Thermal and Pressure Pain Sensitivity in Patients With Unilateral Shoulder Pain: Comparison of Involved and Uninvolved Sides

Shoulder pain is a common symptom that prompts patients to seek healthcare and, particularly, outpatient physical therapy. Shoulder disorders have 1-year prevalence rates ranging from 5% to 47% and point prevalence rates from 14% to 21%. As in the management of patients with low back pain, there are ongoing efforts to improve diagnostic and prognostic approaches to managing patients with shoulder disorders. Currently there is an abundance of special tests and measures used to investigate shoulder pain. Physical therapists routinely use provocative tests to reproduce their patients’ shoulder pain and compare the results from one side of the body to the other side, to distinguish normal from abnormal. The findings of these special tests assist clinical decision making in differential diagnosis, identification of regional impairments, and/or treatment selection.

Recent efforts to investigate the validity of pain provocation in common musculoskeletal conditions have presented evidence suggesting the excitability of the central nervous system in unilateral musculoskeletal conditions. When compared to healthy controls, individuals with unilateral epicondylalgia, carpal tunnel syndrome, and patellofemoral pain syndrome have demonstrated decreased pain thresholds bilaterally, indicating generalized pain sensitivity beyond the involved extremity. These findings of bilateral similarity in pain perception bring into question the validity of side-to-side comparisons of pain-reproducing tests for musculoskeletal conditions.
METHODS

Participants

Patients seeking operative treatment for shoulder pain, who showed evidence of having rotator cuff pathology, were considered for enrollment in the study.29 Participants provided informed consent, in keeping with guidelines set forth by The University of Florida Institutional Review Board for Human Subjects. The participants recruited for this study were identified at an orthopaedic and sports medicine practice affiliated with the University of Florida.

All participants were required to meet the following inclusion criteria: (a) between 18 and 85 years of age; (b) complaints of pain limited to the anterior, lateral, or posterior shoulder; (c) 1 of the following documented or suspected conditions, based on evidence from clinical examination or imaging studies: rotator cuff tendinopathy, including small (<1 cm), medium (1-3 cm), and large (3-5 cm) tears, adhesive capsulitis, or labral lesion; and (d) scheduled for an arthroscopic procedure.

Exclusion criteria, as determined from the subjective history of the patients, consisted of the following: (a) current complaints of neck, elbow, hand, low back, hip, knee, or ankle pain for more than the previous 3 months; (b) massive or complete rotator cuff tear, defined as a tear greater than 5 cm; (c) documented shoulder osteoarthritis; (d) prior shoulder surgery within the past year or current complaints of pain from prior shoulder surgery; (e) current shoulder fracture, tumor, or infection; (f) previously diagnosed chronic pain disorder, including, but not limited to, irritable bowel syndrome, fibromyalgia, temporomandibular disorder, and chronic low back pain; (g) current medical management for psychiatric disorder, defined as taking 2 or more psychiatric medications; and (h) current gastrointestinal or renal illness.

Procedures

The study protocol was approved by The University of Florida Institutional Review Board. All study procedures were completed 3 to 5 days prior to scheduled shoulder surgery. After providing informed consent, participants were administered demographic questionnaires. Experimental pain testing commenced with bilateral pain sensitivity measures taken on the participant’s right upper extremity first. Initially obtaining pain measures on the right upper extremity allowed standardization of the experimental pain protocol, regardless of side of clinical pain. Testing then proceeded to the left extremity. As it is not desirable to have consecutive tests on one side, each new stimulus was applied to the right extremity first, which allowed for adequate intervals between applications of the painful stimuli. During testing, the examiner was blinded to the patient’s questionnaire history and side of clinical shoulder pain.

Self-Report Measures

Each participant provided information on age, sex, race, employment status, education level, and side of involved arm, and answered yes/no questions on marital status, current medications taken, and whether the current episode of shoulder pain was work-related. Clinical shoulder pain was assessed with the Brief Pain Inventory, which uses an 11-point numerical rating scale for pain intensity, with 0 as “no pain at all” and 10 as the “worst pain imaginable.” Participants rated their shoulder pain intensity for 3 conditions: current pain intensity, worst pain intensity over the last 24 hours, and best pain intensity over the last 24 hours. The values of the pain ratings were summed and divided by 3, to obtain an average clinical pain rating.

Pain Sensitivity Measures

Pressure Pain Threshold (PPT) A Fis-Schner pressure algometer (Pain Diagnostics and Thermography, Inc, Great Neck, NY) was used to assess PPT bilaterally at the muscle belly of the supraspinatus, infraspinatus, brachioradialis, and masseter, and at the acromion process. Mechanical pressure was applied at a rate of 1 kg/s, until the participant reported the first sensation of pain from the pressure, at which point, the amount of pressure was recorded. This process was repeated 3 times bilaterally at each site, and the average of these measures was used in the data analysis. PPT recordings have demonstrated good test-retest and interrater reliability in healthy and clinical popula-
Local PPT was defined as the average of the 3 shoulder measures (supraspinatus, infraspinatus, and acromion process), and distal PPT was defined as the average of the 2 nonshoulder measures (brachioradialis and masseter).

**Thermal Pain Threshold and Tolerance**

Thermal stimuli were delivered to the involved and uninvolved volar forearms, using a contact thermode and a computer-controlled neurosensory analyzer (TSA-2001; Medoc, Inc, Ramat Yishai, Israel), with a peltier element stimulator. Temperature of the thermode was increased at a rate of 0.5°C/s, until the participant reported the first sensation of pain (threshold). In a separate trial to determine pain tolerance, using the same temperature parameters, participants reported when the heat became intolerable. Between trials, the thermode was applied alternately to the right and left arms, and shifted, to avoid sensitization or habituation to the thermal stimuli. Temperature of the thermode was recorded at the time participants reported threshold and tolerance. Two trials each of threshold and tolerance were repeated, and the average of these trials was used for data analysis. Previous studies investigating the reliability of thermal pain testing have revealed minimal intraindividual differences and good test-retest reliability across days.

**Thermal Temporal Summation**

Temporal summation was measured using a contact thermode with a 2.5-cm² surface area, which delivered a series of 10 consecutive heat pulses less than 1 second in duration to the thenar eminence of the involved and uninvolved hands. An interpulse interval of 2.5 to 3.0 seconds (0.33 Hz) was used to ensure the development of temporal summation. At a rate of 10° per second, each heat pulse rapidly increased from a baseline temperature of 35°C to a maximum temperature of 49°C, followed by a return to the 35°C baseline temperature. Participants verbally rated the intensity of each thermal pulse on a numerical pain rating scale from 0 (“no pain”) to 100 (“worst pain imaginable”). To determine temporal summation, only the ratings of the first 5 pulses were analyzed. These ratings are believed to measure the progressive increase in magnitude of C-fiber input as a result of repeated neural firing. We included temporal summation, because it is a dynamic measure thought to capture the pain modulation ability of the central nervous system. Temporal summation measures provide a contrast to static psychophysical measures, such as pain threshold and tolerance, which measure a single point in the pain-processing continuum.

**Statistical Analysis**

Data were analyzed with SPSS for Windows, Version 17.0 (SPSS Inc, Chicago, IL). Descriptive statistics for demographics and experimental pain responses are reported as mean ± SD. For the pressure pain measures, we used a repeated-measures analysis of variance (ANOVA), with side (involved and uninvolved) and location (local and distal) as the within-subject factors. For the thermal measures, we used a repeated-measures ANOVA as well, with side as the within-subject factor. To investigate its influence on side-to-side differences, sex was included in the ANOVA as a between-subject factor for the static psychophysical measures. As appropriate, post hoc comparisons were performed for statistically significant effects (α<.05). A Pearson correlation was used to analyze the association between pain sensitivity measures and average pain intensity.

**RESULTS**

Descriptive data for the 59 participants on demographics and self-reported incidence of pain and average clinical pain intensity are presented in Table 1.
TABLE 2

Pressure Pain Threshold (PPT) and Thermal Pain Threshold and Tolerance Measures Between the Involved and Uninvolved Sides and Sex*

<table>
<thead>
<tr>
<th>Measures</th>
<th>Involved Side</th>
<th>Uninvolved Side</th>
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<tbody>
<tr>
<td><strong>Pressure Pain Threshold</strong></td>
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<tr>
<td><strong>Local PPT (kg)</strong></td>
<td></td>
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<tr>
<td>Female</td>
<td>3.09 ± 1.46 (95% CI: 2.38, 3.80)</td>
<td>3.70 ± 1.52 (95% CI: 2.92, 4.48)</td>
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<tr>
<td>Male</td>
<td>5.29 ± 1.83 (95% CI: 4.72, 5.87)</td>
<td>5.45 ± 2.07 (95% CI: 4.82, 6.09)</td>
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<tr>
<td><strong>Distal PPT (kg)</strong></td>
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<tr>
<td>Female</td>
<td>1.88 ± 0.81 (95% CI: 1.52, 2.24)</td>
<td>2.05 ± 0.76 (95% CI: 1.65, 2.45)</td>
</tr>
<tr>
<td>Male</td>
<td>2.68 ± 0.90 (95% CI: 2.38, 2.97)</td>
<td>2.79 ± 1.07 (95% CI: 2.46, 3.11)</td>
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<tr>
<td><strong>Thermal Pain Threshold and Tolerance</strong></td>
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<tr>
<td><strong>Thermal Pain Threshold (°C)</strong></td>
<td></td>
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<tr>
<td>Female</td>
<td>43.37 ± 3.80 (95% CI: 42.14, 44.60)</td>
<td>43.81 ± 3.52 (95% CI: 42.63, 44.98)</td>
</tr>
<tr>
<td>Male</td>
<td>44.88 ± 2.27 (95% CI: 43.83, 45.93)</td>
<td>44.90 ± 2.32 (95% CI: 43.89, 45.90)</td>
</tr>
<tr>
<td><strong>Thermal Pain Tolerance (°C)</strong></td>
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<td></td>
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<tr>
<td>Female</td>
<td>46.58 ± 2.96 (95% CI: 45.71, 47.45)</td>
<td>46.79 ± 2.36 (95% CI: 46.04, 47.53)</td>
</tr>
<tr>
<td>Male</td>
<td>49.10 ± 1.23 (95% CI: 48.36, 49.85)</td>
<td>48.91 ± 1.30 (95% CI: 48.28, 49.55)</td>
</tr>
</tbody>
</table>

Abbreviation: PPT, pressure pain threshold.
*Values are expressed as mean ± SD (95% CI).
†Significant difference in PPT between the involved side and uninvolved side (P<.05).
‡Local PPT includes supraspinatus, infraspinatus, and acromion process. Distal PPT includes brachioradialis and masseter.
§Significant difference between heat pain threshold and tolerance (P<.05).

**Side-to-Side Assessment of Pressure Pain Sensitivity**

Our primary analysis revealed a main effect for side (F$_{1,15}$ = 4.96, P = .030), which was consistent with our primary hypothesis that participants would report significantly lower PPTs on the involved side compared to the uninvolved side, at both the local and distal locations, indicating enhanced experimental pain sensitivity to pressure pain (TABLE 2). When examining the influence of sex, there was no interaction between side and sex for threshold (F$_{1,15}$ = 1.26, P = .267). However, there was an interaction between PPT location and sex (F$_{1,14}$ = 10.84, P = .002), indicating a sex difference in PPT based on testing location, with female participants reporting lower PPT (ie, enhanced pain sensitivity) than male participants in the local shoulder areas only (FIGURE 1).

**Side-to-Side Assessment of Thermal Pain Sensitivity**

The repeated-measures ANOVA revealed no difference between participants’ involved and uninvolved sides for threshold (F$_{1,15}$ = 2.701, P = .106) or tolerance (F$_{1,15}$ = 0.003, P = .959) (TABLE 2), or temporal summation (F$_{1,15}$ = 1.332, P = .26) (FIGURE 2), indicating no side-to-side difference for measures of thermal pain sensitivity. In addition, there was no interaction between side and sex for threshold (F$_{1,15}$ = 2.286, P = .136) or tolerance (F$_{1,15}$ = 1.931, P = .168).

**Association Between Experimental Pain Sensitivity Measures and Average Clinical Pain Intensity**

Average clinical pain intensity was not associated with any static experimental pain sensitivity measure except PPT at the involved local site (r = –0.284, P = .029). As expected, participants with greater clinical pain intensity exhibited lower PPTs locally, at the site of shoulder pain. Average clinical pain intensity for the dynamic experimental pain sensitivity measure of temporal summation was correlated with the first (r = 0.310, P = .034) and fifth (r = 0.354, P = .016) heat pulses on the involved side and the first (r = 0.291, P = .047) and fifth (r = 0.291, P = .050) heat pulses on the uninvolved side.

**DISCUSSION**

In the current study, we compared experimental pain sensitivity of the involved and uninvolved sides in patients with unilateral shoulder pain. Results for the pressure stimulus, but not the thermal stimuli, supported our primary hypothesis of higher pain sensitivity in the involved side of patients with unilateral shoulder pain. Consistent with our secondary hypothesis, females with unilateral shoulder pain, as compared to males, demonstrated higher local pressure pain sensitivity only; they did not demonstrate enhanced sensitivity to the entire extremity or to thermal stimuli.

Prior studies have investigated bilateral pressure pain sensitivity in unilateral musculoskeletal conditions. In contrast to our findings, most of these studies reported bilateral decreases in the...
PPTs of those with unilateral musculoskeletal conditions, as compared to control participants, and found no differences between the involved and uninvolved sides. For example, previous studies have demonstrated a general state of hyper-sensitivity in patients with lateral epicondylalgia, carpal tunnel syndrome, migraine, and temporomandibular disorder. These conditions may exhibit similar underlying alterations in pain processing or co-occur with subclinical states of widespread pain. The primary intent of our study was not to determine the presence of centrally mediated pain processes, for which it is best to include comparisons between healthy and clinical samples. However, our side-to-side comparisons suggest that peripheral pain processes may be implicated in patients with unilateral shoulder pain.

Several possibilities may explain the conflict between the PPT findings from our study and those previously mentioned. It may be that there is a difference in the pathologic pain mechanisms of the respective conditions, the degree to which the central nervous system is affected, or where in the continuum of disease progression the individuals are. Central alterations in pain processing resulting in hyperalgesia in the contralateral side have been shown to occur after a unilateral peripheral insult. In a study examining bilateral pressure sensitivity for patients with chronic unilateral shoulder pain, Ge et al reported lower PPTs and multiple active trigger points in the infraspinatus muscle of the involved side. However, Ge et al also reported a similar number of latent trigger points between the involved and uninvolved sides, suggesting the development of a central sensitized state. Therefore, it is possible that varying stages of the same disease process may yield different results in experimental pain sensitivity; that is, peripheral sensitization may be easier to detect in acute and subacute stages, while central sensitization may be easier to detect in chronic stages.

Clinically, our study supports the use of pressure stimuli for pain provocation if the objective is to assess side-to-side pain response. Such use of pressure stimuli is also supported by the association between local PPT and clinical pain intensity. Pain threshold at multiple sites in patients with temporomandibular disorder and carpal tunnel syndrome, respectively, found no difference between sides. Similarly, Fernandez-Carnero et al reported no difference in heat pain threshold at multiple sites in patients with temporomandibular disorder and carpal tunnel syndrome, respectively, but found no difference between sides. Furthermore, it may be possible to distinguish between altered peripheral and central pain processes with the application of pressure stimuli. For example, if a clinician is concerned about heightened central pain processing (central sensitization), additional palpation testing at tissue sites away from the local pain region may be performed. There have been fewer studies assessing thermal stimuli in side-to-side comparisons of pain sensitivity in patients with musculoskeletal conditions. Fernandez de las Penas et al and de la Llave Rincon et al found bilateral decreases in heat pain threshold at multiple sites in patients with temporomandibular disorder and carpal tunnel syndrome, respectively.

FIGURE 1. Differences in local and distal pressure pain threshold (PPT) based on sex. Values are composite means of involved and uninvolved sides. Error bars represent 95% confidence intervals for mean values. *Significant difference between groups (P<.05).
However, they do yield new information. To the pressure pain are not surprising; patient population. Make conclusions about the presence of implications if these patterns are used to for testing. Pain sensitivity, based on the stimuli used exhibit different patterns of experimental stimulus. It is possible that individuals recognize, as many prior studies comparisons utilized only a single type of stimulus. It is possible that individuals exhibit different patterns of experimental pain sensitivity, based on the stimuli used for testing. This could have important implications if these patterns are used to make conclusions about the presence of central sensitization in a particular patient population.

The sex differences noted in response to the pressure pain are not surprising; however, they do yield new information. It has been observed that females display greater sensitivity to pressure stimuli, and that, in comparison to other stimuli, pressure pain yields the largest sex difference. Conversely, while a majority of studies support similar findings with the application of thermal stimuli, sex differences with thermal stimuli are not as consistent. Prior studies of pain sensitivity differences between sexes have generally enhanced pain sensitivity. The clinical implication of this finding is that sex differences in pain sensitivity may be most evident in females reporting increased pain with local palpation more often than males. Future research in clinical populations will determine if the location affects sex differences in experimental pain sensitivity.

Overall, these data highlight future clinical and research considerations in musculoskeletal pain assessment. Nijs et al. have introduced guidelines for clinicians for identifying altered central pain processing in patients with musculoskeletal disorders. One of their primary recommendations in the examination is the use of multiple modalities for pain sensitivity in locations local and distal to the area of the initial injury (or primary pain complaint). Our study followed that recommendation by not only assessing local and distal locations but utilizing more than 1 pain stimulus. Had we used only 1 stimulus, we might have drawn faulty conclusions regarding the pain processing of patients with unilateral shoulder pain. For example, if we had only used thermal stimuli in our study, the data would have been indicative of a central sensitization model, as in studies of lateral epicondylalgia and carpal tunnel syndrome. In contrast, if we had only used pressure stimuli, a peripheral sensitization model might have been the logical conclusion. The inconsistency between our pressure and thermal findings highlights the necessity of utilizing multiple stimuli, as it provides a more complete picture of pain processing in clinical conditions. In addition, variable sensitivity among individuals across different pain stimuli has been reported, which challenges the notion of a generalized state of heightened pain sensitivity. Zhou et al. compared differences in responses to various pain stimuli across different body sites in patients with irritable bowel syndrome and found enhanced pain sensitivity with thermal heat, cold, and ischemic stimuli, but not with mechanical pressure. These findings also varied across body sites, with the greatest pain sensitivity noted in the foot as compared to the hand. Future studies should incorporate multiple stimuli when characterizing the pain profile of patients with musculoskeletal conditions. To assist clinical decision making, future studies should not only determine which profiles are indicative of central and peripheral processing but also which profiles are associated with poor clinical outcomes.
Limitations

There are several limitations in this study that should be noted. As mentioned previously, it was not the intention of the study to examine the presence of central sensitization or hyperalgesia; therefore, the study did not include a healthy control group. A control group would have enabled us to compare experimental pain sensitivity measures between groups and to determine if the patient group was more or less sensitive to pain. A competing hypothesis for this study might state that central sensitization is present if the unaffected side PPTs were lower than those of healthy controls. With the current data, we can only conclude that the affected side is more pain sensitive than the other side. In addition, the pressure pain stimulus was administered over locations local and distal to the shoulder, while the thermal stimuli were applied only to the distal forearm and hand locations. Pressure pain stimuli were applied to general pain-producing anatomical landmarks, with no intended specificity of location in producing a familiar or concordant pain complaint. It has been suggested that a nonuniform distribution of painful points may exist within some muscles of the upper quarter, which could potentially influence the results of pressure testing. The results of this study are not generalizable to all clinical samples seen in a physical therapy setting but limited to those of the specific patient population examined, which included patients with rotator cuff pathology, adhesive capsulitis, and labral lesion, as diagnosed by a physician, and determined to be candidates for surgery. That the clinical cohort contained multiple pathologies could be a limitation as well, as we did not track the specific pathological diagnoses of these patients and could not assess any specific interaction between the outcomes of this study and shoulder pathology. However, we did not have a specific hypothesis about this, nor did we feel that this would have been a vital component of the study, as most analytical comparisons between sides were made within individuals. Additional information regarding duration of pain, level of disability, and special test results was not available to the researchers.

Conclusion

The results of this study provide evidence for higher experimental pain sensitivity in the involved side of patients with unilateral shoulder pain. However, findings differed with stimulus applied, sex of patient, and location of testing. Side-to-side differences were noted only with pressure stimuli. Compared to males, females demonstrated higher pain sensitivity to pressure stimuli at the local shoulder region. In terms of clinical application, these results suggest that pressure stimuli, such as palpation and mechanical stress testing, in patients with shoulder pain may be used to elicit side-to-side differences but not to make determinations about the existence of a state of central sensitization. The inconsistency between our findings on the use of pressure and thermal stimuli supports the need for multiple-modality testing in determining elevated states of pain sensitivity, even in patients with local pain complaints. Future studies should incorporate multiple stimuli when examining the pain profile of clinical populations and link these profiles to clinical outcomes.

Key Points

Findings: Higher experimental pain sensitivity to pressure stimuli but not thermal stimuli was found in the involved side of patients with unilateral shoulder pain. Female participants reported higher experimental pain sensitivity than male participants for local testing on the involved side only.

Implication: A pressure stimulus, such as palpation and mechanical stress testing, may be a suitable clinical tool for determining side-to-side differences. However, multiple stimuli should be incorporated if the goal is to determine central sensitization.

Caution: These findings are limited to patients with preoperative shoulder pain due to rotator cuff pathology, adhesive capsulitis, or labral lesion, who are candidates for surgery. Lack of a control group prohibits definitive conclusions regarding central and peripheral pain processing in this sample.

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