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Published in:
European Journal of Pain

DOI (link to publication from Publisher):
10.1002/ejp.2183

Publication date:
2024

Document Version
Publisher's PDF, also known as Version of record

Received: 24 April 2023 | Revised: 20 August 2023 | Accepted: 27 August 2023

DOI: 10.1002/ejp.2183

EJP European Journal of Pain

ORIGINAL ARTICLE

Quantitative sensory testing, psychological profiles and clinical pain in patients with psoriatic arthritis and hand osteoarthritis experiencing pain of at least moderate intensity

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Funding information
Danish Psoriasis Foundation, Grant/Award Number: 210417; Danish Rheumatism Foundation, Grant/Award Number: R179-A6299; Aalborg University; Aalborg University hospital, Grant/Award Number: 2016-017615; Danish National Research Foundation, Grant/Award Number: DNRF121; Novo Nordisk Foundation, Grant/Award Number: NNF21OC0065373

Abstract

Background: Chronic pain is the hallmark symptom of joint diseases. This study examined the differences in quantitative sensory testing between patients with psoriatic arthritis (PsA), hand osteoarthritis (hand-OA) and a pain-free control group and differences between patients with and without concomitant fibromyalgia (cFM).

Methods: All patients and pain-free controls were assessed using pressure pain thresholds (PPT), temporal summation of pain (TSP), conditioned pain modulation (CPM) and clinical pain intensities. Psychological distress was assessed with the Hospital Anxiety and Depression Scale, Pain Catastrophizing Scale, and Pittsburgh Sleep Quality Index. Disability was assessed with the Health Assessment Questionnaire and pain quality with the painDETECT questionnaire. cFM was identified using the revised 2016 American College of Rheumatology diagnostic criteria.

Results: Patients with hand-OA ($n = 75$) or PsA ($n = 58$) had statistically significant lower PPTs and CPM, greater TSP, and higher scores of psychological distress ($p < 0.05$) than controls ($n = 20$). Patients with cFM (58%) had higher scores of depression ($p = 0.001$), anxiety ($p = 0.004$), catastrophizing ($p = 0.012$), disability ($p < 0.001$), higher painDETECT score ($p = 0.001$), TSP ($p = 0.027$), and reduced sleep quality ($p = 0.021$) when compared to patients without cFM.

Conclusion: Patients with hand-OA and PsA exhibited signs of pain sensitization and a higher degree of psychological distress and disability than pain-free individuals. Patients with cFM had greater TSP, painDETECT score, disability, catastrophizing, and reduced sleep quality, than patients without, indicating greater degree of pain sensitization, psychological burden, and disability.

Statement of Significance: This paper shows that a significant proportion of patients with hand osteoarthritis and psoriatic arthritis with moderate pain intensity have significantly increased signs of pain sensitization and markers of psychological distress. A large proportion of these patients fulfil the criteria for concomitant fibromyalgia and these patients show even greater propensity towards pain sensitization and psychological distress.

1 | INTRODUCTION

Psoriatic arthritis (PsA) and hand osteoarthritis (hand-OA) represent two joint pain conditions, where chronic pain is prevalent and underlying pain mechanisms are less well understood (Panter et al., 2021; Rifbjerg-Madsen, Christensen, et al., 2017; Rifbjerg-Madsen, Wæhrens, et al., 2017). PsA is an inflammatory joint disease characterized by peripheral arthritis, enthesitis, dactylitis, axial arthritis and psoriasis in the skin (Ritchlin et al., 2017). Even though effective anti-inflammatory treatment options exist more than 30% of patients with PsA experience moderate pain (Kilic et al., 2018) and widespread pain is common in PsA (Højgaard et al., 2019).

Hand-OA is a degenerative joint disease with a female preponderance (Marshall et al., 2018). Cardinal symptoms are joint pain, stiffness, and loss of function. Hand-OA can affect different joints especially the first carpometacarpal joint and the distal and proximal interphalangeal joints (Kloppenburg & Kwok, 2012). In contrast to PsA, no disease-modifying treatment for hand-OA is available and data from a recent study indicates that altered nociceptive signal processing may explain some of the pain experienced by patients with OA (Pettersen et al., 2019).

At present, however, there is a dearth of studies examining the differences and similarities in pain experience and mechanisms among different joint pain conditions especially with regard to PsA and Hand-OA.

Fibromyalgia is a chronic pain condition with complex symptomatology and unclear aetiology (Sarzi-Puttini et al., 2020). It is characterized by widespread musculoskeletal pain and is associated with clinical signs of sensitization including quantitative sensory testing (QST) parameters representing widespread pain hypersensitivity (Palmer et al., 2019), facilitated temporal summation of pain (TSP) (Price et al., 2002; Staud et al., 2007) and inhibited conditioned pain modulation (CPM; Normand et al., 2011; Paul-Savoie et al., 2012), but also increased risk of depression (Løge-Hagen et al., 2019), catastrophizing (Hassett et al., 2000) and sleep disturbances (Wu et al., 2017). The 2016 diagnostic criteria for fibromyalgia states that fibromyalgia is a valid diagnosis regardless of concomitant disease (Wolfe et al., 2016) and research has shown that concomitant fibromyalgia (cFM) is prevalent in patients with inflammatory arthritis (Zhao et al., 2019) and knee osteoarthritis (Mahgoub et al., 2020).

However, the underlying pain mechanisms are less studied in joint pain conditions with cFM and whether this leads to increased pain, increased signs of sensitization, psychological distress or disability remains largely unknown.

The aim of this exploratory study was to compare QST and psychological factors in patients with hand-OA and PsA with pain-free controls. Furthermore, to explore whether a difference in QST and psychological factors exists in patients with and without cFM.

2 | METHODS

2.1 | Study population

The present study is a secondary analysis based on the patient cohort from the NordCAN trial, a randomized controlled trial examining the analgesic effects of cannabidiol (Vela et al., 2022). Patients with Hand-OA or PsA were included between November 2018 and September 2020 after obtaining written informed consent. All participants were ^{3} 18 years of age, had a pain intensity of ≥ 30/100 mm measured by visual analogue scale (VAS) and fulfilled either the 2006 Classification Criteria for

Psoriatic Arthritis (CASPAR) (Taylor et al., 2006) or the 1990 American College of Rheumatology (ACR) (Altman et al., 1990) criteria for Hand-OA. Participants with PsA did not have active peripheral disease (swollen joints evaluated by a trained rheumatologist/physician using clinical examination and ultrasound.) or signs of systemic inflammation (assessed by serological markers of systemic inflammation). Detailed inclusion and exclusion criteria and study population are previously described (Vela et al., 2022) Patients with PsA had psoriasis severity measured using the Psoriasis Area Severity Index (Fredriksson & Pettersson, 1978). Controls were recruited from the Department of Rheumatology staff and were eligible for inclusion if they were $^{3} \geq$ 18 years of age, did not experience daily pain intensity of $^{3} \leq$ 10/100 mm measured by VAS and reported no pain conditions.

This trial was conducted at the Department of Rheumatology, Aalborg University Hospital, Denmark and approved by the regional Danish Human Ethics Committee (N-20170074) and was registered on clinicaltrials.gov (NCT03703934).

Reporting is done according to the Strengthening the Reporting of Observational Studies in Epidemiology Statement (Von Elm et al., 2007).

2.2 | Clinical assessment of pain

Patients with Hand-OA and PsA were asked to rate their average pain intensity experienced during the last 24 h with a 100 mm visual analogue scale (VAS). The scale was anchored with 0 mm indicating no pain and 100 mm indicating the worst pain imaginable.

2.3 | Quantitative sensory testing

A hand-held algometer equipped with a 1 cm^2 rubber probe (Somedic, Hørby, Sweden) was used to measure the pressure pain threshold (PPT) by pressing laterally at 90° on the most painful finger joint (local site) and 5 cm distally to the tibial tuberosity of the right leg (shin, distal site). Pressure was applied gradually at 30 kPa and the PPT was defined as the point when the patient verbally indicated that the pressure stimulus became painful (Arendt-Nielsen et al., 2016; Pettersen et al., 2019).

Additionally, cuff PPT and cuff pain tolerance threshold (cuff PTT) were assessed using a computer-controlled cuff algometer (Cortex Technology and Aalborg University, Denmark) fitted with two 13-cm wide tourniquets on both legs (VBM, Sulz, Germany) and connected to an electronic 100 mm VAS.

TSP was measured by applying 10 pressure stimuli (with a pressure equal to the PTT) to the right leg. The duration of each stimulus was one second and the pause between stimuli had a duration of one second. Patients rated the pain intensity continually and TSP was defined as the difference between measured pain intensity at the first and the 10th stimulus (Petersen et al., 2015). If a patient stopped the test before the last stimulus was given, a pain intensity score of 10 at the 10th stimulus was assigned.

CPM was measured by applying pressure (conditioning stimulus) to the left leg and simultaneously measuring cuff PPT on the right leg as done in previous studies (Petersen et al., 2016; 2019). A pressure equal to 70% of cuff PTT was used as the conditioning stimulus. The CPM effect was defined as the difference between conditioned cuff PPT and unconditioned cuff PPT (i.e., CPM effect = cuff PPT conditioned minus cuff PPT unconditioned).

QST measurements were completed by one examiner (JV), not blinded to the index joint disease of patients.

2.4 | Patient-reported outcomes

All participants were assessed with the Hospital Anxiety and Depression Scale (HADS). A scale with an anxiety and a depression domain each rated from 0 to 21 where a higher score equals a greater involvement of psychiatric comorbidity (Zigmond & Snaith, 1983). A score of ≥8 was previously identified as the optimal cut-off for identifying patients with clinical depression or anxiety related disorders, in both domains (Bjelland et al., 2002).

The Pittsburgh Sleep Quality Index (PSQI) questionnaire was used to evaluate sleep quality. The PSQI is rated from 0 to 21 with a greater score indicating reduced sleep quality (Buysse et al., 1989).

The Pain Catastrophizing Scale (PCS) questionnaire was used to evaluate catastrophizing yielding a score from 0 to 52 with a higher score indicating greater pain catastrophizing (Mjl et al., 1995).

Self-reported disability was assessed with the Health Assessment Questionnaire Disability Index (HAQ-DI) yielding a global score of zero to three with a higher score indicating more severe disability (Bruce & Fries, 2003).

In addition, patients with hand-OA and PsA filled out the painDETECT questionnaire (PDQ) (Freynhagen et al., 2006). A questionnaire designed to screen for neuropathic pain in musculoskeletal conditions. Scored from −1 to 38, a score above 18 indicating a likely neuropathic component. The PDQ has also been used as a surrogate for central sensitization (Rifbjerg-Madsen, Christensen, et al., 2017; Rifbjerg-Madsen, Wæhrens, et al., 2017).

2.5 | Classification of concomitant fibromyalgia

Patients were classified as having cFM if they fulfilled the 2016 revised American College of Rheumatology (ACR) diagnostic criteria for fibromyalgia (Wolfe et al., 2016). The 2016 diagnostic criteria consist of a Widespread Pain Index (WPI), a Symptom Severity Score (SSS), and a generalized pain criterion. The criteria are satisfied if symptoms have been present at a similar level for at least three months and the patient has a WPI of at least seven and an SSS of at least five or a WPI of four–six and a SSS of at least nine. Furthermore, a generalized pain criterion must be satisfied, defined as pain in a minimum of four out of five body regions.

2.6 | Statistical analysis

Baseline variables were described for all participants with means and standard deviations (SD) for continuous variables after accessing normality with a quantile plot. Discrete variables were reported with counts and percentages.

Differences in continuous outcomes between groups were compared using an independent two-sided t-test for normal distributed variables and a bootstrap *t*-test with 10,000 replicates for continuous non-normally distributed variables (Efron & Tibshirani, 1993). Normality of the variable's sample distribution was assessed visually by a Q-Q plot. Discrete variables were compared using a Chi^2 test. Comparison between three or more groups was done using one-way ANOVA and pairwise comparisons were performed post hoc with Tukey's test. Multiple linear regression analysis was performed to control for confounding using each patient-reported outcome measure and QST variable as the dependent and age, sex and group (Hand-OA, PsA or control) as independent variables. Test statistics were considered significant with a *p*-value of <0.05.

All data management and analyses were carried out using R version 3.5.1 (R Foundation for Statistical Computing).

3 | RESULTS

One-hundred and fifty-three participants were included in the analysis (see Table 1). Eleven percent of patients with hand-OA reported "Base of thumb" as their most painful joint while 79% reported a "distal finger joint" as their most painful joint. Twenty-four patients with PsA had active psoriasis. The mean Psoriasis Area Severity Index score was 1.2 with a range of 0.0 to 14.5. Patients with hand-OA where older than patients with PsA (mean difference 13 years 95% CI 9 to 17 years; $p<0.001$) and the pain free controls and a larger proportion of pain-free controls were female compared with the PsA and hand-OA group.

Patients with hand-OA and PsA had significantly lower PPTs, CPM and greater TSP when compared with controls and had significantly higher scores in all patients reported outcomes (See Table 1). Patients with PsA had higher HADS depression score than patients with OA, with mean difference 1.33 (95% CI 0.39 to 2.28; $p=0.004$), but no other significant differences were found between patients with OA and PsA. Adjusting for age and sex did not change the results.

3.1 | Patients without fibromyalgia

3.1.1 | Patients with psoriatic arthritis versus patients with hand osteoarthritis

When comparing patients with PsA and OA, both without cFM, patients with PsA had higher depression score (mean difference 1.58 95% CI 0.39 to 2.77; $p=0.005$) anxiety score (mean difference 1.48 (95% CI 0.03 to 2.90; $p=0.045$) compared to patients with OA and patients with OA had reduced CPM effect −9.33 (95% CI −17.58 to −1.04; $p=0.029$) compared to patients with PSA.

3.1.2 | Patients with hand osteoarthritis versus controls

When comparing patients with OA without cFM with controls, patients with OA had significantly higher scores of depression (mean difference 1.03 95% CI 0.10 to 1.97; $p=0.027$), anxiety (mean difference 1.78 95% CI 0.023 to 3.33; $p=0.028$), disability (mean difference 0.6 95% CI 0.36 to 0.83; $p<0.001$), catastrophizing (mean difference 10.82 95% CI 6.51 to 15.13; $p<0.001$), and sleep problems (mean difference 3.25 95% CI 1.31 to 5.2; $p=0.001$). Patients with OA demonstrated significantly lower PPTs at the painful joint (mean difference − 143.24 kPa 95% CI −221.37 to −65.10; $p<0.001$) and at a distal site (mean difference − 139.16 kPa 95% CI −231.89 to −46.43; $p=0.003$, greater TSP (mean difference 1.39 95% CI 0.3 to 2.07; $p=0.007$), and reduced CPM effect (mean difference −16.51 95% CI −25.03 to −7.98; $p<0.001$).

3.1.3 | Patients with psoriatic arthritis versus controls

When comparing patients with PsA without cFM with controls, patients with PsA had significantly higher scores of depression (mean difference 2.61 95% CI 0.5 to 3.11;

TABLE 1 Demographic and study specific outcomes.

	Hand-OA	PsA	Controls
N	75	58	20
Females (%)	48 (64%)*	39 (75%)*	18 (90%)
Age, years (SD)	66.07 (7.73)*	53.16 (11.62)*,**	58.10 (8.32)
Pain intensity, 0 to 100 mm (SD)	56.6 (18.3)*	58.6 (18.0)*	—
Quantitative sensory testing			
Pressure pain threshold joint, kPa[a] (SD)	214.60 (127.27)*	260.60 (178.24)*	369.85 (180.74)
Pressure pain threshold shin, kPa[a] (SD)	284.40 (152.18)*	281.36 (154.18)*	446.25 (180.40)
Temporal summation of pain (SD)	2.68 (2.35)*	2.51 (1.91)*	1.13 (1.34)
Conditioned pain modulation, kPa[b] (SD)	3.13 (15.78)*	7.70 (18.02)*	19.03 (14.35)
Patient reported outcomes			
HADS depression, 0 to 21 (SD)	2.09 (2.16)*	3.43 (2.68)*,**	0.50 (0.95)
HADS anxiety, 0 to 21 (SD)	4.34 (3.37)*	5.55 (3.32)*	1.79 (2.82)
Pain Catastrophizing Scale, 0 to 52 (SD)	16.52 (9.26)*	16.95 (7.80)*	3.75 (5.23)
Pittsburgh Sleep Quality Index, 0 to 21 (SD)	8.23 (3.84)*	9.02 (4.18)*	4.42 (2.41)
Health Assessment Questionnaire, 0–3 (SD)	0.77 (0.56)*	0.86 (0.61)*	0.01 (0.04)
painDETECT questionnaire, −1 to 38 (SD)	17.95 (6.04)	18.73 (5.51)	—
Widespread pain index (SD)	5.81 (4.35)	6.79 (4.66)	—
Fibromyalgia (%)	29 (38.7)	30 (51.7)	—

Abbreviations: Hand-OA, Hand osteoarthritis; PsA, Psoriatic arthritis; SD: HADS, Hospital anxiety and depression scale.

[a]Assessed using handheld algometer.

[b]Calculated using bootstrap.

*$p < 0.05$ when compared with control.; **$p < 0.05$ when compared with Hand-OA.

$p < 0.001$), anxiety (mean difference 3.25 95% CI 1.41 to 5.09; $p < 0.001$), disability (mean difference 0.71 95% CI 0.43 to 0.96; $p < 0.001$), catastrophizing (mean difference 12 95% CI 3.75 to 15.75; $p < 0.001$), and sleep problems (mean difference 3.7 95% CI 1.72 to 5.73; $p < 0.001$). Patients with PsA did not demonstrate lower PPTs at the painful joint (mean difference −91.17 kPa 95% CI -199.40 kPa to 17.06 kPa; $p = 0.096$) but did at a distal site (mean difference −139.25 kPa 95% CI −238.67 kPa to −39.83 kPa; $p = 0.007$), with greater TSP (mean difference 0.98 95% CI 0.06 to 1.90 $p = 0.037$), but not reduced CPM effect (mean difference −7.2 kPa 95% CI −16.97 kPa to 2.57 kPa; $p = 0.145$).

3.2 | Concomitant fibromyalgia

Fifty-nine out of 133 patients (44%) fulfilled the criteria for fibromyalgia. Out of these, 30 patients (52%) were diagnosed with PsA and 29 (39%) were diagnosed with hand-OA. In total 38% of patients with hand-OA and 52% with PsA fulfilled the criteria for fibromyalgia (see Table 2).

3.2.1 | Concomitant fibromyalgia versus non-concomitant fibromyalgia

Patients fulfilling the fibromyalgia criteria had significantly facilitated TSP compared with those without (mean difference 0.83 95% CI 0.09 to 1.57; $p = 0.027$) but otherwise no significant difference in QST scores were observed. Patients with cFM did, however, have higher depression (mean difference 1.22 95% CI 0.38 to 2.06; $p = 0.005$), anxiety (mean difference 1, 71 95% CI 0.57 to 2.85; $p = 0.004$), catastrophizing (mean difference 3.85 95% CI 0.88 to 6.82; $p = 0.012$, PSQI (mean difference

1.64 95% CI 0.25 to 3.03; $p = 0.021$), HAQ (mean difference 0.35 95% CI; 0.16 to 0.55 $p < 0.001$) and painDETECT scores (mean difference 3.55 95% CI 1.6 to 5.5; $p = 0.001$) when compared to those without cFM. There was no significant difference in the use of analgesics between groups (see Table 3).

TABLE 2 Demographic and study specific outcomes based on concomitant fibromyalgia status.

	No fibromyalgia	Fibromyalgia	*p*
N	74	59	
Female (%)	43 (58%)	44 (75%)	0.072
Age, years	61 (11.53)	59 (11.56)	0.360
PsA (%)	28 (37.8)	30 (50.8)	0.184
Pain intensity, mm	55.4 (17.8)	60.0 (18.4)	0.149
Quantitative sensory testing			
Pressure pain threshold (Joint), kPa[a]	245.48 (147.55)	220.00 (157.13)	0.351
Pressure pain threshold (Shin), kPa[a]	307.06 (160.01)	254.54 (138.85)	0.055
Temporal summation of pain (0–10)	2.24 (1.74)	3.07 (2.53)	**0.027**
Conditioned pain modulation, kPa	6.06 (17.45)	4.03 (16.27)	0.499
Patient reported outcomes			
HADS depression	2.09 (2.16)	3.43 (2.68)	**0.005**
HADS anxiety	4.12 (3.07)	5.83 (3.57)	**0.004**
Pain catastrophizing scale	15.03 (8.42)	18.88 (8.44)	**0.012**
Pittsburgh Sleep Quality Index	7.86 (3.87)	9.50 (4.01)	**0.021**
Health Assessment Questionnaire	0.65 (0.53)	1.00 (0.59)	**<0.001**
painDETECT questionnaire	16.67 (5.58)	20.22 (5.52)	**<0.001**
Widespread pain index	3.28 (2.79)	9.95 (3.33)	**<0.001**

Bold indicates significance level at *p*-value ≤ 0.05.

Abbreviations: HADS, Hospital anxiety and depression scale; PsA, Psoriatic Arthritis.

[a]Assessed using handheld algometer.

TABLE 3 Analgesic and DMARD use.

	Hand-OA	PsA	*p*	No fibromyalgia	Fibromyalgia	*p*
Analgesics						
N	75	58		74	59	
Paracetamol	54 (72%)	46 (79%)	0.444	51 (69%)	49 (83%)	0.094
NSAIDs	23 (33%)	29 (50%)	0.078	33 (45%)	21 (36%)	0.383
Codein	4 (5%)	1 (2%)	0.532	2 (3%)	3 (5%)	0.796
Tramadol	7 (9%)	6 (10%)	≈1	2 (3%)	8 (14%)	0.308
Anticonvulsants	7 (9%)	8 (14%)	0.596	5 (7%)	10 (17%)	0.116
Opioids	2 (3%)	2 (4%)	0.932	2 (3%)	2 (4%)	0.900
DMARDs						
N (PsA only)		58		28	30	
csDMARDs (%)	—	23 (40%)	—	11 (40%)	12 (40%)	≈1
bDMARDs (%)	—	7 (12%)	—	4 (14%)	3 (10%)	0.922

Abbreviations: bDMARDs, Biological disease modifying antirheumatic drugs; csDMARDs, Conventional synthetic disease modifying antirheumatic drugs; Hand-OA, Hand osteoarthritis; NSAID, Non-steroidal anti-inflammatory drugs; PsA, Psoriatic arthritis.

Besides age and gender distribution there were no significant differences between patients with PsA or Hand-OA with cFM.

3.2.2 | Concomitant fibromyalgia versus non-concomitant fibromyalgia in patients with hand osteoarthritis

When limiting the analysis to patients with Hand-OA there were no significant differences in QST measures but those with cFM had higher scores of depression (mean difference 1.86 95% CI 0.46 to 2.41; $p=0.005$), anxiety (mean difference 1.44 95% CI 0.49 to 3.59; $p=0.011$), and catastrophizing (mean difference 5.13 95% CI 0.76 to 9.51; $p=0.021$). Patients with cFM also scored higher on HAQ (mean difference 0.4 95% CI 0.15 to 0.65; $p=0.002$) and painDETECT (mean difference 3.29 95% CI 0.5 to 6.09 $p=0.021$).

3.2.3 | Concomitant fibromyalgia versus non-concomitant fibromyalgia in patients with psoriatic arthritis

When limiting the analysis to patients with PsA there were no significant differences in measures except a higher painDETECT score in patients with cFM (mean difference 3.79 95% CI 0.96 to 6.61; $p=0.010$). No significant differences were found in the proportion of patients using classical disease modifying antirheumatic drugs or biological disease modifying antirheumatic drugs (see Table 3).

4 | DISCUSSION

The present exploratory study showed that patients with hand-OA or PsA and pain of at least moderate intensity exhibited signs of central sensitization and a higher degree of psychological distress and disability when compared with pain-free individuals. Furthermore, patients also fulfilling criteria for concomitant fibromyalgia presented with the strongest facilitation of temporal summation of pain, the highest painDETECT score, and the highest level of psychological distress and disability.

4.1 | Patients with psoriatic arthritis and hand osteoarthritis compared with controls

Patients with hand-OA or PsA with moderate pain intensity experienced hypersensitivity at a distal site, had facilitated TSP and inhibited CPM when compared with a pain-free control group.

In previous studies, researchers have examined pressure pain detection thresholds in patients with PsA compared with non-arthritic controls and found decreased PPT, but the authors did not disclose whether the tested joints were affected with active arthritis or near a joint with active arthritis, making a conclusion of hypersensitivity due to central sensitization difficult (Bagnato et al., 2015; Giudice et al., 2018). Patients with PsA in the present study exhibited low PPT at a distal site, had facilitated TSP and inhibited CPM indicating involvement of spinal and supraspinal mechanisms.

Decreased pressure pain detection thresholds have previously been observed in patients with hand-OA but results have been inconsistent (Chiarotto, Fernandez-de-las-Peñas, Castaldo, Negrini, & Villafañe, 2013; Chiarotto, Fernandez-de-Las-Peñas, Castaldo, & Villafañe, 2013; Pedersini et al., 2020; Wajed et al., 2012) possibly owing to the heterogenous nature of the disease. Petterson et al. identified 42% of patients in a hand-OA cohort displaying facilitated TSP. This is in line with the present study where patients with hand-OA exhibited facilitated TSP, inhibited CPM and lower PPT at a distal non-joint site when compared with pain-free controls indicating the presence of augmented central pain processing.

Patients with PsA displayed clinically significant higher scores of depression and anxiety when compared with controls while patients with hand-OA displayed clinically significant higher scores of anxiety when compared with controls. However, the mean scores for depression and anxiety for all groups were below the proposed threshold of seven for clinical disorders (Bjelland et al., 2002). This indicates a higher level of psychological distress rather than clinical depression/anxiety disorder. This observation aligns with the higher scores typically found in populations of patients with chronic pain (Andersen et al., 2014).

More disturbed sleep, disability and pain catastrophizing were also found in patients with hand-OA and PsA when compared with pain-free controls. Besides a greater but non clinically significant difference in depression score, no significant differences in patient reported outcome measures or QST between patients with hand-OA and PsA were observed. Studies comparing QST profiles between patients with osteoarthritis and other inflammatory joint conditions are sparse. A study compared the PPT at different non-joint sites between 36 patients with RA, 36 patients with OA and 18 patients with spondylarthritis and found lower PPT in patients with RA compared to OA and spondylarthritis (Gerecz-Simon et al., 1989). Notably, these authors did not present data on markers of systemic inflammation in the patients which hampers

interpretation of the results. Lack of inflammatory activity, proven by ultrasound and biomarkers, could account for the observed lack of difference between patients with OA and PsA found in the present study.

Overall, these findings indicate that patients with persistent moderate pain and hand-OA or PsA (with no signs of inflammatory activity) could share certain characteristics with regards to underlying pain mechanisms and psychological factors related to the pain experience.

4.2 | Concomitant fibromyalgia

A large proportion of patients in the present study fulfilled the criteria for fibromyalgia (39% for hand-OA and 52% for PsA). These observations are similar to those reported in previous studies examining patients with PsA with prevalence in cFM ranging from 17% to 64% (Brikman et al., 2016; Elsawy et al., 2021; Kancharla et al., 2021;Ulus et al., 2019; Ulutatar et al., 2021). The large variation in prevalence of cFM could be due to difference in detection criteria for fibromyalgia or heterogeneity of patients with PsA (active arthritis, number of female participants etc.). No previous studies have examined the proportion of cFM among patients with hand-OA, but the prevalence is estimated to be 10% to 35% (Dzekan & Stanislavchuk, 2018; Haliloglu et al., 2014; Mahgoub et al., 2020) in patients with knee-OA. Greater co-occurrence in hand-OA in this study could be anticipated due to the greater number of women affected by hand-OA or due to participants experiencing at least moderate pain intensity.

Although patients with cFM experienced decreased PPT at a local painful site and distal site these finding were not significantly different from those of patients without fibromyalgia. Joharatnam et al. (2015) compared patients with rheumatoid arthritis (RA) and cFM to patients without and observed significantly reduced PPT at three distal sites in patients with cFM. Contrary to the present trial Joharatnam et al. (2015) did not exclude participants with active arthritis (swollen joints), and patients with cFM reported greater pain intensity in general raising the question of whether these patients had a greater degree of disease activity.

Pain intensity scores were identical between the cFM and non-fibromyalgia group and a statistically significant but small difference in catastrophizing score was observed. Patients with cFM reported significantly greater disability, when compared to those without fibromyalgia. This finding could indicate that cFM represents patients further along a severity continuum as proposed by Wolfe et al. (Wolfe & Michaud, 2009). The difference in disability was not present when selecting only those patients with PsA.

The results are confirmed by similar studies which report greater disability (Brikman et al., 2016) and poorer QoL (Ulus et al., 2019; Ulutatar et al., 2021) among patients with PsA and OA (Mahgoub et al., 2020) with cFM. However, Elsawy et al (Elsawy et al., 2021) found no significant difference in HAQ-DI between patients with PsA with cFM and those without. They did however include patients with active arthritis and patients in the non-fibromyalgia group had up to 23 swollen joints indicating severe inflammatory activity, which could explain why no difference in HAQ-DI was seen.

Reduced sleep quality was also observed among patients with fibromyalgia but could be due to confounding by indication as reduced sleep quality is a component of the fibromyalgia diagnostic criteria.

Patients with cFM scored significantly higher on the PDQ. The PDQ was originally designed to identify a neuropathic pain component among patients with musculoskeletal disease (Freynhagen et al., 2006). But the specificity of the instrument has been questioned (Finnerup et al., 2016) especially in light of the new International Association for the Study of Pain criteria requiring a demonstrable lesion or disease of the somatosensory system to be present (Scholz et al., 2019). However, high PDQ scores are observed in a range of joint pain conditions (Kurien et al., 2018; Rifbjerg-Madsen et al., 2018; Rifbjerg-Madsen, Christensen, et al., 2017; Rifbjerg-Madsen, Wæhrens, et al., 2017) including fibromyalgia (Amris et al., 2010) and researchers have shown that high PDQ score could indicate altered pain mechanisms (Amris et al., 2010; Hochman et al., 2013). In the present study patients with cFM had a significantly higher PDQ score and significantly greater facilitation of TSP indicating that cFM could represent patients with a greater degree of sensitization. However, it is not yet clarified whether altered pain mechanisms and increased psychological distress is a result of fibromyalgia or contributing to the development of fibromyalgia.

4.3 | Limitations

Patients included in this study attended the randomized clinical trial, the NordCAN study. Patients willing to participate in a randomized controlled trial might represent a population subgroup and extrapolation of results should be done with caution.

An inclusion criterion for participation in the NordCAN study was a pain intensity of at least 30 mm on a 100 mm VAS. Thus, the comparison between patients with or without fibromyalgia conducted in the present study is in patients with at least moderate joint pain which might not represent the general patient population.

The current study utilized a recruitment criterion of VAS <10/100 mm for the inclusion of healthy pain-free subjects. This criterion was utilized to ensure sufficient recruitment of subjects and this cut-off has previously been utilized in other studies but this should be kept in mind when interpreting the results. (Arendt-Nielsen et al., 2014; 2015).

As the examiner was not blinded to the specific diagnosis of the patients it could potentially bias the results but as no studies have compared the three conditions the examiner had no pre-determined idea of possible differences between the patient groups and hence the possible bias – if any - is assumed very minimal.

Some of the controls knew the investigator but did not have any background knowledge of the study measures prior to participating and how those measures were used in the overall analysis.

Pain from multiple sites was not an exclusion criterion in the present study as polyarticular disease is common in PsA and OA. While participants did report pain from finger joints as their primary problem, one cannot with certainty isolate the origin of sensitization from these sites. Consequently, the results of this study should be interpreted within the context of multi-site pain often observed in PsA and Hand-OA patients.

An aspect of joint pain not examined in the present paper is menopausal status among the female participants (Watt, 2018). This factor could contribute to the large number of participants experiencing widespread pain and should be taken into account when extrapolating the results to different populations.

Due to the cross-sectional design causality cannot be inferred from the observation. Thus, it remains to be seen whether altered pain mechanisms and increased psychological distress are a result of or leads to fibromyalgia – or both.

5 | CONCLUSION

Patients with hand-OA or PsA and chronic pain of at least moderate intensity display widespread hyperalgesia, facilitated TSP, inhibited CPM, increased catastrophizing, decreased sleep quality and increased disability when compared with pain-free controls. A large proportion of these patients fulfilled the criteria for cFM and this subgroup exhibited greater catastrophizing, reduced sleep quality, greater disability and facilitated TSP compared to patients without cFM potentially indicating a greater degree of pain sensitization, more psychological distress, and increased disability. Further studies are needed to explore the temporal association between arthritis and fibromyalgia and whether patients with cFM profit from different treatment modalities than patients without.

AUTHOR CONTRIBUTION

J. Vela was the primary contributor to the conception and design of the study and J. Vela is responsible for drafting the manuscript. S. Kristensen, K. K. Petersen, L. Dreyer, K. Skjærbæk Duch, K. Amris and L. Arendt-Nielsen contributed to the conception and design of the trial. S. Kristensen, K. K. Petersen, L. Dreyer, K. Skjærbæk Duch, K. Amris and L. Arendt-Nielsen have all contributed substantially during manuscript revision and approved the final draft.

FUNDING INFORMATION

This work was supported by the Danish Psoriasis Foundation Grant number 210417, the Danish Rheumatism Foundation Grant number R179-A6299, from Aalborg University and Aalborg University hospital (2016-017615). Centre for Neuroplasticity and Pain (CNAP) is supported by the Danish National Research Foundation (DNRF121). The Center for Mathematical Modeling of Knee Osteoarthritis (MathKOA) is funded by the Novo Nordisk Foundation (NNF21OC0065373)

CONFLICT OF INTEREST STATEMENT

All authors report nothing to declare.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

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How to cite this article: Vela, J., Dreyer, L., Petersen, K. K., Arendt-Nielsen, L., Duch, K. S., Amris, K., & Kristensen, S. (2024). Quantitative sensory testing, psychological profiles and clinical pain in patients with psoriatic arthritis and hand osteoarthritis experiencing pain of at least moderate intensity. *European Journal of Pain*, *28*, 310–321. https://doi.org/10.1002/ejp.2183