HHS Public Access

Author manuscript

Exp Gerontol. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

Exp Gerontol. 2017 November ; 98: 186–191. doi:10.1016/j.exger.2017.08.026.

Physical performance and movement-evoked pain profiles in community-dwelling individuals at risk for knee osteoarthritis

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Abstract

Background—Knee pain associated with osteoarthritis is a significant contributor to decreased physical function. Recent evidence supports the inter-individual heterogeneity associated with knee pain presentation, but whether there is similar heterogeneity in physical performance among these individuals has not been previously examined. The aim of the present study was to characterize the variability in physical performance profiles and the pain evoked by their performance (i.e., movement-evoked pain).

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Methods—In a secondary analysis of the community-based study Understanding Pain and Limitations in Osteoarthritic Disease (UPLOAD), individuals (n=270) completed functional, pain, psychological, and somatosensory assessments. Hierarchical cluster analysis was used to derive physical function profiles that were subsequently compared across several clinical, psychological and experimental pain measures.

Results—Our results support the hypothesis that among persons with knee OA pain, three different physical performance profiles exist with varying degrees of movement-evoked pain. Even as all three groups experienced moderate to severe levels of spontaneous knee pain, those individuals with the most severe movement-evoked pain and lowest physical functional performance also had the least favorable psychological characteristics along with increased mechanical pain sensitivity and temporal summation.

Conclusions—Our findings support the need for the assessment and consideration of movement-evoked pain during physical performance tasks as these have the potential to increase the value of functional and pain assessments clinically. The identification of the mechanisms driving pain burden within homogeneous groups of individuals will ultimately allow for targeted implementation of treatments consistent with a biopsychosocial model of pain.

Keywords

pain; physical function; inter-individual variability

Introduction

The incidence of osteoarthritis (OA) is dramatically increasing worldwide as the aging population grows. In particular, the knee is the most commonly affected joint where multiple cellular and molecular mechanisms underlie loss of synovial tissue structure and function ultimately leading to reduced physical functioning and pain (Mobasheri et al., 2015; Musumeci et al., 2015; Jinks et al. 2007; Neogi et al. 2009). Lower self-reported and performance-based physical function has been consistently observed in older adults with knee pain (Hopman-Rock et al. 1996; Sharma et al. 2003). Indeed, pain-associated reduction in physical function is a strong predictor of future disability and dependency in elderly people (Zakoscielna & Parmelee 2013).

Recent evidence demonstrates considerable inter-individual heterogeneity among people with knee pain across a number of clinical, experimental and psychological variables (Cruz-Almeida et al. 2013; Cardoso et al. 2016; Frey-Law et al. 2016). There is likely similar heterogeneity in physical functional performance *among* individuals with knee pain that accounts for distinct functional trajectories (i.e., get worse or recover over time) (van Dijk et al. 2006). While it is common to classify individuals into categories of high versus low physical function, a more sophisticated approach would consider patterns of responses across multiple functional domains. Additionally, common measures of physical performance do not routinely assess pain during task performance, i.e. movement-evoked pain, which is likely one of the drivers of the observed physical performance outcomes. Although abundant evidence exists that pain impacts physical functional performance, no studies to date have examined potential differences in physical functional performance and

movement-evoked pain *among* persons with knee OA pain. Therefore, the primary aims of the present study were: 1) to identify subgroups in persons with knee pain based on physical performance and movement evoked-pain measures, and 2) to compare these subgroups with respect to clinical pain, as well as psychological and somatosensory function measures. Identification of subgroups among persons with knee OA would ultimately allow for targeted treatment approaches.

Methods

This is a secondary data analysis including 270 individuals with knee pain who participated in the community-based study Understanding Pain and Limitations in Osteoarthritic Disease (UPLOAD) at the University of Florida (UF) and the University of Alabama at Birmingham (UAB). The aim of the parent study was to understand ethnic differences in pain and functional limitations in persons with knee pain. The sample was between 45 and 85 years of age who identified as either African American (AA) or non-Hispanic whites (NHW). Participants had knee postero-anterior and lateral radiographs to assess severity of radiographic OA (i.e., KL score). A detailed description of the screening, inclusion/exclusion criteria has been reported previously (King et al. 2013; Cruz-Almeida et al., 2014). Participants were excluded if they: 1) had cognitive impairment; 2) used opioids on a daily basis; 3) were hospitalized for a psychiatric illness in the preceding year; 4) had a history of acute myocardial infarction, heart failure or uncontrolled hypertension (BP >150/95 mm Hg); 5) had bilateral prosthetic knee replacements or other clinically significant surgery to the affected knee; 6) had peripheral neuropathy; 7) had systemic diseases including rheumatoid arthritis, systemic lupus erythematosus or fibromyalgia. After consent, subjects underwent a general health assessment (HAS) session followed by a quantitative sensory testing (QST) session no more than 4 weeks apart. During the HAS, participants completed questionnaires (detailed below) and physical function assessments and a physician/nurse practitioner conducted a health history/examination including weight and height measurements for BMI calculation. During the QST, a multimodal experimental pain battery was administered (details previously reported) (Cruz-Almeida et al. 2014; King et al. 2013). Both UF and UAB IRBs approved the study (IRB# 201400209).

Physical Function

Short Physical Performance Battery (SPPB)—The SPPB consists of three measures of lower-extremity function: standing balance, 4-meter walking speed, and ability to rise from a chair. Participants were asked for an overall numerical pain rating for their knee using a visual analogue scale (VAS) of 0–100, where 0 = no pain sensation and 100 = the most intense pain sensation imaginable. These measures have been standardized and are widely used in older populations (Guralnik et al. 1995).

QST

Heat Pain Threshold (HPT)—Stimulation was administered by a computer-controlled Medoc PATHWAY Pain & Sensory Evaluation System with a 16×16 mm Advanced Thermal stimulator. HPT was assessed on the most painful knee and ipsilateral ventral forearm. HPT trials started with the thermode at 32°C increasing at 0.5°C/s until the participant pressed a

button indicating the sensation “first became painful.” HPT was repeated 3 times and averaged for analysis.

Temporal Summation of Heat Pain—Heat stimuli were applied to the most painful knee and ipsilateral forearm using the CHEPS thermode of the PATHWAY system. The experimenter moved the thermode between trials to avoid sensitization/habituation of cutaneous nociceptors. Participants were asked to rate their heat pain using a VAS (0–100). Stimulations lasted <1 second with a 2.5-second inter-stimulus interval with target temperature of 44°C. If a subject gave a rating of 100 the procedure was stopped. The first pain rating was subtracted from the fifth pain rating as the change score.

Pressure Pain Threshold (PPT)—PPT was assessed on the most affected knee, the ipsilateral quadriceps, extensor carpi radialis longus and trapezius. Order of testing was counterbalanced and randomized. For all test sites, a handheld digital pressure algometer (AlgoMed; Medoc) was applied at a constant rate of 30kPa/s. Participants were instructed to press a button when the pressure sensation “first became painful”. PPTs were repeated 3 times on each site to create a mean PPT for that site. The maximum pressure for the knee was 600kPa and 1000kPa for other sites. Maximum pressures were based on safety considerations for our knee pain participants. For individuals reaching maximum pressure levels without reporting pain, a value of 600/1000 was assigned.

Punctate Pain—Subjects underwent a punctate mechanical stimulation procedure using a calibrated nylon monofilament with 300 grams of force. Punctate mechanical testing was performed on the patella of the index knee and the back of the ipsilateral hand, in randomized order. Participants were instructed to provide a verbal pain rating on a 0–100 scale after a single contact. The single pain ratings were averaged together separately at knee and hand dorsum).

Immediately following the single stimulus, a series of 10 stimuli were administered and participants provided a verbal rating of the greatest pain intensity experienced. Two series of stimulations were administered at a rate of one contact per second. The ratings were averaged separately by site. The averages of the single pain ratings were subtracted from the averages of the 10 trials to calculate temporal summation at each location.

Cold Pressor Task (CPT)—Participants were asked to submerge their right hand up to the wrist in cold water during 3 separate trials of 16°C, 12°C, and 8°C, separated by 10-minute breaks. Temperatures were maintained (+0.1°C) by a refrigeration unit (Neslab) that constantly circulated water to prevent warming around the immersed hand. The time the participants could keep their hand in the water was recorded for each individual temperature (seconds).

Clinical and Psychosocial Assessments

Graded Chronic Pain Scale (GCPS)—The GCPS measures knee pain severity over the past 6 months. The GCPS contains 7-items related to pain intensity and pain-related interference with activities. We used pain frequency and characteristic pain intensity scores (Von Korff et al. 1992).

Number of painful sites—Participants indicated areas besides the knee where they felt pain including head, neck, shoulders, chest, stomach, upper and lower back, arms, hands, legs and feet. The total number of sites was used for analysis.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)—The WOMAC assesses knee OA symptoms in the preceding 48 hours, including pain, stiffness and physical function (Bellamy et al. 1988). Higher scores indicate greater levels of pain, stiffness, and functional limitations.

Coping Strategies Questionnaire-Revised (CSQ-R)—The CSQ-R measures pain-related active and passive coping techniques (Robinson et al. 1997). The CSQ's catastrophizing subscale has been validated and is commonly used to assess catastrophizing (Sullivan et al. 2001).

Pain Vigilance and Awareness Questionnaire (PVAQ)—The PVAQ assesses attention to pain, as well as preoccupation and vigilance related to pain over the past few weeks (McCracken 1997). Greater scores represent greater pain vigilance (Roelofs et al. 2003).

The Center for Epidemiologic Studies Depression Scale (CES-D)—The CES-D measures the frequency of depressive symptoms during the preceding week (Radloff 1977). Higher scores indicate greater levels of depressive symptomatology.

Positive and Negative Affect Scale (PANAS)—The PANAS is comprised of 20-items rated on a 5-point scale (Watson et al. 1988; Crawford & Henry 2004). Higher scores on positive items indicate higher positive affect, while higher scores on negative items indicate higher negative affect.

Statistical Methods

Cluster Analysis of SPPB Measures—To identify homogenous subgroups, we entered the 3 SPPB subscales (i.e., Balance, Gait, Chair Stands) along with their movement-evoked pain ratings into a hierarchical cluster analysis using Ward's clustering method with squared Euclidean distances. The optimal number of clusters was determined by examining the agglomeration coefficients and analysis of the dendogram. We used ANOVAs to assess the internal validity of the final cluster solution on the raw variables.

External Validation of the Cluster Solution—The empirically derived clusters were compared across the total SPPB score, clinical pain, psychological and somatosensory function measures using ANCOVA procedures with Bonferroni post-hoc adjustments. Race and study site were included as covariates given their differential distribution across the clusters. Chi-square analyses were used to compare the clusters on categorical data. Normality assumption was determined by a combination of the Shapiro Wilk test and examination of the Quantile-Quantile (Q-Q) Plots. Alpha was set to 0.05 for all hypothesis testing. All analyses were conducted in IBM-SPSS24 software for MacOS.

Results

Our study sample was mostly female (63.1%) and AA (56.3%) with an average age of 57 years (45–85 years old). Three clusters emerged and were significantly different across clustering variables. Table 2 details the variables used for clustering and how they were significantly different between the clusters, ($p<0.05$). Cluster 1 was the largest (n=143) and consisted of individuals with the highest physical function and minimal performance-evoked pain, Cluster 2 (n=101) consisted of individuals with moderate physical function and mild performance-evoked pain and Cluster 3 was a small group of individuals (n=24) with the lowest functional performance along with severe performance-evoked pain. Clusters differed significantly in their race composition and recruitment study site ($p<0.05$), but not in age, BMI, sex, KL scores or educational attainment (Table 1, $p>0.05$).

Clusters also differed significantly across most clinical and psychological measures, even after adjusting for race and study site (Table 3, $p<0.05$). Individuals in Cluster 3 had significantly greater spontaneous pain intensity and frequency during the past 6 months, more painful sites and higher WOMAC scores than individuals in Cluster 1. Similarly, participants in Cluster 3 reported significantly greater depressive symptomatology, greater use of active and passive coping strategies, more catastrophizing, pain hypervigilance and negative affect than individuals in Cluster 1. However, all three clusters reported similar levels of positive affect ($p>0.05$).

Clusters also differed significantly across most QST measures even after adjusting for race and study site (Table 4, $p<0.05$). Individuals in Cluster 3 had significantly lower pressure and cold pain sensitivity and higher punctate pain sensitivity at the knee and at other distal sites compared to individuals in Cluster 1. Individuals in Cluster 3 also experienced greater temporal summation of heat and punctate pain than individuals in Cluster 1.

Discussion

We sought to identify physical performance profiles among a sample of community-dwelling individuals with knee pain and to determine the relationship between these profiles with clinical, psychological and somatosensory function measures. While ample evidence demonstrates decreased physical performance in individuals with versus without knee pain, our finding of functional subgroups *among* individuals with knee pain is novel. In particular, clinically meaningful differences in functional performance (Perera et al. 2006) were highly associated with the severity of the pain evoked by the functional tasks (i.e., performance-associated pain, movement-evoked pain). The subgroup with the highest functional performance across all tasks experienced minimal movement-evoked pain, while the lowest functional group across all tasks experienced the most severe movement-evoked pain. Movement-evoked pain measures enhance functional assessments by providing additional insight regarding the adverse effects of movement rather than simply measuring the functional performance alone. Recent evidence suggests that movement-evoked pain might represent a dimension of the pain experience that is more disability-relevant than spontaneous pain (Mankovsky-Arnold et al. 2014). This is further supported by our findings. While all three groups experienced moderate to severe levels of spontaneous knee pain

during the past six months, those with the most severe movement-evoked pain and lowest physical function also experienced more frequent pain at multiple body sites. This is consistent with evidence from the MOBILIZE Boston study where multisite pain was a strong predictor of poorer lower body function (Eggermont et al. 2009). In addition, pain at the knee was the joint location most strongly associated with poor function (Eggermont et al. 2009). However, our findings may also support the idea that an individual's overall pain experience is encompassed by the combined burden of their spontaneous and evoked pain types. For example, the highest functional group in our sample experienced the lowest combination of both spontaneous and evoked pains while the lowest functional group experienced the highest severity of both spontaneous and evoked pain types. Thus, the latter group had the greatest overall burden of pain, highlighting the importance of assessing both pain types in clinical and research settings. It is also interesting that differences in pain and function among these clusters closely mirrored differences in the WOMAC-pain measure. This finding may possibly indicate that this brief, validated, self-report assessment may be useful in predicting movement-evoked pain and function in clinical settings where task performance is not feasible.

Our participants with the lowest physical functional performance along with severe movement-evoked pain also reported more depressive symptoms, increased pain hypervigilance, and more pain-related catastrophizing than the other clusters. Previous studies have reported associations between psychological measures and activity-related pain (Sullivan et al. 2002; Swinkels-Meewisse et al. 2006) including associations with treatment outcomes (Lindberg et al. 2016). Indeed, multiple psychological factors in people with knee OA pain are associated with the development of disability and longer term worsening of pain (Helminen et al. 2016). On the other hand, the most important predictor of catastrophizing, anxiety and depression after total joint replacement was preoperative pain and self-reported physical function (Wood et al. 2016), supporting reciprocal complex associations between pain, psychological and physical functioning. It is possible that a set of psychological behaviors (i.e., hyper-attentiveness to pain, depression, catastrophizing) contributes to maladaptive movement avoidance and physical inactivity patterns that are similar to those proposed in the fear-avoidance model in persons with low back pain (Beneciuk et al. 2012). Future research is needed to determine whether similar patterns are present in persons with knee pain and whether targeted psychological interventions are complementary and beneficial with respect to pain and physical function.

The participants with the lowest overall physical functional performance were also the most pain sensitive to pressure, cold and punctate stimuli across several body sites. Similarly, previous research has demonstrated increased generalized pressure pain sensitivity in patients with knee OA pain, suggesting the presence of central sensitization to mechanical stimuli (Arendt-Nielsen et al. 2010; Frey-Law et al. 2016). These lower functioning participants also exhibited greater heat and mechanical temporal summation. Studies have also reported a tendency for individuals with knee OA pain to experience greater temporal summation of pain, thought to reflect pain amplification at the spinal cord (Skou et al. 2013; Arendt-Nielsen et al. 2010). That mechanical experimental pain measures differed most consistently between the functional groups likely reflects differences in joint-activated nociceptor sensitization. Indeed, movement-evoked pain is associated with sensitization of

peripheral Aδ and C-fiber afferents (Brucini et al. 1981; Hendiani et al. 2003), while spontaneous pain or pain at rest is related to sensitization at the dorsal horn and spinal cord (Schaible et al., 2002). Also, increased heat temporal summation implicates centrally-mediated mechanisms, and evidence suggests that in some individuals, peripheral and central nervous system mechanisms significantly contribute to knee OA pain (Murphy et al. 2011; Arendt-Nielsen et al. 2010; Frey-Law et al. 2016; Cardoso et al. 2016). Future mechanism-based research is needed incorporating measures of temporal summation of movement-evoked pain and their associations with physical function and intervention outcomes.

The current study has some limitations. First, most of our sample was highly functional, consistent with community-dwelling individuals not necessarily seeking care for knee pain. This is further reflected by the small sample size in the lowest functional group. Thus, it is unknown whether the same analyses in more severe clinical samples would yield similar results. Studies are needed to determine whether these profiles can be replicated across different settings and samples, including the oldest old. Furthermore, treatment response across profiles such as these may provide important mechanistic and predictive information supporting a personalized medical approach.

Despite the limitations, our findings support the need for consideration of movement-evoked pain during physical performance tasks as these have the potential to increase the value of functional, clinical and experimental pain assessments. These findings may be relevant both for research in order to identify potential biological mechanisms as well as in the clinic. The identification of the biopsychosocial mechanisms driving pain burden within homogeneous groups of individuals will ultimately allow for targeted implementation of treatments. For example, it is possible that individuals such as those in the lowest functional group would benefit from a combination of surgical, pharmacological and psychological therapies to reduce movement-evoked pain and optimize physical function. Future research is needed to test such hypotheses.

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Highlights

- We found significant heterogeneity in physical performance and movement-evoked pain among community-dwelling individuals with knee osteoarthritis.
- Profiles based on physical performance and movement-evoked pain differed significantly in psychological and somatosensory function.
- Movement-evoked pain needs to be considered clinically in persons with knee OA.

Table 1

Demographic & socioeconomic measures across the clusters.

	Cluster 1 (n=145)	Cluster 2 (n=101)	Cluster 3 (n=24)	P
Age, mean ± SD years	57.2 ± 7.4	55.9 ± 7.6	56.3 ± 7.4	0.402
BMI, mean ± SD kg/m^2	30.9 ± 7.1	32.0 ± 7.6	33.9 ± 9.7	0.151
Sex, no. (%), X^2				0.191
Female	98 (67.6)	57 (56.4)	16 (66.7)	
Male	47 (32.4)	44 (43.6)	8 (33.3)	
Race, no. (%), X^2				<0.0001
African American	71 (49.0)	67 (66.7)	20 (83.3)	
Non-Hispanic White	74 (51.0)	34 (33.3)	4 (16.7)	
Right Knee KL Score, no. (%), X^2				0.208
0	76 (57.1)	43 (47.8)	11 (45.8)	
1	18 (13.5)	16 (17.8)	3 (12.5)	
2	20 (15.0)	8 (8.9)	3 (12.5)	
3	14 (10.5)	11 (12.2)	4 (16.7)	
4	5 (3.8)	12 (13.3)	3 (12.5)	
Left Knee KL Score, no. (%), X^2				0.114
0	80 (60.2)	44 (48.4)	9 (37.5)	
1	17 (12.8)	21 (23.1)	5 (20.8)	
2	15 (11.3)	13 (14.3)	2 (8.3)	
3	15 (11.3)	11 (12.1)	5 (20.8)	
4	6 (4.5)	2 (2.2)	3 (12.5)	
Education, no (%), X^2				0.163
High school or less	58 (40.0)	57 (56.4)	12 (50.0)	
2 years of college	33 (22.8)	23 (22.8)	6 (25.0)	
Bachelor's degree and above	54 (37.2)	21 (20.8)	6 (25.0)	
Site, no (%), X^2				<0.0001
University of Florida	75 (54.7)	73 (76.8)	19 (82.6)	
University of Alabama at Birmingham	62 (45.3)	22 (23.2)	4 (17.4)	

Table 2

Physical functional measures across the clusters.

	Cluster 1 Highest Function Minimal Movement-Evoked Pain (n=145)	Cluster 2 Moderate Function Mild Movement-Evoked Pain (n=101)	Cluster 3 Lowest Function Severe Movement-Evoked Pain (n=24)	p-value
Chair Stand Score, mean ± SD	2.9 ± 1.1	2.0 ± 1.3	1.5 ± 1.1	<0.0001
Pain Chair Stand, mean ± SD	4.5 ± 5.4	31.7 ± 17.8	75.7 ± 25.2	<0.0001
Gait Score, mean ± SD	3.7 ± 0.7	3.6 ± 0.8	3.0 ± 1.0	0.001
Pain Gait, mean ± SD	2.2 ± 3.5	24.4 ± 15.5	73.8 ± 16.0	<0.0001
Balance, mean ± SD	3.9 ± 0.3	3.8 ± 0.6	3.6 ± 0.7	0.012
Pain Balance, mean ± SD	1.8 ± 2.6	22.3 ± 14.2	72.7 ± 16.8	<0.0001
SPPB Total Score *	10.5 ± 1.5	9.4 ± 1.9	8.0 ± 2.0	<0.0001

*SPPB Total Score was NOT entered into the clustering procedure

Table 3

Clinical pain and psychological measures across the clusters adjusted for race and study site.

	Cluster 1 Higher Function Minimal Movement-Evoked Pain (n=145)	Cluster 2 Moderate Function Mild Movement-Evoked Pain (n=101)	Cluster 3 Lower Function Severe Movement-Evoked Pain (n=24)	Adjusted p-value
Characteristic Pain Intensity, mean ± SD	41.8 ± 20.0	57.5 ± 18.2	79.2 ± 11.6	<0.0001
WOMAC-Pain, mean ± SD	5.4 ± 3.4	8.6 ± 3.5	13.2 ± 3.3	<0.0001
WOMAC- Stiffness, mean ± SD	2.8 ± 0.7	3.9 ± 0.8	5.5 ± 1.0	<0.0001
WOMAC-Function, mean ± SD	17.8 ± 11.9	27.6 ± 12.6	42.0 ± 10.5	<0.0001
# of Pain Sites, mean ± SD	4.5 ± 3.8	5.8 ± 3.7	9.0 ± 4.8	<0.0001
# of Pain Days Past 6 mo., mean ± SD	7.5 ± 14.8	20.7 ± 38.9	40.3 ± 56.9	<0.0001
CES-D, mean ± SD	8.2 ± 6.7	10.8 ± 7.9	12.9 ± 7.2	0.003
CSQ- Active Coping, mean ± SD	2.7 ± 0.9	3.2 ± 0.9	3.4 ± 1.0	0.001
CSQ- Passive Coping, mean ± SD	2.8 ± 1.2	2.9 ± 1.1	3.6 ± 1.0	0.004
CSQ- Catastrophizing, mean ± SD	1.5 ± 0.9	1.7 ± 1.1	2.4 ± 1.2	<0.0001
PVAQ, mean ± SD	44.6 ± 14.7	45.4 ± 13.7	56.3 ± 10.3	<0.0001
Positive Affect, mean ± SD	35.4 ± 7.5	35.6 ± 7.8	36.4 ± 8.7	0.832
Negative Affect, mean ± SD	13.7 ± 4.6	15.7 ± 6.5	15.1 ± 6.5	0.050

Table 4

QST measures across clusters adjusted for race and study site.

	Cluster 1 Higher Function Minimal Movement-Evoked Pain (n=145)	Cluster 2 Moderate Function Mild Movement-Evoked Pain (n=101)	Cluster 3 Lower Function Severe Movement-Evoked Pain (n=24)	Adjusted p-value
PPT- Medial Knee, mean ± SD	293 ± 159	275 ± 161	191 ± 118	0.014
PPT- Lateral Knee, mean ± SD	312 ± 173	293 ± 164	208 ± 105	0.019
PPT- Arm, mean ± SD	247 ± 169	248 ± 170	152 ± 74	0.028
PPT- Trapezius, mean ± SD	275 ± 175	255 ± 172	189 ± 89	0.070
PPT- Quadriceps, mean ± SD	434 ± 229	405 ± 218	311 ± 142	0.043
Punctate Pain, Hand, mean ± SD	11.9 ± 16.7	11.0 ± 14.9	20.4 ± 24.2	0.044
Punctate Pain, Knee, mean ± SD	16.1 ± 19.8	13.9 ± 16.6	32.6 ± 28.5	<0.0001
CPT-16°C, mean ± SD seconds	34.0 ± 19.3	33.7 ± 17.8	29.6 ± 16.1	0.587
CPT-12°C, mean ± SD seconds	54.8 ± 11.9	49.5 ± 15.9	49.0 ± 15.5	0.008
CPT-8°C, mean ± SD seconds	48.6 ± 16.7	41.6 ± 20.5	39.0 ± 19.3	0.004
HPT- Arm, mean ± SD	41.7 ± 3.3	41.7 ± 3.3	41.1 ± 3.5	0.710
HPT- Knee, mean ± SD	42.1 ± 3.1	41.7 ± 3.5	41.1 ± 3.9	0.334
Heat TS- Knee, mean ± SD	0.3 ± 14.0	0.6 ± 14.3	8.7 ± 20.1	0.045
Punctate TS- Arm, mean ± SD	13.3 ± 16.1	19.4 ± 22.6	24.1 ± 20.5	0.009
Punctate TS- Knee, mean ± SD	18.4 ± 18.0	23.6 ± 21.5	25.2 ± 18.0	0.084