Table: Relation of PSI Score vs. Individual QST Measures to Developing of Constant Pain Over Two-year Period

	Development of Constant Pain
Per 10-unit increase	*Odds ratio (95% CI)*
Pain Sensitivity Index	**1.49 (1.08, 2.04)**
PPT, wrist	1.23 (1.01, 1.49)
PPT, patella	1.19 (1.03, 1.37)
TS, wrist	1.00 (0.77, 1.30)
CPM	1.25 (0.68, 2.27)
Analyses were adjusted for age, sex, race, body mass index (BMI), widespread pain, sleep, depressive symptoms, pain catastrophizing, and use of opioids. QST: quantitative sensory testing, PPT: pressure pain threshold, TS: temporal summation, CPM: conditioned pain modulation,	

PRESENTATION NUMBER: 442
WEIGHT-BEARING AND NON-WEIGHT-BEARING PAIN MAY REFLECT DIFFERENT PAIN MECHANISMS IN KNEE OSTEOARTHRITIS

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Purpose: Knee osteoarthritis (OA) is predominantly characterized by pain with weight-bearing (**WB**) activities, which is thought to be reflective of nociceptive pain. However, pain at rest, i.e., non-weight bearing (**NWB**), is also common in individuals with knee OA. Why NWB pain may occur in a disease that is largely biomechanically driven is not clear, though altered neurobiological functioning of pain pathways is hypothesized to play a role, such as ascending pain facilitation (pain sensitization) and inefficient descending pain modulation. We, therefore, sought to determine whether pain sensitization or inefficient conditioned pain modulation (**CPM**) may have different associations with WB pain and NWB pain in knee OA.

Methods: We used data from The Multicenter Osteoarthritis Study (MOST), a NIH-funded longitudinal cohort of older adults with or at risk of knee OA. To assess pain sensitivity and CPM, we employed the following quantitative sensory testing (**QST**) measures: 1) pressure pain threshold (**PPT**) at the wrist and patellae using a handheld algometer, defined as the point at which pressure first changed into slight pain, and categorized into sex-specific tertiles. Low PPT at the wrist is thought to reflect greater central sensitization while low PPT at the patella is thought to reflect greater peripheral +/- central sensitization; 2) mechanical temporal summation (**TS**) assessed using a weighted punctuated probe applied as a train at 1Hz over 10 seconds. An increase in pain rating at the end of the train indicates central sensitization; 3) Efficiency of CPM assessed using forearm ischemia as the conditioning stimulus. A ratio of the post-conditioning stimulus PPT to the pre-conditioning stimulus PPT being $\leq$1 indicates inefficient CPM. WB pain was defined as presence of at least moderate pain on each of the WOMAC pain subscale questions regarding stairs, standing, and walking; a similar approach was used to define NWB pain based upon the questions regarding sitting/lying, and sleeping at night. We evaluated the relation of each QST measure to each of the WOMAC pain questions in separate models, using logistic regression with generalized estimating equations to account for correlations between two knees within an individual, adjusting for potential confounders (age, sex, body mass index (BMI), catastrophizing, depressive symptoms, poor sleep quality, widespread pain).

Results: 2749 subjects (5479 knees) were included (mean age 64±11, 57% female, mean BMI 29.5±5.7 kg/m^2). Lower patellar PPT was associated with greater odds of both WB and NWB pain (**Table**). Lower wrist PPT was associated with greater odds of WB pain but not with NWB pain while facilitated TS was associated with greater odds of only pain with stairs. CPM was not associated with any of the outcomes.

Conclusions: Greater peripheral sensitization, as measured by patellar PPT, was associated with both WB and NWB pain while PPT at the wrist and TS, both measures of central sensitization, were associated with WB pain only. CPM, a surrogate measure of descending pain modulation, was not associated with either type of pain. Our findings challenge the hypothesis that NWB pain may reflect greater pain sensitization and inefficient CPM than WB pain, and suggest that other mechanisms may be responsible for NWB pain that merit further examinations, such as inflammation or psychological factors.

Table 1. Results for the logistic regression analyses of the association between QST measures and individual WOMAC pain questions (n=5479 knees)

At least moderate pain with:	Odds Ratio (95% Confidence Interval)							
	PPT tertiles (patella)			PPT tertiles (wrist)			TS (per SD unit increase)	%CPM (per SD unit increase)
	Highest (Ref)	Middle	Lowest [most pain sensitized]	Highest (Ref)	Middle	Lowest [most pain sensitized]		
Walking n=465 (8.5%)	1.0	1.47* (1.08, 2.00)	2.26* (1.68, 3.05)	1.0	1.58* (1.14, 2.17)	1.95* (1.44, 2.64)	1.09 (0.98, 1.21)	0.96 (0.87, 1.06)
Standing n=443 (8.1%)	1.0	1.19 (0.86, 1.64)	1.98* (1.45, 2.70)	1.0	1.25 (0.88, 1.78)	1.85* (1.32, 2.58)	1.06 (0.95, 1.20)	1.04 (0.94, 1.14)
Stairs n=1280 (23.5%)	1.0	1.28* (1.07, 1.52)	1.79* (1.49, 2.15)	1.0	1.37* (1.12, 1.68)	1.56* (1.27, 1.90)	1.11* (1.02, 1.19)	1.00 (0.93, 1.07)
Sitting n=309 (5.6%)	1.0	1.31 (0.92, 1.87)	1.88* (1.32, 2.68)	1.0	1.06 (0.73, 1.55)	1.39 (0.96, 2.00)	1.00 (0.88, 1.14)	1.03 (0.92, 1.14)
Lying in bed n=359 (6.6%)	1.0	1.39* (1.00, 1.93)	1.60* (1.16, 2.21)	1.0	1.10 (0.78, 1.55)	1.20 (0.86, 1.68)	1.04 (0.93, 1.16)	0.99 (0.88, 1.10)

All models adjusted for age, sex, BMI, catastrophizing, depressive symptoms, poor sleep quality and widespread pain.
*: significant results
Abbreviations: PPT, pain pressure thresholds; TS, temporal summation; %CPM, % efficiency of conditioned pain modulation

PRESENTATION NUMBER: 443
ASSOCIATIONS OF PERIPHERAL AND CENTRAL PAIN MECHANISMS WITH VOLUNTARY MUSCLE STRENGTH IN PEOPLE WITH KNEE PAIN

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Purpose: Knee pain is a major cause of disability and approximately 25% of people, aged 55 years and over in the UK, experience knee pain. Pain might be caused by local structural changes or inflammation linked to knee osteoarthritis (OA), and might be associated with alterations in central nervous system pain processing. People with knee pain commonly report weakness or giving way of their knees, despite often a lack of evidence of structural instability. Knee pain can reduce quadriceps voluntary contractions, a process referred to as reflex inhibition. "Central mechanisms trait" (CMT), a composite self-report tool, was designed to measure central pain augmentation in individuals with knee pain (Akin-Akinyosoye et al. Osteoarthritis Cartilage 2020; 28(2):173-81). It can be measured using 8 questionnaire items addressing anxiety, depression, catastrophizing, neuropathic-like pain, fatigue, sleep disturbance, pain distribution, and cognitive impact. This study aimed to explore possible effects of central and peripheral pain mechanisms on muscle strength in people with knee pain.

Methods: This is a sub-study embedded in the Nottingham Knee Pain and Health in the Community (KPIC) cohort study in the East Midlands region of the UK including 9506 men and women aged $\geq$ 40 years at baseline. 322 participants that reported knee pain took part in additional baseline clinical assessments and were invited for repeat assessment at 1 year. The “Early Knee Pain” group at baseline was defined as pain commencing within the past 3 years, with the “Established Knee Pain” group being those reporting moderate to severe knee pain that lasted more than 3 years. Clinical assessment related to central pain mechanisms comprised CMT and pressure pain detection thresholds (PPT) at the proximal tibia ipsilateral to the index knee. Assessment related to peripheral pain mechanisms were total radiographic OA score (Nottingham Line Drawing Atlas), and ultrasound synovitis score. The mean value of 3 repeats of maximum quadriceps voluntary contraction (MVC) for index knee was assessed by ‘Nicholas Manual Muscle Tester’ (Lafayette Instruments, Indiana). The index knee was selected based on the only (unilateral) or most painful knee (bilateral). A knee was randomly selected if all scores were the same. The index knee was the only knee that was analysed in this study. The dominant hand grip strength was measured by the mean value of 3 repeats using a JAMAR hydraulic dynamometer (Lafayette, Indiana). Associations were explored using Spearman’s correlation coefficient and multiple linear regression models. Results were presented with standardized coefficients beta (β value), 95% Confidence Interval (CI), and p-value.

Results: Of the 322 participants that provided baseline data, 219 had early and 103 had established knee pain. Quadriceps and hand grip strength were each associated with knee pain severity both at baseline and in longitudinal analyses. In cross-sectional analyses at baseline, PPT and CMT were associated with quadriceps strength, more strongly than were radiographic OA scores, while ultrasound synovitis score was not significantly associated with muscle strength. CMT was associated with hand grip strength. At 1 year, 255 people were reassessed (181 with early knee pain and 74 with established knee pain). The correlations between baseline variables and year 1 quadriceps strength were examined for baseline index knee pain (r=-0.32, p<0.001), age (r= -0.08, p=0.2), female sex (r=-0.46, p<0.001), study group (r= -0.25,

p<0.001), CMT (r=-0.44, p<0.001), PPT (r=0.29, p<0.001), global X-ray score (r=-0.13, p=0.001) and total ultrasound score (r=-0.01, p=0.9). In longitudinal regression analysis (after adjustment for the above variables plus baseline quadriceps strength) baseline CMT was associated with year 1 quadriceps strength (β=-0.20 (95%CI:-0.34 to -0.06); p=0.005; Table 1). Baseline CMT was also associated with year 1 hand grip strength (Table 1).

Conclusions: Central mechanisms of pain are associated with reduced muscle strength, both at the index knee and at a distant site (hand). Central pain mechanisms appeared to drive these associations, whereas local radiographic changes did not appear to be strongly linked. Addressing central pain augmentation has potential to improve muscle strength and reduce frailty in people with knee pain.

Analyses	Dependent variable	Independent variables	Beta	95% CI	p
Baseline regression	Baseline quadriceps strength	CMT	-0.19	-0.33 to -0.04	0.012
		PPT	0.13	0.01 to 0.25	0.037
		Global X-ray	-0.11	-0.24 to 0.02	0.102
		Total ultrasound score	0.03	-0.10 to 0.16	0.645
	Baseline hand grip strength	CMT	-0.21	-0.33 to -0.08	0.001
		PPT	0.19	0.08 to 0.30	0.001
Longitudinal regression	Year 1 quadriceps strength	CMT	-0.20	-0.34 to -0.06	0.005
		PPT	0.04	-0.07 to 0.15	0.485
		Global X-ray	0.01	-0.12 to 0.14	0.831
		Total ultrasound score	-0.03	-0.15 to 0.09	0.637
	Year 1 hand grip strength	CMT	-0.24	-0.40 to -0.08	0.004
		PPT	0.04	-0.07 to 0.16	0.454

Baseline and longitudinal regression analyses for muscle strength

Osteoarthritis and Cartilage

PRESENTATION NUMBER: 444

PRE-TREATMENT PAIN SENSITIVITY IS ASSOCIATED WITH OUTCOME FOLLOWING EXERCISE THERAPY IN PATIENTS WITH KNEE OSTEOARTHRITIS - AN OBSERVATIONAL STUDY

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Purpose: Exercise therapy in combination with education is recommended as first-line treatment for painful knee osteoarthritis (KOA). In clinical practice, supervised exercise therapy and education demonstrate approx. 25% pain relief following an 8-week treatment program. Studies indicate that some patients with KOA experience larger pain relief compared to others. Assessments of peripheral and central pain mechanisms has been used to predict responders and non-responders to treatment. Studies on surgery and treatment with non-steroid anti-inflammatory drugs in patients with KOA have indicated that patients with higher levels of pain sensitivity might respond less positive. The primary aim of this observational study was to investigative if measures of pre-treatment pain sensitivity was associated with clinical outcomes after supervised exercise therapy and education.

Methods: Patients with painful KOA (numeric rating scale [NRS, 0-10] $\geq$ 3) were included, and examined before and 1-2 weeks after 6-8 weeks of supervised exercise therapy (2 sessions of 1 hour per week) and 2 sessions of patient education. Handheld pressure pain threshold (PPT) was assessed locally at the most painful knee at 4 peripatellar sites (knee) and at two remote sites at the m. tibialis anterior (TA) and the contralateral m. extensor carpi radialis longus (ECRL). Further, computer-controlled cuff algometry at the lower leg with the most intense knee pain was used to assess pain detection threshold (cPDT), pain tolerance threshold (cPTT) and conditioned pain modulation (cCPM). Peak pain intensity within the last 24 hours (NRS, 0-10), PainDetect questionnaire (PDQ, 0-38) and Knee injury and Osteoarthritis Outcome Score (KOOS) were assessed as clinical measures. PDQ assesses the pain phenotype with a score $\leq$ 12 indicating probably nociceptive pain, 13-18 uncertain pain phenotype and $\geq$ 19 probably neuropathic pain. $KOOS_4$ was defined as the average score of the subscale scores for Pain, Symptoms, Activity of Daily Living and Quality of Life (0-100 with 0 indicating extreme problems and 100 indicating no problems). Physical performance was assessed using the 40-meter walk test (40MWT). A treatment attendance score (%) was calculated for each patient by dividing the number of sessions attended by the number of sessions scheduled (twice per week). This study was approved by the local ethical committee (N-20190045) and pre-registered at clinicaltrials.org (NCT04123756). All participants gave oral and written informed consent prior to enrollment.

Results: This interim analysis reports on the first patients recruited for this observational study. Eleven KOA patients (6 women) with mean peak pain intensity of 6.0 ± 1.5, median pain duration 17.0 months (range: 5-120) and body mass index of 30.3 ± 5.7 were included in this interim analysis. In one subject, follow-up was made by telephone due to the COVID-19 situation, leaving 10 subject for the analysis on changes in pain sensitivity measures. Attendance score was 98.1 ± 18.1% during 7.1 ± 0.7 weeks. Following treatment, improvements were observed in $KOOS_4$ (57.1 ± 10.0 at baseline vs. 65.3 ± 13.1 at follow-up, $P < 0.01$), and peak pain intensity (6.0 ± 1.5 vs. 3.2 ± 2.3, $P < 0.001$). No differences were seen for PDQ (7.6 ± 2.6 vs 6.8 ± 3.6, $P = 0.77$) and 40MWT (27.1 ± 6.6 sec vs. 25.8 ± 5.2 sec, $P = 0.29$). Further, no changes in any of the pain sensitivity measures were found following treatment (all $Ps > 0.15$). Pre-treatment cPDT ($r_s < 0.73$, $P < 0.05$) and cPTT ($r_s < 0.72$, $P < 0.05$) were associated with post-treatment $KOOS_4$. No significant associations were found between pre-treatment PPT or CPM effects and post-treatment peak pain measures or change in KOOS-4 ($P > 0.05$).

Conclusions: These results indicate that patients with higher pre-treatment pressure pain sensitivity have worse $KOOS_4$ scores following supervised exercise therapy and education.

PRESENTATION NUMBER: 445

COMORBIDITIES IN HAND OSTEOARTHRITIS PATIENTS: PREVALENCE AND IMPACT ON PAIN AND PAIN SENSITIZATION

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Purpose: Pain is a hallmark symptom of hand osteoarthritis (OA), and a subset of people with hand OA display centrally driven pain characteristics. It is well-known that pain is largely driven by person-related factors rather than the OA severity, but how comorbidities are related to the pain experience in persons with hand OA is currently undetermined. Comorbidities may be linked to changes in central and peripheral pain pathophysiology and the pain levels through for example low-grade inflammation. Hence, the purpose of this study was to determine whether the burden of comorbidities or the individual comorbidities were associated with pain and pain sensitization in persons with hand OA.

Methods: These cross-sectional analyses included 282 participants from the Nor-Hand study, which is an hospital-based study of hand OA patients. Comorbidities were assessed by a self-administered comorbidity questionnaire (0-45 scale)by Sangha et al., which includes 12 predefined medical conditions and 3 optional conditions. The participant can receive a maximum of 3 points for each comorbidity: 1 point for the presence of the comorbidity, 1 point if one receives treatment for the comorbidity and 1 point for limitation in functioning due to the comorbidity. The index is sub-divided into a Disease, Limitation and Treatment scale. The participants completed questionnaires about pain in their hands, knees/hips and total body. The questionnaires included Numeric Rating Scale (NRS) about hand pain (0-10) and all joints (0-10), the Australian/Canadian (AUSCAN) hand pain subscale (0-20 scale) and