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The associations of psychological symptoms and cognitive patterns with pain and pain sensitization in people with hand osteoarthritis

Elisabeth Mulrooney [a,*], Tuhina Neogi [b], Hanne Dagfinrud [c,g], Hilde Berner Hammer [a,g], Pernille Steen Pettersen [a], Torfinn L. Gaarden [d], Knut Engedal [e,g], Tore K. Kvien [a,g], Karin Magnusson [c,f], Ida K. Haugen [a]

[a] Division of Rheumatology and Research, Diakonhjemmet Hospital, Oslo, Norway
[b] Section of Rheumatology, Boston University School of Medicine, Boston, United States
[c] National Advisory Unit on Rehabilitation in Rheumatology, Division of Rheumatology and Research, Diakonhjemmet Hospital, Oslo, Norway
[d] Department of Geriatric Psychiatry, Diakonhjemmet, Oslo, Norway
[e] Norwegian Centre of Ageing and Health, Vestfold County Hospital, Tønsberg and Oslo University Hospital, Ullevaal, Oslo, Norway
[f] Lund University, Faculty of Medicine, Department of Clinical Sciences Lund, Orthopaedics, Clinical Epidemiology Unit, Lund, Sweden
[g] Faculty of Medicine, University of Oslo, Oslo, Norway

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ABSTRACT

Objective: To examine whether psychological symptoms and cognitive patterns are associated with self-reported pain and pain sensitization in people with hand osteoarthritis (OA).
Design: In the Nor-Hand study (n = 300), people with hand OA self-reported psychological symptoms (Hospital Anxiety and Depression Scale), cognitive patterns (Pain catastrophizing Scale and Arthritis Self-Efficacy Scale) as well as their pain severity in hands, overall pain and multi-joint pain. Central pain sensitization was measured clinically by temporal summation and pressure pain threshold tests. We examined whether psychological symptoms and cognitive patterns were cross-sectionally associated with pain using linear regression. Beta coefficients (β) per one standard deviation of the independent variable were presented. Stratified analyses were performed in cases of significant interactions ($p < 0.10$).
Results: Higher levels of anxiety, depressive symptoms and pain catastrophizing and low levels of self-efficacy were statistically significantly associated with higher levels of hand pain by Numeric Rating Scale (β = 0.43, 0.48 and −0.57, respectively). Similar associations were found for overall pain, but not for measures of central pain sensitization. In stratified analyses, anxiety and depressive symptoms were more strongly related with pain in subgroups with younger age and higher comorbidity burden. Pain catastrophizing was more strongly related with pain in subgroups with younger age, overweight/obesity, higher comorbidity burden and poor sleep.
Conclusion: Psychological symptoms and cognitive patterns were associated with self-reported OA pain, especially in people with younger age, overweight/obesity, higher comorbidity burden and poor sleep. No associations were found for psychological symptoms and cognitive patterns with pain sensitization.

1. Introduction

Pain is a prominent symptom for people with hand osteoarthritis (OA) and the main reason why people with hand OA seek help from clinical health services [1]. Currently, no disease-modifying agents are available for OA, and most patients continue to experience pain, despite non-pharmacological interventions and treatment with conventional analgesic drugs [2].

Pain in hand OA has traditionally been viewed as nociceptive, i.e. pain caused by actual or threatened tissue damage, due to structural joint damage or inflammation. However, studies have shown discordance or weak associations between the total amount of hand OA pathology and pain severity [3–5]. These findings suggest that other mechanisms than structural alterations and inflammation of the joint, are relevant to the

* Corresponding author. Division of Rheumatology and Research, Diakonhjemmet Hospital, PB 23 Vinderen, 0370, Oslo, Norway.
E-mail addresses: elisabethmulrooney@gmail.com (E. Mulrooney), tneogi@bu.edu (T. Neogi), Hanne.Dagfinrud@diakonsyk.no (H. Dagfinrud), hbham@online.no (H.B. Hammer), pernille.steen.pettersen@gmail.com (P.S. Pettersen), TorfinnLodoen.Gaarden@diakonsyk.no (T.L. Gaarden), knut.engedal@aldringoghelse.no (K. Engedal), t.k.kvien@medisin.uio.no (T.K. Kvien), magnusson_karin@outlook.com (K. Magnusson), ida.k.haugen@gmail.com (I.K. Haugen).

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pain experience. Mechanisms of nociplastic pain, which is defined as pain that arises from altered nociception despite no tissue damage or disease/lesion of the somatosensory system, have recently been acknowledged as important contributors to the OA pain experience [6,7]. In the Nor-Hand study of people with hand OA, central pain sensitization was common and associated with more severe hand OA pain [8]. Nociceptive and nociplastic pain are not mutually exclusive and may co-exist in chronic painful diseases, such as hand OA.

According to the biopsychosocial model by Engel, pain cannot be explained by focusing on biological mechanisms alone without the integration of social and psychological processes [9]. Despite the recognition of a biopsychosocial framework for pain, few studies have explored associations between psychological symptoms and pain in people with hand OA. Anxiety and depressive symptoms were associated with more severe hand pain in two previous cross-sectional studies of people with hand OA [10,11], while no previous hand OA studies have explored how cognitive patterns such as pain catastrophizing or self-efficacy relate to pain. The determinants of central pain sensitization are not fully understood, and no previous studies have explored whether psychological symptoms and cognitive patterns are associated pain sensitization in persons with hand OA.

Assuming psychological symptoms and cognitive patterns are associated with pain, the temporality is likely complex and bi-directional. There is evidence that psychological symptoms may influence the pain experience. Psychological symptoms, such as depression and anxiety, and cognitive patterns, such as pain catastrophizing and self-efficacy, may influence how pain is perceived. In people with knee OA, depression and pain catastrophizing predicted changes in pain severity [12,13]. Furthermore, cognitive therapy intervention focusing on pain coping skills may improve pain severity in people with OA [14].

Hence, the scope of the psychological symptoms or cognitive patterns may influence the experience of pain and pain sensitization. The primary aim of this study is to explore whether psychological symptoms and cognitive patterns are associated with self-reported pain and pain sensitization in people with hand OA.

2. Materials and methods

The Nor-Hand study is a hospital-based observational cohort study following 300 participants with hand OA, as described in the protocol [15]. These analyses are based on baseline data collected in 2016–17. Participants were recruited consecutively from the Rheumatology outpatient clinic at Diakonhjemmet Hospital, Oslo, Norway. Men and women between 40 and 70 years with hand OA in at least one finger or thumb base joint, confirmed by ultrasound and/or clinical examination, were included. Clinical examination criteria for hand OA included Heberden/Bouchards nodes and/or bony enlargement, squaring and/or deformity of the thumb base and no clinical signs of inflammatory arthritis, while the ultrasound criteria included osteophytes in interphalangeal joints and/or thumb base, and no signs of inflammatory arthritis. Participants with inflammatory arthritic disease, for example, seropositive or seronegative rheumatoid arthritis, psoriatic arthritis, reactive arthritis, spondylarthritis, arthritis related to connective tissue disorders, diagnosis of psoriasis, erythrocyte sedimentation rate >40 mm/h and/or C reactive protein >20 mg/L, without known ongoing infection, anti-cyclic citrullinated protein and/or rheumatoid factor positivity, ferritin>200 μg/L for women and>300 μg/L for men and s-iron/stotal iron binding capacity above 50% to rule out haemochromatosis were excluded [16].

2.1. Psychological symptoms and cognitive patterns

The participants completed three questionnaires about psychological symptoms and cognitive patterns. The Hospital Anxiety and Depression Scale (HADS, range: 0–42) includes seven questions each for anxiety and depressive symptoms [17]. A previous systematic review identified a cut-off point of eight or more on each subscale (subscale range: 0–21) were higher scores indicate a need for further evaluation of possible anxiety or depression [18]. The Pain Catastrophizing Scale (PCS, range: 0–52) is a 13-item questionnaire divided into three subscales of magnification, rumination and helplessness [19]. Higher HADS and PCS scores indicate worse status. The first part of the Arthritis Self Efficacy scale (ASES, range: 10–100) includes five questions about the ability to influence pain, and the second part includes six questions about the ability to influence other symptoms of rheumatic disease [20]. Higher ASES scores indicates greater self-efficacy.

2.2. Pain severity in the hands and other joints

The participants reported their hand pain severity by two instruments; the Numeric Rating Scale (NRS) for hand pain the last 24 hours ("How would you describe the joint pain you have had in your hands for the last 24 h?", range: 0–10), and pain severity in all joints combined ("How would you describe the joint pain you have had in the last 24 h? Take all joints into account.", range: 0–10) [21]. For the NRS pain instruments, higher score represents more pain. In addition, as a measure of multi-joint pain the participants marked their painful or aching joints (bilateral shoulders, elbows, wrists, hips, knees, and ankles as well as the neck, upper, middle and lower back) the previous six weeks on a homunculus. The painful or aching hand joints the previous six weeks were marked on a hand diagram. All painful hand joints were accumulated and counted as one "hand joint" in a total body painful joint count (range: 0–18).

2.3. Measures of central pain sensitization

Quantitative sensory testing (QST) is a tool to assess pain sensitivity and an indirect measure of pain sensitization. Two trained medical students performed QST to assess pain sensitization as described in detail in the published protocol [15]. The testing was conducted based on the same predefined protocol throughout the data collection period, which always was available for the examiner in printed format whilst testing.

Temporal summation (TS) is defined as an increase in pain intensity during the repetition of identical noxious stimuli and is thought to reflect central pain sensitization (i.e., ascending nociceptive facilitation). A set of punctuate probes with different exerted forces (8, 16, 32, 64, 128, 256 and 512 Nm) was used. The probe that first evoked NRS pain of 4 or more was identified by tapping the left distal radioulnar joint starting with the lowest weight. If none of the probes evoked NRS pain of 4 or more, the 512 Nm probe was used. The selected probe was then applied ten times with a pace of one tap/second to the skin overlying the left distal radioulnar joint. The participant rated the pain severity of the first, fifth and tenth tap on the NRS [15]. TS was calculated by subtracting the first pain rating from the highest pain rating of either the fifth or tenth tap [6,22]. Pressure pain detection threshold (PPT) as a marker of central pain sensitization, was tested at the mid-portions of tibialis anterior muscle using a hand-held algometer (FPIX25 Wagner; Wagner Instruments, Greenwich, USA). The examination was repeated three times with the algometer placed at slightly different positions over the muscle with a pause of 30 seconds between the measurements. The average of the three measurements were used in analyses.

Nine subjects were examined by both examiners the same afternoon. Moderate inter-observer reliability (intraclass correlation coefficient (ICC), two-way mixed-effects model, absolute agreement, individual measure) was found for PPT tibialis anterior (0.43) and TS (0.56).

2.4. Co-variates

Potential confounders included age, sex, body mass index (BMI), comorbidities, sleep disturbance and education. Information about age and sex was collected from medical records. Height (without shoes) and weight (in light clothing) was measured by medical students and BMI

was calculated (kg/m^2). Burden of comorbidities were measured by a self-administered comorbidity index (range: 0–45) [23]. Greater scores indicate higher total burden of comorbidities. The questionnaire assesses the presence of 12 predefined conditions and three additional self-reported comorbidities in addition to whether the person receives treatment for the condition and if it limits their activity level. The participants self-reported their degree of sleep disturbance by choosing one out of five statements describing either normal sleep (no problems), slight problems (e.g. difficulty in falling asleep, or sometimes waking at night), moderate problems (e.g. disturbed sleep, or feeling I have not slept enough), greater problems (e.g. having to use sleeping pills often or routinely, or usually waking at night and/or too early in the morning) or severe sleeplessness (e.g. sleep is almost impossible even with full use of sleeping pills, or staying awake most of the night) [24]. Level of education was reported on a seven-point scale, and dichotomized into lower or higher education (at least four years of university or higher education).

2.5. Statistical analysis

We examined if psychological symptoms and cognitive patterns were associated with self-reported pain and pain sensitization in these explorative analyses as follows. Prior to all analyses, we checked whether the assumptions of regression where met. Due to sex differences in pain sensitivity [25], we standardized the TS and PPT values by subtracting the group mean value from the observed value for each participant and then divide this value by the standard deviation (SD). Mean values and SDs were calculated for each sex separately due to the differences in pain sensitization between men and women. As an example, a value of 0 in a female participant corresponds to the mean PPT or TS value among women, while a value of −1 and 1 corresponds to a value that is one SD below and above the mean value for women, respectively. We conducted sensitivity analyses using the raw data of the PPT tibialis and temporal summation variables.

We examined the relation of the psychological symptoms and cognitive patterns variables (HADS, PCS and ASES as explanatory variables) to self-reported pain and pain sensitization (outcome variables) using linear regression. Separate models were performed for HADS, PCS and ASES before the three variables were entered into the same multivariable model. Data were presented as beta coefficient values (95% confidence interval) per one SD of the explanatory variable. All analyses were adjusted for age, sex, BMI, comorbidities, sleep disturbance and education. After fitting the regression models, we inspected the plotted residuals to evaluate any deviation from normal distribution, and no strong deviations was observed. Due to the explorative nature of this study, multiple comparisons were not corrected for. We repeated the analyses stratified by levels of the confounder (poor vs. normal sleep, old vs. young age, overweight/obesity vs normal weight, and high vs. low comorbidity burden). Poor sleep was defined as slight to severe sleep disturbances. Participants were divided into two age groups based on the median of 61 years. Overweight/obesity was defined as BMI$\geq$25 kg/m^2, where normal weight was defined as BMI<25 kg/m2. Participants were grouped into high or low comorbidity burden based on the median of seven on the comorbidity index (range: 0–45). We then conducted tests of interaction ($p < 0.1$) between the confounders, to assess possible differences in effect of the explanatory variables depending on the level of the confounders. A series of Mann-Whitney U tests were conducted to assess whether participants with younger age, overweight/obesity, higher comorbidity burden and poor sleep differed significantly from participants with older age, normal weight, lower comorbidity burden and normal sleep.

We performed complete case analyses as missing data was less than 5%. P-values <0.05 were considered statistically significant. Stata/IC 16.0 was used for all statistical analyses.

2.6. Ethics

The study was approved by the Norwegian Regional Committee for Medical and Health Research Ethics (Ref. no: 2014/2057) and registered at https://clinicaltrials.gov (Ref. no: NCT03083548). The participants received oral and written information about the study and gave their informed consent. They were informed that they could withdraw from the study at any time. A user representative was involved during study planning and throughout the study period.

3. Results

All 300 Nor-Hand study participants were included in these explorative analyses. The median age was 61 years and most participants were women and had ≥1 year of college/university (Table 1). The study participants demonstrated a wide range in radiographic hand OA severity and pain severity. Most participants reported low levels of anxiety, depressive symptoms and pain catastrophizing (Table 1). Anxiety was more common than depressive symptoms, as 56 (20.4%) and 45 (8.7%) of the participants scored above the cut-off value on the HADS subscale for possible anxiety and depression, respectively. Among those, 20 participants (6.9%) scored above the cut-off value on both subscales. Only nine participants (3.1%) had a PCS sum score of ≥30, which has been suggested as clinically relevant level of pain catastrophizing [26]. A large proportion of the participants reported moderate to severe sleeping disturbances (Table 1).

Table 1
Baseline participant characteristics (n = 300).

Sex, n (%) women	266 (89)
Age, median (IQR) years	61 (57–66)
BMI, mean (SD) kg/m^2	26.5 (5.0)
Fulfil ACR hand criteria, n (%)	278 (93)
Education ≥1 year of higher education/university, n (%)[a]	173 (58)
Slight to severe sleep disturbance, n (%)[a]	223 (75)
Comorbidity index, median (IQR) [0–45]	7 (5–11)
ASES sum score, median (IQR) [10−100][a]	69 (60–78)
ASES Pain, median (IQR) [10−100]	62 (52–74)
ASES Symptom, median (IQR) [10−100]	74 (65–83)
PCS sum score, median (IQR) [0–52][a]	9 (5–15)
PCS rumination, median (IQR) [0–16]	3 (1–6)
PCS magnification, median (IQR) [0–12]	2 (1–3)
PCS helplessness, median (IQR) [0–24]	4 (2–6)
HADS sum score, median (IQR) [0–42][a]	6 (3–10)
HADS Anxiety, median (IQR) [0–21]	4 (1–6)
HADS Depression, median (IQR) [0–21]	2 (1–4)
NRS hand pain, mean (SD) [0–10][a]	3.8 (2.3)
NRS all joint pain, mean (SD) [0–10][a]	4.1 (2.3)
Number of painful joints (whole-body) previous six weeks, median (IQR) [0–18]	4 (2–8)
TS, median (IQR)[a]	1 (0–2)
PPT Tibialis anterior muscle, mean (SD) (kg/cm2)[a]	5.5 (2.5)
Kellgren-Lawrence sum score, median (IQR) [0–128][a]	27 (15–43)

IQR = interquartile range; SD = standard deviation; BMI=Body Mass Index; ACR = American College of Rheumatology; PCS=Pain Catastrophizing Scale; ASES = Arthritis Self-Efficacy Scale; HADS=Hospital Anxiety & Depression Scale; NRS=Numeric Rating Scale; TS = Temporal Summation; PPT=Pressure detection Pain Threshold; Brackets present possible ranges.

[a] N = 2 missing for Education, Sleep, TS and NRS hand pain; n = 4 missing for NRS all joints; n = 5 missing for ASES; PCS; n = 8 missing for Kellgren Lawrence sum score; n = 9 missing for PPT tibialis anterior; n = 11 missing for HADS.

3.1. Psychological symptoms and cognitive patterns and their relation to self-reported pain severity

Greater values of self-reported anxiety and depressive symptoms, pain catastrophizing and lower values of self-efficacy were significantly related to greater self-reported pain severity in the hands, overall joints and the number of painful joint sites (Table 2). Similar results were found for subscales of HADS (anxiety and depression), PCS (helplessness, rumination, and magnification) and ASES (pain and symptoms) (Supplementary table 1). When HADS, PCS and ASES were included in the same model, PCS and ASES remained statistically significantly associated with most measures of pain, despite a reduction in the strength of associations. HADS remained significantly associated with the number of painful joints only (Table 3).

The associations between HADS and self-reported pain variables showed a tendency to be stronger in people with younger age and high comorbidity burden than their counterparts, and the associations reached statistical significance. However, the interaction analyses showed no significant differences between subgroups. Similarly, pain catastrophizing was significantly associated with pain in people with younger age, overweight/obesity and high comorbidity burden (Supplementary Table 1-4). The interaction effect was only statistically significant for PCS and comorbidities (for one pain outcome: number of painful joints), and no statistical difference was found between overweight/obesity and normal weight subgroups. While the association between pain catastrophizing and pain were significant, and tended to be stronger in people with poor vs. normal sleep, the opposite was observed for anxiety and depressive symptom. The interaction effects for HADS and sleep (for two pain outcomes: NRS hand pain and NRS all joints) reached statistical significance. No consistent differences between subgroups were found for ASES (Supplementary Table 1-4).

Participants with younger age, overweight/obesity, higher comorbidity burden and poor sleep reported significantly higher levels of anxiety, depressive symptoms, and pain catastrophizing in comparison with their counterparts. Participants with younger age and poor sleep had significantly lower levels of self-efficacy than participants with higher age (Supplementary table 11).

3.2. Psychological symptoms and cognitive patterns and their relation to central pain sensitization

Anxiety, depressive symptoms, pain catastrophizing and self-efficacy were not significantly associated with PPT or TS (Table 4). The sensitivity analyses conducted with the raw data yielded similar results, and we found no significant associations. In the stratified analyses, the associations were overall weak and with doubtful clinical relevance (Supplementary tables 7-10).

Table 2
The associations of psychological symptoms and cognitive patterns with self-reported pain outcomes.
Beta values (95% CI) per one SD[a] of the psychological factors are reported[b].

	NRS hand pain (0–10)	NRS all joints (0–10)	Homunculus 6 weeks (0–18)
HADS	**0.43 (0.19, 0.68)**	**0.37 (0.12, 0.62)**	**0.87 (0.43, 1.30)**
PCS	**0.48 (0.32, 0.79)**	**0.48 (0.24, 0.72)**	**0.72 (0.24, 1.11)**
ASES	**−0.57 (-0.85, -0.28)**	**−0.57 (-0.85, -0.42)**	**−0.71 (-1.27, -0.28)**

NRS=Numeric Rating Scale; HADS=Hospital Anxiety and Depression Scale; PCS=Pain Catastrophizing Scale; ASES = Arthritis Self Efficacy Scale; CI = confidence interval.
[a] Standard deviation for the exposure variables: HADS: 6.1; PCS: 7.9; ASES: 14.1.
[b] Adjusted for age, sex, BMI, comorbidity, sleep and education; Separate models for each explanatory variable; **Bold** indicates statistically significant associations.

Table 3
The multivariable associations between the psychological factors and self-reported pain outcomes.
Beta values (95% CI) per one SD[a] of the psychosocial factor are reported[b].

	NRS hand pain (0–10)	NRS all joints (0–10)	Homunculus 6 weeks (0–18)
HADS	0.19 (−0.12, 0.43)	0.04 (−0.25, 0.31)	**0.62 (0.12, 1.11)**
PCS	**0.24 (0.16, 0.56)**	**0.24 (0.001, 0.56)**	0.32 (−0.16, 0.79)
ASES	**−0.42 (-0.71, -0.07)**	**−0.56 (-0.85, -0.28)**	−0.42 (−0.99, 0.04)

NRS=Numeric Rating Scale; HADS=Hospital Anxiety and Depression Scale; PCS=Pain Catastrophizing Scale; ASES = Arthritis Self Efficacy Scale; CI = confidence interval.
[a] Standard deviation for the exposure variables: HADS: 6.1; PCS: 7.9; ASES: 14.1.
[b] Adjusted for age, sex, BMI, comorbidity, sleep and education; All three psychological factors included in the same model for each pain outcome; **Bold** indicates statistically significant associations.

Table 4
The associations of psychological symptoms and cognitive patterns with sex-standardized pain sensitization variables.
Beta values (95% CI) per one SD[a] of the psychological factors are reported[b].

	PPT Tibialis Anterior	TS
HADS	−0.06 (−0.19, 0.06)	0.05 (−0.06, 0.19)
PCS	−0.03 (−0.16, 0.08)	0.02 (−0.08, 0.16)
ASES	0.65 (−1.14, 0.16)	−0.15 (−0.13, 0.13)

PPT=Pressure detection Pain Threshold; TS = Temporal Summation; HADS=Hospital Anxiety and Depression Scale; PCS=Pain Catastrophizing Scale; ASES = Arthritis Self Efficacy Scale; CI = confidence interval.
[a] Standard deviation for the exposure variables: HADS: 6.1; PCS: 7.9; ASES: 14.1.
[b] Adjusted for age, sex, BMI, comorbidity, sleep and education; Separate models for each explanatory variable; **Bold** indicates statistically significant associations.

4. Discussion

The Nor-Hand study is the first to comprehensively explore whether psychological symptoms and cognitive patterns are associated with self-reported pain and pain sensitization in people with hand OA. We found that higher levels of anxiety, depressive symptoms, pain catastrophizing and lower levels of self-efficacy were significantly related to pain by questionnaires, but not to measures of pain sensitization.

The frequency of possible depression (8.7%) by HADS was identical to the prevalence of self-reported depression in the Norwegian general population [27]. However, our estimate was lower compared with previous estimates of depression in people with knee OA (24.5%) and rheumatoid arthritis (RA) (34.2%) [28,29]. These results may indicate that knee OA and RA are associated with more depressive symptoms, but different definitions of depression across studies make it challenging to directly compare estimates.

A total PCS score of ≥30 (range: 0–52) has been suggested as a clinically relevant level of catastrophizing [26]. The cut-off was based on normative distribution and the 75th percentile in a chronic pain population that was not specified. Only 3.1% of our study participants reported PCS of ≥30, and 75th percentile for this study was 15. Differences in the 75% percentile across studies may be explained by differences in study populations, as we did not specifically recruit patients with chronic and disabling pain. Importantly, the strong observed associations between PCS and pain variables in our study suggest that pain catastrophizing below the suggested cut-off is of clinical relevance. Additional studies to explore the cut-off for clinically meaningful pain catastrophizing are warranted.

In our current study, we found significant associations for emotional and cognitive variables with self-reported pain severity and number of painful joints. A similar hospital-based hand OA study found that

participants with self-reported depression and/or anxiety reported higher levels of hand pain severity compared with participants without depression and/or anxiety [11]. Furthermore, Magnusson et al. found a statistically significant association between mental health by the Short Form (SF)-36 questionnaire and AUSCAN hand pain in a population-based study of people with radiographic hand OA [10]. The SF-36 mental component scale has been suggested to detect presence of anxiety and depression with good sensitivity and specificity in RA patients [30], and certain questions in the SF-36 are comparable to questions included in the HADS questionnaire. Despite the use of different questionnaires, the association observed by Magnusson et al. was of similar magnitude as our results [10].

It is unclear how psychological states and symptoms influence pain, but inflammation has been hypothesized to be the link between depression and pain. Hospitalized elderly psychiatric patients with major depression had higher levels of inflammatory markers than healthy controls in a previous study [31]. As our hand OA population had mostly no or mild depressive symptoms, a similarly strong association between depression and inflammation cannot be expected. The weaker relations between HADS and pain variables in multivariate analyses including pain catastrophizing and self-efficacy suggest that these cognitive patterns may partly explain the observed association between HADS and pain.

Cognitive patterns, such as pain catastrophizing and self-efficacy, are relevant for how pain is perceived by patients and pain catastrophizing has been suggested to be critical in understanding the pain experience in rheumatic diseases [32]. Pain catastrophizing was associated with most self-reported pain measures in our study, which is in line with previous studies of people with knee OA and RA [33,34]. Higher self-efficacy might be considered as a protective factor against pain. In line with other cross-sectional studies of patients with knee OA [35,36], we found that higher self-efficacy was associated with less self-reported pain severity. A proposed theory suggests that pain catastrophizing and self-efficacy are related, although they may function independently of each other [37].

Anxiety, depressive symptoms and pain catastrophizing were more strongly associated with the majority of self-reported pain outcomes in participants with younger age, overweight/obesity (only pain catastrophizing) and higher number of comorbidities. Younger people referred to the rheumatology outpatient clinic may present a more complex etiology of symptoms, as their hand OA is likely of less severe disease severity in comparison with people of older age and more extensive disease progression [38]. Indeed, the younger participants in our study reported overall higher levels of anxiety, depressive symptoms and pain catastrophizing and lower levels of self-efficacy than people of higher age. In line with our results, a knee OA study found that younger people had more frequently depression than people of higher age [28]. Furthermore, we found that participants with overweight/obesity or higher comorbidity burden had higher levels of self-reported anxiety, depressive symptoms and pain catastrophizing. Being burdened with overweight/obesity and several medical conditions may influence the emotional wellbeing and abilities to cope with joint pain. Our results are clinically relevant, as overweight/obesity and certain comorbidities are modifiable factors that might be of importance in pain management.

There were no statistically significant associations of the emotional and cognitive variables with QST measures of central pain sensitization. Our results suggests although psychological symptoms and cognitive patterns are related to pain, they may not be of importance for mechanisms of pain sensitivity. In contrast, in these analyses we found that psychological symptoms and cognitive patterns were significantly related to multi-joint pain, which might be within a spectrum of widespread pain. A link between pain catastrophizing and measures of QST is also previously established in musculoskeletal disorders such as chronic low back pain [39]. Further, a small study of orthopaedic clinic patients with either neck, shoulder, low back or knee pain suggested that central pain sensitization could mediate the association between psychological factors and pain intensity [40]. The divergent results may be explained by different study populations and the lower levels of anxiety, depressive symptoms and pain catastrophizing in our study population. It is also possible our measures of QST did not sufficiently detect pain sensitization. Further, psychological factors have previously been found to affect pain tolerance [41]. Thus, it is possible that there is a relation of psychological symptoms and cognitive patterns with pain tolerance, but this was not assessed.

With regard to the biopsychosocial model, we focused on aspects of mental health, but we acknowledge that pain may be generated and modified by a multitude of factors. Social context, as for example community and family-relations may impact how pain is perceived and experienced. The lack of data regarding social support in our data set prevented us from assessing this relationship.

The following limitations should also be acknowledged. Due to cross-sectional design, we were unable to draw conclusions about whether pain is the cause or consequence of the psychological states. Further, the results would need to be replicated by a separate cohort considering the explorative nature of these analyses. We did not correct for multiple comparison due to the nature of the analyses. However, the multiple analyses does render the results in higher risk of Type 1 error. The majority of the participants in this study were women with higher level of education, generally good physical and mental health, probably representing a selection bias. With a larger variation in physical and mental health, stronger association than found in this study could have been expected. Participants with fibromyalgia ($n = 28$) where not excluded from the study, and participants with widespread pain may influence the strength of the associations. Another limitation is the fair to moderate reliability of the quantitative sensory testing. This may influence the lack of associations between the exposure variables and the measures of QST, and the results we found should be interpreted accordingly as we cannot be certain the QST measures were sufficiently reliable to detect sensitivity. Previous reliability studies including healthy participants, found ICC's ranging from very good to excellent [42,43]. When we excluded participants, who were examined by the least experienced medical student the results remained similar, suggesting that sub-optimal inter-observer reliability did not affect the results. Data on intra-observer reliability was not available.

In summary, we found that higher measures of self-reported anxiety, depressive symptoms, pain catastrophizing and lower measures of self-efficacy were significantly related to increased self-reported pain hand OA, especially in people with younger age, overweight/obesity, higher comorbidity burden and poor sleep. Further, psychological symptoms and cognitive patterns were not significantly associated with QST measures of pain sensitivity. These findings underlines the complexity of the multifactorial nature of the pain. Although we cannot assess any causal relationships, our results suggest that management of pain in hand OA patients should not only focus on joint pathology but consider psychological symptoms and cognitive patterns, in addition to modifiable factors such as overweight/obesity, comorbidities and sleep.

Author contributions

Substantial contributions to the conception and design of the study: EM, TN, HD, PSP, TKK and IKH, or acquisition/analysis of data: EM, HBH, PSP, TLG, KE, KM, and IKH. Interpretation of data and drafting of the manuscript or revising it critically: EM, TN, HD, HBH, PSP, TLG, KE, KM, TKK and IKH and IKH. Final approval of the publication: EM, TN, HD, HBH, PSP, TLG, KE, KM, TKK and IKH.

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Declaration of competing interest

Tuhina Neogi reports consulting fees from Pfizer/Lilly and Regeneron outside the submitted work during the past 36 months. Hilde Berner Hammer reports speaker honorarium from AbbVie, Novartis, Lilly and Roche, as well as participation in AbbVie Advisory Board outside the submitted work during the past 36 months. Ida Kristin Haugen reports grants from Pfizer, consulting fees from Novartis and a leadership/fiduciary role related to OARSI (unpaid) outside the submitted work during the past 36 months. Elisabeth Mulrooney, Hanne Dagfinrud, Pernille Steen Pettersen, Torfinn L. Gaarden, Knut Engedal, Tore Kvien and Karin Magnusson have nothing to disclose.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ocarto.2022.100267.

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