mechanistically-based therapeutic strategies that could be individualized based upon patient sex. Further, methods by which to effectively evaluate and diagnose centrally-mediated pain (e.g., developing diagnostic criteria for central sensitization) (12), both in the research and clinical setting, merits attention as this could optimize pain treatment and ultimately reduce pain management disparities existing among men and women.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovations

- In community-dwelling older adults with symptomatic knee osteoarthritis, women exhibit hyperalgesia to multiple experimental pain modalities and greater widespread pain, relative to men.
- The enhanced pain sensitivity observed in women with knee osteoarthritis may have a strong central component to its pathology.
- Select age-related differences were detected in pain sensitivity; however, sex differences in pain varied minimally across middle- and older-aged adults.

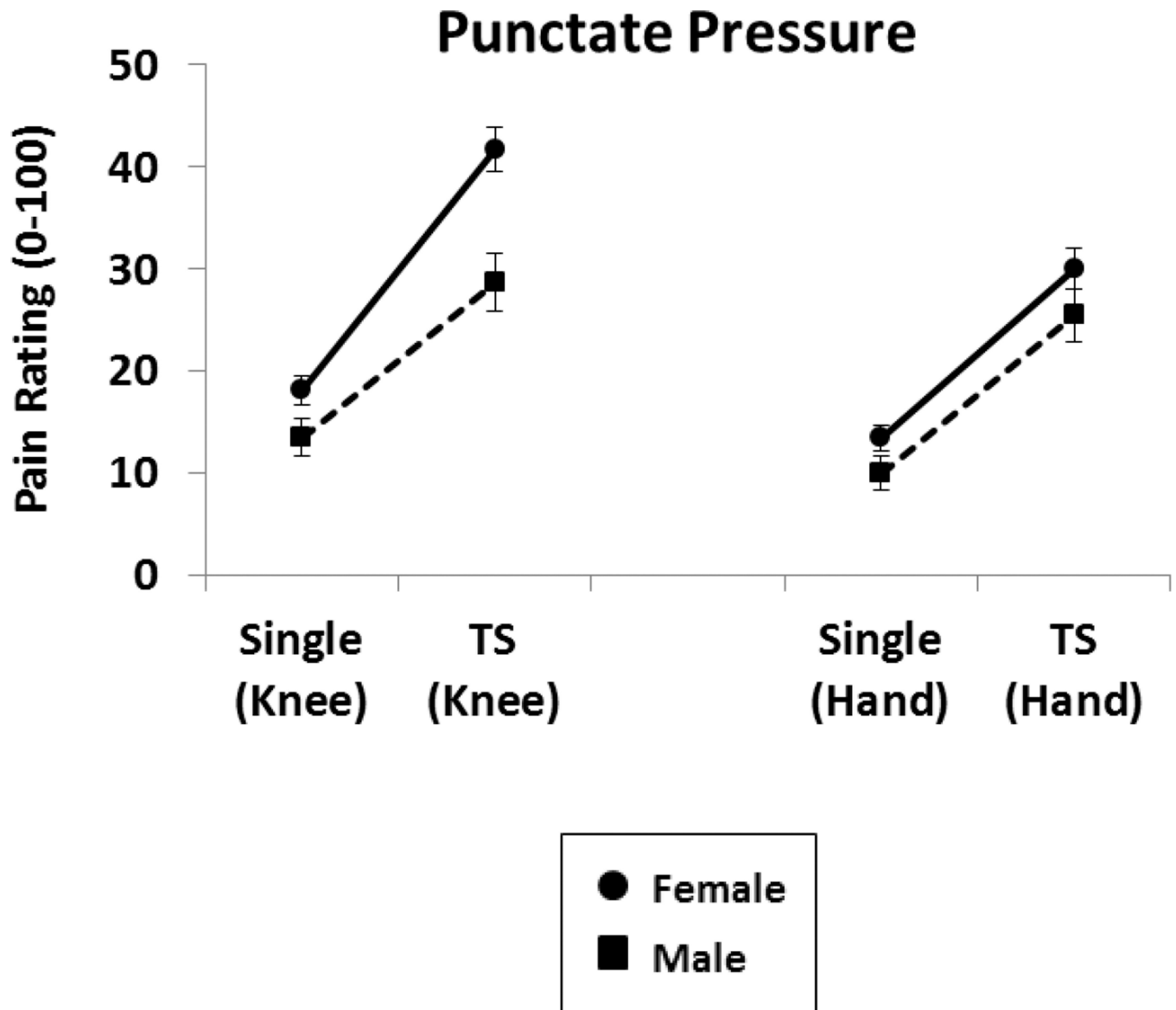


Figure 1. Adjusted means and standard errors for punctate pressure across sex. For punctate pressure at the hand, the main effect of sex was non-significant for the single stimulus and temporal summation (TS). For punctate pressure at the knee, women had higher pain ratings for the single stimulus compared to men, and had greater TS of punctate pressure pain.

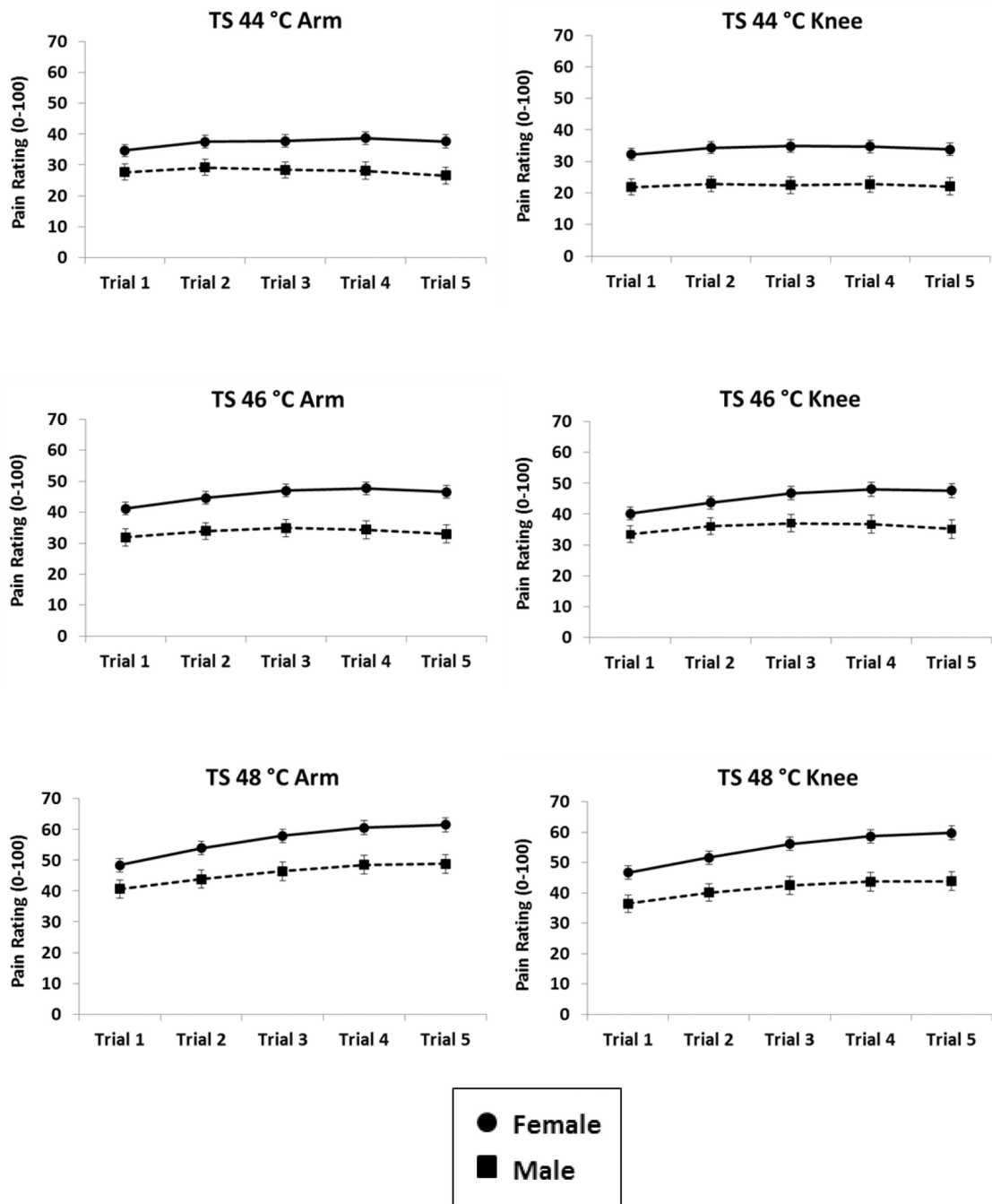


Figure 2. Adjusted means and standard errors for temporal summation (TS) across sex. Women had overall higher heat pain ratings than men. The Sex × Trial interaction for 46 °C (knee) and 48 °C (arm, knee) was significant indicating that women had greater TS across the 5 repeated trials.

Table 1

Demographic and clinical characteristics of participants across sex and age

| | Women N=183 | | Men N=105 | | Group Comparison | | Middle-Age N=161 | | Older-Age N=127 | | Group Comparison | |
|------------------------|----------------|----------------|--------------|-----|---------------------|----------------|---------------------|------|--------------------|----------------|---------------------|-------|
| | M or % (SD) | M or % (SD) | p | d | M or % (SD) | M or % (SD) | p | d | M or % (SD) | M or % (SD) | p | d |
| Age | 56.8(7.8) | 56.5(7.2) | .69 | .05 | 51.1(3.3) | 63.9(5.2) | <.001 | 2.89 | | | | |
| Sex | | | | | | | | | | | | .82 |
| Female | 63.5 | | | | 64.0 | 62.7 | | | | | | |
| Male | | 36.5 | | | 36.0 | 37.3 | | | | | | |
| Race | | | 1.00 | | | | | | | | | <.001 |
| White/Caucasian | 42.9 | 42.9 | | | 29.2 | 60.6 | | | | | | |
| Black/African-American | 57.1 | 57.1 | | | 70.8 | 39.4 | | | | | | |
| Income (\$) | | | .20 | | | | | | | | | .27 |
| 20,000 | 29.2 | 47.1 | | | 39.9 | 30.4 | | | | | | |
| 20,000–39,999 | 34.8 | 18.3 | | | 25.3 | 33.6 | | | | | | |
| 40,000–59,999 | 15.2 | 12.5 | | | 13.3 | 15.2 | | | | | | |
| 60,000 | 20.8 | 22.1 | | | 21.5 | 20.8 | | | | | | |
| Education | | | .02 | | | | | | | | | .02 |
| High School degree | 41.2 | 57.2 | | | 52.2 | 40.9 | | | | | | |
| 2-year college degree | 24.2 | 19.0 | | | 20.5 | 24.4 | | | | | | |
| 4-year college degree | 19.8 | 14.3 | | | 19.3 | 15.7 | | | | | | |
| Graduate degree | 14.8 | 9.5 | | | 8.0 | 19.0 | | | | | | |
| BMI | 32.7(8.1) | 30.9(6.8) | .06 | .24 | 32.7(8.4) | 31.3(6.4) | .13 | .18 | | | | |
| Marital Status | | | .80 | | | | | | | | | .01 |
| Married | 37.4 | 48.6 | | | 39.2 | 44.9 | | | | | | |
| Not Married | 60.4 | 50.4 | | | 58.9 | 53.5 | | | | | | |
| Other | 2.2 | 1.0 | | | 1.9 | 1.6 | | | | | | |
| Employment | | | .01 | | | | | | | | | <.001 |
| Employed | 55.3 | 32.2 | | | 56.3 | 35.4 | | | | | | |
| Other | 2.8 | 4.8 | | | 1.9 | 5.5 | | | | | | |
| GCPS | | | .72 | | | | | | | | | <.001 |

| | Women N=183 | | Men N=105 | | Middle-Age N=161 | | Older-Age N=127 | | Group Comparison | |
|---------|----------------|---|----------------|---|---------------------|---|--------------------|---|---------------------|---|
| | M or % (SD) | d | M or % (SD) | d | M or % (SD) | d | M or % (SD) | d | p | d |
| Grade 0 | 0.0 | | 2.0 | | 0.6 | | 0.8 | | | |
| Grade 1 | 38.9 | | 41.1 | | 29.9 | | 52.4 | | | |
| Grade 2 | 27.8 | | 16.7 | | 24.9 | | 22.2 | | | |
| Grade 3 | 17.2 | | 19.6 | | 22.9 | | 11.9 | | | |
| Grade 4 | 16.1 | | 20.6 | | 21.7 | | 12.7 | | | |

Note. BMI=Body Mass Index; GCPS=Graded Chronic Pain Scale.

Table 2
Descriptive and inferential statistics for measures of mechanical pressure across sex and age

| Pain Outcome | Women | | Men | | Sex (S) | | Middle-Age | | Older-Age | | Age (A) | | SexA | | |
|----------------------------------|--------------|--------------|----------------|-----------|--------------|--------------|---------------|-----------|-----------|-----------|---------|----------|------|----------|--|
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | F | η^2 | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | F | η^2 | F | η^2 | |
| Mechanical Pressure (kPa) | | | | | | | | | | | | | | | |
| Medial joint line (knee) | 243.8(145.4) | 357.0(167.8) | * 37.10 | .12 | 304.5(162.5) | 296.3(165.0) | .17 | .00 | 2.32 | .01 | | | | | |
| Lateral joint line (knee) | 254.5(153.9) | 386.3(167.8) | * 47.97 | .15 | 322.8(165.8) | 318.1(176.3) | .05 | .00 | 1.98 | .01 | | | | | |
| Quadriceps | 373.2(200.5) | 490.5(243.9) | * 18.39 | .06 | 460.9(237.5) | 402.8(203.5) | * 3.93 | .01 | .01 | .00 | | | | | |
| Trapezius | 226.0(142.8) | 331.0(200.5) | * 25.30 | .09 | 298.8(186.4) | 258.2(152.2) | 3.30 | .01 | .74 | .00 | | | | | |
| Epicondyle | 202.2(114.0) | 309.7(212.5) | * 29.40 | .10 | 277.0(177.9) | 234.8(145.0) | * 3.95 | .01 | .05 | .00 | | | | | |

Note. kPa=kilopascals.

* $p < .05$.

Table 3

Descriptive and inferential statistics for measures of thermal heat and cold pain across sex and age

| Pain Outcome | Women | | Men | | Sex (S) | | Middle-Age | | Older-Age | | Age (A) | | SxA | |
|---------------------------------|------------|------------|---------------|----------|------------|------------|------------|----------|-----------|-----------|--------------|----------|-----|----------|
| | Mean (SD) | Mean (SD) | F | η^2 | Mean (SD) | Mean (SD) | F | η^2 | Mean (SD) | Mean (SD) | F | η^2 | F | η^2 |
| Heat Trials (Knee) | | | | | | | | | | | | | | |
| Warmth Thr (°C) | 37.0(2.7) | 37.9(3.0) | *5.41 | .02 | 37.1(2.7) | 37.8(2.9) | 2.89 | .01 | 2.89 | .01 | .28 | .00 | | |
| Pain Thr (°C) | 41.6(3.2) | 42.5(3.4) | *4.93 | .02 | 42.2(3.3) | 41.8(3.3) | .79 | .00 | .79 | .00 | .42 | .00 | | |
| Pain Tol (°C) | 45.1(2.7) | 46.7(2.7) | *25.65 | .09 | 46.0(2.9) | 45.9(2.8) | .05 | .00 | .05 | .00 | .66 | .00 | | |
| Heat Trials (Arm) | | | | | | | | | | | | | | |
| Warmth Thr (°C) | 35.3(2.1) | 36.2(2.9) | *9.78 | .03 | 36.0(2.7) | 35.5(2.2) | 1.81 | .01 | 1.81 | .01 | .40 | .00 | | |
| Pain Thr (°C) | 41.2(3.2) | 42.3(3.3) | *7.34 | .03 | 42.0(3.3) | 41.6(3.3) | .62 | .00 | .62 | .00 | .59 | .00 | | |
| Pain Tol (°C) | 45.2(2.5) | 46.7(2.7) | *25.88 | .09 | 46.1(2.6) | 45.8(2.7) | .49 | .00 | .49 | .00 | 2.38 | .01 | | |
| Heat Pain Ratings (Knee) | | | | | | | | | | | | | | |
| Pain Thr (0–100) | 24.0(21.5) | 28.8(22.5) | 2.63 | .01 | 26.0(22.2) | 27.8(21.9) | .06 | .00 | .06 | .00 | .65 | .00 | | |
| Pain Tol (0–100) | 55.0(27.7) | 66.4(24.9) | *9.79 | .04 | 62.4(27.5) | 59.0(27.1) | .73 | .00 | .73 | .00 | .20 | .00 | | |
| Heat Pain Ratings (Arm) | | | | | | | | | | | | | | |
| Pain Thr (0–100) | 22.7(19.9) | 27.0(22.1) | 2.39 | .01 | 25.7(21.8) | 23.9(19.8) | .36 | .00 | .36 | .00 | .43 | .00 | | |
| Pain Tol (0–100) | 52.7(25.5) | 62.0(25.0) | *7.28 | .03 | 59.0(26.1) | 55.8(25.2) | .71 | .00 | .71 | .00 | .26 | .00 | | |
| Cold Pressor (12 °C) | | | | | | | | | | | | | | |
| Pain Thr (in sec) | 18.2(15.1) | 21.1(15.8) | 2.19 | .01 | 21.3(15.4) | 18.0(15.4) | 2.24 | .01 | 2.24 | .01 | 1.99 | .01 | | |
| Withdrawal (in sec) | 51.4(14.3) | 54.3(12.8) | 2.95 | .01 | 53.1(13.4) | 52.5(14.4) | .12 | .00 | .12 | .00 | .76 | .00 | | |
| Intensity @ 60-sec | 62.2(31.0) | 56.2(34.6) | 2.08 | .01 | 55.8(32.9) | 62.5(31.8) | 2.16 | .01 | 2.16 | .01 | 2.44 | .01 | | |
| Unpl. @ 60-sec | 65.8(31.0) | 60.4(32.8) | 1.77 | .01 | 62.9(32.1) | 63.3(31.3) | .93 | .00 | .93 | .00 | 2.12 | .01 | | |
| Cold Pressor (8 °C) | | | | | | | | | | | | | | |
| Pain Thr (in sec) | 11.1(10.9) | 13.8(11.7) | 3.46 | .01 | 13.8(11.9) | 11.1(10.4) | 2.81 | .01 | 2.81 | .01 | *6.67 | .03 | | |
| Withdrawal (in sec) | 43.3(19.3) | 48.3(18.1) | *4.79 | .02 | 45.7(18.9) | 46.0(19.1) | .01 | .00 | .01 | .00 | .94 | .00 | | |
| Intensity @ 60-sec | 76.5(27.1) | 68.0(31.2) | *5.37 | .02 | 71.2(29.9) | 73.3(27.6) | .27 | .00 | .27 | .00 | *5.54 | .02 | | |
| Unpl. @ 60-sec | 78.2(26.4) | 73.2(29.5) | 1.98 | .01 | 75.7(27.5) | 75.6(27.6) | .00 | .00 | .00 | .00 | *3.85 | .02 | | |

Note. Thr=Threshold; Tol= Tolerance.

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Table 4

Descriptive and inferential statistics for measures of clinical pain across sex and age

| Pain Outcome | Women | | Men | | Sex (S) | | Middle-Age | | Older-Age | | Age (A) | | SxA | | Cronbach's Alpha |
|-----------------------------|------------|------------|-----------|-----------|---------|----------|------------|------------|-----------|-----------|---------|----------|------|----------|------------------|
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | F | η^2 | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | F | η^2 | F | η^2 | |
| WOMAC | | | | | | | | | | | | | | | |
| Total Score (0-96) | 34.5(20.5) | 34.1(20.7) | | | .03 | .00 | 35.2(21.1) | 33.3(19.5) | | | .53 | .00 | .00 | .00 | .00 |
| WOMAC Subscales | | | | | | | | | | | | | | | |
| Pain (0-20) | 7.3(4.2) | 7.1(4.6) | | | .13 | .00 | 7.4(4.5) | 7.0(4.2) | | | .54 | .00 | .46 | .00 | .88 |
| Stiffness (0-8) | 3.3(2.0) | 3.5(1.9) | | | .88 | .00 | 3.5(2.0) | 3.4(2.0) | | | .13 | .00 | .92 | .00 | .91 |
| Physical Function (0-68) | 23.7(15.1) | 23.3(14.9) | | | .07 | .00 | 24.2(15.5) | 22.8(14.2) | | | .52 | .00 | .01 | .00 | .97 |
| GCPS | | | | | | | | | | | | | | | |
| Pain Intensity (0-100) | 50.8(22.4) | 49.8(23.6) | | | .16 | .00 | 53.9(22.4) | 46.7(22.0) | | | *7.00 | .03 | .18 | .00 | .83 |
| Disability (0-100) | 43.2(29.1) | 44.3(29.5) | | | .10 | .00 | 48.1(28.5) | 39.4(29.0) | | | *5.47 | .02 | .00 | .00 | .92 |
| Number of Pain Sites | 6.0(4.7) | 4.3(3.2) | | | *11.42 | .04 | 5.4(4.6) | 4.9(3.8) | | | .99 | .00 | 1.37 | .01 | |
| SPPB | | | | | | | | | | | | | | | |
| Total Score (0-12) | 9.6(1.9) | 9.9(1.7) | | | 1.13 | .00 | 10.0(1.8) | 9.5(2.0) | | | 3.15 | .01 | 1.16 | .00 | |

Note. WOMAC=Western Ontario and McMaster Universities Index of Osteoarthritis; GCPS=Graded Chronic Pain Scale; SPPB=Short Physical Performance Battery.

* $p < .05$.