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THE EXTENT OF PAIN IS ASSOCIATED WITH SIGNS OF CENTRAL SENSITIZATION IN PATIENTS WITH HIP OSTEOARTHRITIS

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Key words: Pain drawings, pain extent, central sensitization, hip osteoarthritis

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28 ABSTRACT

29 Background: Central sensitization may be present in some patients with hip osteoarthritis (OA),
30 often reflected as widespread pain. We examine the association between pain extent with signs
31 of central sensitization and other clinical and psychological features in patients with hip OA.

32 Methods: Thirty patients with hip OA were recruited for this cross-sectional observational study.
33 Participants completed pain drawings on a digital tablet, which displayed frontal and dorsal
34 views of the body. The pain extent (%) for each participant was determined by combining the
35 frontal and dorsal pixels shaded and dividing by the total pixels of the body chart area.

36 Participants completed patient reported outcome measures to assess for signs and symptoms of
37 central sensitization and psychosocial factors. Quantitative sensory testing including pain
38 pressure thresholds (PPTs) and Thermal Pressure Thresholds (TPTs) was performed at points
39 anatomically local and distant from the hip.

40 Results: Women had significantly greater pain extent (6.71%) than men (2.65%) ($z = -2.76$, p
41 < 0.01). Across all participants, increased pain extent was significantly associated with higher
42 scores on the Widespread Pain Index ($r_2 = 0.426$, $p < 0.05$), Pain Detect ($r_2 = 0.394$, $p < 0.05$) and
43 Pain Catastrophising Scale ($r_2 = 0.413$, $p < 0.05$), and with lower PPTs at the thenar eminence ($r_2 = -$
44 0.410 , $p < 0.05$), vastus lateralis ($r_2 = -0.530$, $p < 0.01$), vastus medialis ($r_2 = 0.363$, $p < 0.05$) and
45 greater trochanter ($r_2 = -0.373$, $p < 0.05$).

46 Conclusions: Greater pain extent was associated with several measures of signs and symptoms of
47 central sensitization in patients with hip OA. These results support the utility of the pain drawing
48 for identifying signs of central sensitization in patients with hip OA.

49

50

51 INTRODUCTION

52 Osteoarthritis (OA) is the largest cause of individual level disability and costs for
53 healthcare systems worldwide.¹ With populations living longer, healthcare costs related to OA
54 are likely to escalate further.² The hip is the second most common site for OA after the knee^{3,4}
55 with a lifetime prevalence of approximately 25% in adults.⁵ The prevalence of hip OA increases
56 with age with women generally more likely to have painful hip OA and to seek treatment than
57 men.⁴ In addition to pain, patients with hip OA complain of physical symptoms including
58 stiffness and muscle weakness³, and may present with psychological features including anxiety
59 and low mood, which negatively affect quality of life.⁶ Early diagnosis of OA is critical to
60 successful management. Diagnosis of OA can however be challenging as symptoms do not
61 always correlate well with the degree of articular damage present on imaging.⁷ There is
62 increasing evidence that central sensitization may be present in a sub-group of patients with hip
63 OA,⁸⁻¹⁰.

64 Central sensitization involves several complex neurological reactions ultimately leading
65 to an increased responsiveness of the neurons within the central nervous system to painful
66 stimuli.¹¹ Patients who present with central sensitization as their dominant pain mechanism likely
67 require specific/tailored treatment strategies to improve clinical outcomes.⁸ Features of central
68 sensitization include symptoms of high severity and irritability,¹² including an increased
69 sensitivity to painful stimuli (hyperalgesia),^{13,14} and the maintenance of symptoms in the absence
70 of associated physical damage.¹⁵ A further feature of central sensitization is widespread pain,
71 which is pain experienced beyond the expected anatomical distribution of the pathology.¹⁶
72 Widespread pain has been identified as a common symptom in patients with hip OA^{10,17,18}. And

73 enlarged pain extent has been associated with magnified pain levels¹⁹⁻²¹ and psychological
74 distress²¹ in patients with knee OA .

75 Pain drawings offer a practical way of quantifying pain extent and have been used to
76 quantify the distribution of pain in patients with hip²² and knee²³ OA, greater trochanteric pain
77 syndrome,²⁴ low back pain,²⁵ fibromyalgia,²⁶ carpal tunnel syndrome,²⁷ chronic spinal pain,²⁸
78 whiplash associated disorder,²⁹ migraine,³⁰ and tension type headaches.³¹ To date, only one study
79 has examined the association between pain extent and clinical features of central sensitization in
80 patients with OA.²³ Lluch Girebres et al.,²³ found that pain extent was greater in women, and
81 associated with increased local pain severity and stiffness and reduced local and distant pain
82 pressure thresholds in patients with knee OA. The authors suggested that pain drawings could be
83 used easily in the clinic and recommended that further research was needed to better understand
84 the association between greater pain extent and other clinical features in patients with OA.²³

85 Although pain drawings have been used in patients with hip pain,^{17,18,22,32,33} these studies
86 have used pain drawings to describe but not quantify the distribution of symptoms. The most
87 common pain distributions found in patients with hip OA were the groin, gluteal area, and
88 anterior thigh,^{17,18,22,32,33} with the greater trochanter also documented as an important site of
89 symptoms.^{18,22} Interestingly, larger pain areas were noted in approximately half of patients with
90 hip OA who were either awaiting arthroplasty,¹⁷ or had dysplasia.¹⁸

91 In this study we use a contemporary method to quantify the location and extent of pain in
92 people with hip OA from a digital pain drawing and evaluate the association between pain extent
93 and both clinical and psychological features. Specifically, we aimed to investigate whether an
94 association exists between pain extent and perceived symptom severity, disability, and
95 psychological features (through patient reported outcome measures) and physical measures of

96 pain perception (through quantitative sensory testing) in people with hip OA. Additionally, we
97 evaluated whether differences in pain extent exists between men and women with hip OA.

98 METHODS

99 *Study Design and setting*

100 This cross-sectional observational study was conducted in the Pain Clinic of the
101 Department of Anesthesiology, University Medical Center Gottingen, in the Georg-August-
102 University of Gottingen in Germany, and is reported in line with the Strengthening the Reporting
103 of Observational Studies in Epidemiology statement (STROBE).³⁴ The study was approved by
104 the University Medical Center Gottingen ethics committee (reference number 27815) and was
105 conducted according to the Declaration of Helsinki.

106 *Participants*

107 A convenience sample of thirty participants with hip OA were recruited via flyers placed
108 in the University Hospital Gottingen Orthopedic Department, local orthopedic and physiotherapy
109 practices, and by advertisements taken out in local newspapers. Based on the primary study aim
110 of investigating associations between pain extent and signs and symptoms of central
111 sensitization, a power level of 95% (β), an alpha level of 0.05 (α) and a significant ‘moderate’
112 correlation ($r = 0.6$), a minimum sample of 25 participants was originally targeted. Participants
113 were aged between 40-70 years, with a primary diagnosis of hip OA based on the International
114 Classification of Diseases (ICD). Participants were excluded if they had other painful conditions
115 (e.g. chronic cervical or lumbar pain, fibromyalgia, or rheumatic conditions). co-morbidities,
116 such as severe cardiovascular, cognitive or neurological dysfunctions, or if their body-mass
117 index (BMI) was >32 . Those who were ingesting centrally acting analgesics were excluded,

118 while those taking non-opioid medication in moderate doses, or as needed, were included.
119 Participants were requested to not take any non-opioid medications on the day of testing and
120 were required to be able to give informed written consent to participate.

121 *Digital pain drawings*

122 Participants used a stylus pen (CS100B, Wacom, Vancouver, WA, USA) to define areas
123 of pain on a digital tablet (iPad 2, Apple Computer, Cupertino, CA, USA) using a commercially
124 available sketching software (SketchBook Pro) as previously described.²⁸ Different body charts
125 showing either a male or female body chart with different views (frontal, dorsal) were selected
126 and opened in the sketching software. The type, size, and color of the pen stroke were
127 standardized for all participants. One researcher (MS) instructed the participants on the use of the
128 digital tablet to complete the pain drawing and gave a brief demonstration and training to aid
129 familiarization. The researcher emphasized the importance of comprehensively shading all
130 painful areas, irrespective of their intensity or type.²³ The pain drawing was presented to the
131 participant and the researcher used the standardized instruction ‘Please draw where you felt your
132 usual pain during the last week on this body chart and try to be as precise as possible’.²³ Once the
133 participant had completed the drawing, the researcher asked the participant to confirm that the
134 pain drawing fully corresponded to their pain distribution, and the participants were given an
135 opportunity to edit the drawing prior to being saved.²³ This method has shown good test-retest
136 reliability within lumbar (intraclass correlation coefficients (ICC = 0.97) and cervical (ICC =
137 0.92) pain populations previously.²⁸

138 Pain extent expressed as the combined number of pixels coloured inside the frontal and
139 dorsal body charts (the total area of pain for each participant) was measured using custom
140 software for the analysis of pain drawings which was developed in Matlab®.^{26,28,29,35} Pain

141 frequency and pain location maps were also computed as previously described^{26,28,29,35}. The pain
142 frequency map is a function in which all the pain drawings are overlaid and analyzed
143 simultaneously to indicate the most frequently reported location of pain across all included
144 participants. Pain location was determined by dividing the body charts into 45 anatomical
145 regions (22 frontal and 23 dorsal). The number of participants who reported pain in each region
146 was illustrated using coloured Histograms.²⁸ Pain extent, frequency, and location were computed
147 for women and men separately.

148 *Patient Reported Outcome Measures*

149 All participants were asked to complete the German version of several patient reported
150 outcome measures including:

151 Measures of signs and symptoms of central sensitization and neuropathic pain:

- 152 • Fibromyalgia Survey Questionnaire (FSQ): A validated measure
153 which evaluates physical and emotional distress based on the preliminary
154 American College of Rheumatology (ACR) criteria, indicating a survey based
155 diagnosis of fibromyalgia to be made through patient self-report which, however,
156 may differ from the clinical diagnosis.³⁶ The FSQ combines the symptom
157 severity score (SSS) with the widespread pain index (WPI). The SSS evaluates
158 symptoms relating to sleep, fatigue, troubled thoughts and any additional
159 symptoms on a 0-3 scale (0=not present to 3=extreme), with a score ranging from
160 0 to 12. Patients were also asked if they experienced headaches, depression, or
161 pain in lower abdomen, which were coded to be present (1) or not present (0). The
162 WPI includes 19 non-articular pain sites, with each site being rated as 1 point.

163 Patients who score $\geq 7/19$ on the WPI and $\geq 5/12$ on the SSS or 3-6/19 on the WPI
164 and $\geq 9/12$ on the SSS are considered to have a diagnosis of fibromyalgia
165 according to the Fibromyalgia Survey Diagnostic Criteria (FSDC).³⁷

166 • PainDETECT (PD-Q): A validated measure that can be used as a
167 screening tool for neuropathic pain,³⁸ the PD-Q evaluates pain intensity,
168 characteristics, pattern and distribution to give a combined score out of 38, with a
169 higher score being related to increased pain. A total score of ≥ 19 is indicative of
170 neuropathic involvement with a 90% probability.³⁸ For the purpose of this study,
171 only the descriptive items were analyzed, indicating the level of neuropathic pain
172 like characteristics.³⁹

173

174 Hip Symptoms:

175 • Oxford Hip Score (OSH-D): A 12-item measure which assesses
176 stiffness, pain and physical disability in patients with hip OA with the German
177 version demonstrating reliability and validity. Each item has 5 possible responses
178 (scored 1-5), giving a maximum score of 60, with higher scores indicating
179 increased difficulties with activities of daily living.⁴⁰

180 • The Von Korff Scale (VKS): A measure of chronic pain⁴¹ which
181 grades pain intensity and disability and its German version has shown to be
182 reliable and valid. The tool incorporates 6 items detailing pain intensity and
183 impairment which are measured on 11-point numerical scales (0-10) and the
184 number of disability days.⁴² Patients are then 'graded' as chronic pain grade I

185 (low disability, low pain intensity), II (low disability, high pain intensity), III
186 (high disability, moderately limiting) or IV (high disability, severely limiting).^{41,42}

187 • Visual Analogue Scale (VAS): A widely used measure that
188 evaluates pain intensity⁴³ that has demonstrated reliability and validity for patients
189 with OA.⁴⁴ The VAS uses a 10cm line with ‘no pain’ and ‘worst possible pain’
190 located at each end and participants were asked to indicate their average pain over
191 the past four weeks by applying a vertical mark on the line.⁴³

192

193 Psychosocial symptoms:

194 • Pain Catastrophizing Scale (PCS): A measure that evaluates pain
195 catastrophizing, an important maladaptive psychological mechanism.⁴⁵ The
196 German version has been validated on patients with chronic pain⁴⁵ and has been
197 used extensively to assess knee OA populations.^{46,47} The PCS has 13 items which
198 are rated on a 5 point scale (scored 0-4) for a total score up to 52 points with
199 higher scores equating to increased catastrophizing.⁴⁶

200 • Tampa Scale for Kinesiophobia (TSK): A tool to evaluate fear of
201 movement or re-injury in patients that has been validated and demonstrated
202 reliability in German.⁴⁸ The TSK is a 17 item self-rated measure which uses a 4-
203 point likert scale (1: ‘Strongly disagree; 4: Strongly agree) with higher scores
204 indicating increased apprehension.^{49,50}

205 • Chronic Pain Acceptance Questionnaire (CPAQ): A valid and
206 reliable tool⁵¹ which is the most commonly used self-report method to quantify
207 pain acceptance in chronic pain populations.²³ The CPAQ incorporates two

208 factors: activity engagement and pain willingness, measured on a 7 point scale,
209 from 0 (never true) to 6 (always) across 20 items, with higher scores indicating
210 higher acceptance of chronic pain (Range 0-120).⁵²

211 • Depression, Anxiety, Stress 21 Scale (DASS): A valid⁵³ and
212 reliable⁵⁴ self-report measure to detect psychological factors affecting patients
213 pain experience.⁵⁴ The tool consists of the 21 questions (7 each for depression,
214 anxiety and stress respectively) which are scored on 4-point ordinal scales from 0
215 ‘did not apply to me at all’ to 3 ‘applied very much to me most of the time’. A
216 total score for each domain can be calculated by summing ordinal values and
217 multiplying by 2 and each domain graded as normal, mild, moderate, severe or
218 extremely severe.⁵³

219

220 *Quantitative Sensory Testing*

221 One investigator (MS) conducted Quantitative Sensory Tests on all participants adapting
222 a standardized protocol from the German Research Network on Neuropathic pain (DFNS).⁵⁵ All
223 participants were instructed by the investigator using standardized instructions⁵⁵ and were
224 familiarized with the testing procedures on neutral body sites. Testing was performed ipsilateral
225 to the side of the painful hip with a mean of three scores taken as the final score for each
226 reading.⁵⁵ A 30 second rest period was provided between repetitions.^{56,57}

227 Pain Pressure Thresholds: Pain pressure thresholds (PPTs) were measured using a digital
228 pressure algometer (Somedic Production, Stockholm, Sweden, Probe tip 1cm²) with pressure
229 stimulation increasing at 50 kPa/s. PPTs were assessed at the greater trochanter (5cm distal and
230 2cm anterior to Greater trochanter)⁹, gluteus medius muscle (3cm distally from the Iliac crest of

231 the proximal part of the muscle belly),⁵⁸ vastus medialis (3cm medial to the central point on
232 medial aspect of patella)⁵⁹, vastus lateralis (3cm lateral to the central point of lateral aspect of
233 patella)⁵⁹, tibialis anterior (2.5cm lateral and 5 cm inferior to the tibial tubercle)⁶⁰, and thenar
234 eminence. Participants were asked to state the moment the sensation on their skin changed from
235 one solely of pressure to an additional “burning”, “stabbing”, “piercing” or “tearing” sensation,
236 as described in the protocol of the DFNS. The participants were advised to indicate, by pushing a
237 button, when the sensation on the skin changed from just pressure to pain.

238 Thermal detection and pain thresholds: thermal testing was performed with a Thermal
239 Sensory Analyser II (Medoc, Israel).⁵⁵ A 3x3 cm thermode which applies warm and cold stimuli
240 was placed over the skin and starting at 32°C, the device decreased or increased the temperature
241 by 1°C/s. Thermal detection thresholds and pain thresholds were tested over the greater
242 trochanter (5cm distal and 2cm anterior to greater trochanter),⁹ and the thenar eminence. A
243 temperature limit was set for 50°C and 0°C. For the cold and warm detection thresholds (CDT,
244 WDT respectively), the participant was asked to press a stop button as soon as the perception of
245 cold/warmth occurred respectively. For the cold and heat pain thresholds (CPT, HPT
246 respectively), the participant was advised to press a button as soon as the feeling changed from
247 just cold/heat into an additional “burning”, “stabbing”, “piercing” or “tearing” sensation, as
248 described in the protocol of the DFNS.

249

250 *Statistical Analysis*

251 Descriptive statistics outlined participant symptom characteristics including their pain, hip
252 functional, and psychosocial levels. For descriptive purposes, pain frequency and location maps

253 were created. The data distribution was initially assessed with the Shapiro-Wilk test which
254 demonstrated a non-normal distribution. Therefore, a Mann-Whitney U test was used to assess for
255 differences in pain extent (shown in pain drawings) between men and women and Spearman (non-
256 linear) correlation coefficients were used to investigate the relationship between pain extent and:

257 1) Patient reported outcome measures, including measures of widespread pain
258 and neuropathic pain (FSQ-WPI and PD-Q), hip symptoms (VAS, OHS and VKS), and
259 psychosocial variables (PCS, TSK, CPAQ, and DASS).

260 2) QST data (PPTs and TPTs).

261 The statistical analysis was conducted using International Business Machines Statistical
262 Package for the Social Sciences (IBM Corp, Armonk, NY, USA) version 25 and the level of
263 significance was set at <0.05 .

264

265 RESULTS

266 Thirty participants with hip OA (15 female) were enrolled in the study. Participant
267 characteristics including their descriptive information (gender, age, BMI, VAS score), patient
268 reported outcome scores, and QST data are included in Table 1. Figures 1 and 2 detail the pain
269 frequency and location maps respectively, with dorsal and frontal views for men and women
270 displayed separately. The mean pain extent was 6.71% (of the total body chart area) for women
271 and 2.65% for men respectively. The Mann Whitney U test demonstrated a statistically significant
272 difference ($z = -2.76$, $p < 0.01$) in mean pain extent between men and women. The pain frequency
273 (Figure 1) and location maps (Figure 2) demonstrated that the most common site of symptoms
274 were located around the hip joints, gluteal region and lumbar spine for both male and female

275 participants. However, several participants experienced pain beyond the immediate anatomical
276 regions with women showing higher levels of bilateral and widespread pain than men. In
277 particular, the male participants did not report pain anteriorly above the abdomen or down either
278 arm. Male participants also reported cases of shoulder (4), neck (3), head (2), and distal leg
279 symptoms compared with females. No significant correlation was found between pain extent and
280 participant age ($r_s = -0.1682$) or BMI ($r_s = -.009$) (Table 2).

281 *Relationship between pain extent and patient reported outcome measures*

282 Pain extent scores demonstrated statistically significant positive associations with scores
283 on the Widespread Pain Index ($r_s = 0.426$, $p < 0.05$), Pain Detect ($r_s = 0.394$, $p < 0.05$) and the pain
284 catastrophizing Scale ($r_s = 0.413$, $p < 0.05$). No statistically significant associations were found
285 between pain extent and VAS ($r_s = 0.187$), FMS-SSS ($r_s = 0.354$), OHS ($r_s = 0.314$), VKS ($r_s =$
286 0.308), TSK ($r_s = 0.172$), DASS-D ($r_s = 0.316$), DASS-A ($r_s = 0.312$) or DASS-S ($r_s = 0.245$).

287 *Relationship between pain extent and QST data*

288 Pain extent scores were significantly associated with lower PPTs at the thenar eminence
289 ($r_s = -0.410$, $p < 0.05$), vastus lateralis ($r_s = -0.530$, $p < 0.01$), vastus medialis ($r_s = -0.363$, $p < 0.05$)
290 and greater trochanter ($r_s = -0.373$, $p < 0.05$). Pain extent was also associated with higher CPTs at
291 the greater trochanter ($r_s = 0.503$, $p < 0.01$), reduced HPTs at the greater trochanter ($r_s = -0.382$,
292 $p < 0.05$), and reduced WDTs over the thenar eminence ($r_s = -0.390$, $p < 0.05$). No significant
293 associations were observed between pain extent and PPTs measured over the tibialis anterior ($r_s =$
294 -0.354) or gluteus medius ($r_s = -0.345$). No significant association was measured between pain
295 extent and HPTs ($r_s = -0.337$), CPTs ($r_s = 0.259$), or CDTs ($r_s = 0.079$) over the thenar eminence. No

296 significant association was calculated between pain extent and WDTs ($r_s = -0.085$) or CDTs ($r_s =$
297 -0.134) measured over the greater trochanter.

298

299 DISCUSSION

300 This is the first study to evaluate pain extent and relate it to symptoms of central
301 sensitization in participants with hip OA. The use of digital pain drawings has been shown to be
302 reliable in patients with chronic spinal pain²⁸ and was recommended to reduce errors in transferring
303 images to a digital medium, while allowing for corrections to be made by patients prior to being
304 uploaded.²² Based on our results and similar studies^{22,23}, digital pain drawings offer a convenient
305 method for researchers and clinicians to quantify pain extent in patients with OA. Other studies
306 using pain drawings on patients with hip pain have utilized participants awaiting, or having had,
307 operative procedures with unclear³³ or heterogenous clinical populations.^{17,32,61,62} Only one study
308 has targeted patients with mild to moderate hip OA specifically²², but focused on description of
309 symptom distribution only.

310 The pain frequency maps demonstrated that participants experienced pain beyond the hip
311 region and immediate surrounding anatomical regions. The pain location map demonstrated that
312 the most common areas of pain in both genders were the buttock, lumbar spine, and anterior thighs.
313 Interestingly there were few participants who reported pain in the posterior thigh which is similar
314 to other studies examining pain extent in patients with hip OA.²² In general, women demonstrated
315 greater pain extent bilaterally, anteriorly proximal to the abdomen, and distal to the knee. However
316 men reported minimal symptoms in the thoracic region (especially anteriorly), arms and head or
317 face. The descriptive detail from the pain frequency and location maps was reinforced by the pain

318 extent calculations, which demonstrated that women presented with larger pain extent compared
319 to men. This is consistent with results from studies investigating patients with whiplash²⁹ and knee
320 OA.²³ As an exclusion criteria for this study was other painful conditions, these results have
321 potentially important clinical implications. Therefore, clinicians and researchers should be aware
322 that patients with hip OA, especially women, often present with symptoms of widespread pain.

323 Patient reported outcomes assess components of central sensitization but currently, due to
324 the complexity of patient presentations, the inclusion of key subjective indicators and physical
325 examination techniques are required for diagnosis.¹⁶ The Fibromyalgia Survey Questionnaire
326 (FSQ), which was designed for a patient population with well-recognized signs and symptoms of
327 central sensitization (i.e. fibromyalgia),^{63,64} was chosen as an indirect measure of signs and
328 symptoms of central sensitization for this study. While, no association was found between pain
329 extent and the Symptom Severity Subscale, a significant association was found with the WPI.³⁶
330 As the WPI determines the extent and location of pain distribution it is perhaps not surprising that
331 a significant association was found with pain extent. Increased pain extent was also significantly
332 associated with higher PainDETECT scores. This is consistent with other studies in patients with
333 hip⁹ and knee OA^{65,66} which showed that increased PainDETECT scores were associated with
334 clinical signs of central sensitization.

335 Although this study shows significant associations between increased pain extent and these
336 indirect measures of signs and symptoms of central sensitization, further research is required to
337 consolidate these findings. Currently, there is a lack of consensus over the most appropriate patient
338 reported outcome measure to assess for signs of central sensitization and therefore, the validation
339 of an appropriate tool in patients with hip OA is a research priority.

340 Larger pain extent was associated with reduced PPTs at four of six sites (thumb, vastus
341 lateralis, vastus medialis, and greater trochanter), three of which were remote sites. These results
342 suggest that the participants in this study demonstrated secondary hyperalgesia, which is a key
343 indicator of central sensitization¹⁵ and is in agreement with other studies on patients with hip
344 OA.^{9,67} Taken collectively, these results suggest digital pain drawings could be used clinically as
345 an appropriate screening tool for central sensitization in patients with hip OA.

346 No significant association was found between pain extent and pain intensity (measured
347 on the VAS) or levels of function and disability (measured on the VKS or the OHS respectively)
348 which contrasts studies conducted on patients with knee OA,²³ and women with fibromyalgia.²⁶
349 This may be associated with the mild to moderate symptoms of this studies cohort, or could
350 suggest that the primary pain mechanism underlying hip OA is not from peripheral nociceptive
351 input.^{26,68} The presence of secondary hyperalgesia highlighted above has been associated with
352 dysfunction in the descending inhibitory systems and adds further evidence to the suggestion that
353 central changes may be present in patients with hip OA.²⁴

354 Overall TPT testing showed inconsistent results with with three of eight sites (37.5%)
355 demonstrating a significant correlation with pain extent. Interestingly, local thermal pain
356 threshold (greater trochanter HPT and CPT) showed a significant correlation with pain extent
357 while detection thresholds (greater trochanter WDT and CDT) did not. Although altered
358 processing of thermal stimulus has been associated with both central sensitization⁶⁹ and small
359 fibre dysfunction in neuropathic pain states^{26,28}, these TPT values appeared to be within normal
360 limits. Therefore, limited conclusions can be drawn from the TPT. TPT testing represents a gap
361 in the evidence base that could be explored more thoroughly in future studies.

362 A significant correlation was observed between larger pain extent and the degree of pain
363 catastrophizing, an indication of whether participants fixate on, or feel despondent about their
364 ability to control their pain.⁴⁶ Apprehension to movement has been identified as a predictors for
365 developing chronic pain,⁷⁰ and a previous study demonstrated differences in the Tampa Scale of
366 Kinesiophobia (TSK) scores between patients with hip OA and controls.⁹ However, our study
367 found no correlation between pain extent and TSK scores, which is consistent with previous knee
368 OA²³ or whiplash²⁹ studies. Furthermore, no other significant correlations were identified with
369 the other psychosocial patient reported outcome measures (PAQ and DASS sub-scores). Carnes
370 et al., (2006)⁷¹ systematically reviewed the value of pain drawings in predicting psychosocial
371 distress but found insufficient evidence to support this. Of 19 included studies, only 3 showed
372 significant associations between pain drawings and levels of psychological distress and no
373 studies included patients with hip OA.

374 Central sensitization involves the altered functioning in several overlapping components
375 of the nervous system, including the facilitatory and inhibitory aspects of the descending neurons
376 which moderate nociceptive input,⁶⁴ and increased activity in several supra-spinal centres such as
377 the such as the anterior cingulate cortex , prefrontal cortex, and limbic system.⁷² This
378 neurological complexity leads to great heterogeneity in clinical symptom presentation and
379 although a classification system has been suggested for identification of central sensitization,¹⁶ it
380 has not been validated in OA populations to date. Therefore, the underlying complexity of
381 central sensitization may reflect the infrequent associations measured between increased pain
382 extent and the potential presence of neuropathic pain and psychosocial distress.

383

384 *Methodological considerations*

385 To date, no data exists on pain drawing reliability in patients with hip OA. However, test-
386 retest reliability of pain drawings has already been established for patients with spinal pain²⁸ and
387 during provoked pain in asymptomatic subjects³⁵, which suggests that pain drawings may well be
388 reliable in this study too. The sample size was relatively small in this study and the participants
389 had mild to moderate hip OA. Furthermore, there were no matched control participants in this
390 study. Therefore, the results may not be generalizable to all patients with hip OA, especially
391 those with more severe symptoms, and future research could determine normative TPT values
392 both local and distant to the hip in asymptomatic participants so these results can be placed in
393 context.

394 *Conclusion*

395 Increased pain extent in people with hip OA was associated with higher scores on the
396 Widespread Pain Index, PainDETECT, and the Pain Catastrophising Scale. Additionally, larger
397 pain extent was associated with lower PPT measured both locally and at remote sites. Pain
398 drawings may be useful clinically to identify increased pain extent, thereby contributing to early
399 diagnosis of central sensitization. Future research should determine the reliability and validity of
400 pain drawings and establish a validated patient reported outcome measure to evaluate for the
401 presence of central sensitization in patients with hip OA.

402

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404 All authors declare no conflicts of interest.

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625 FIGURE LEGENDS

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627 Figure 1: Pain frequency maps generated by superimposing the pain drawings of all participants
628 included in the study. Pain frequency maps have been generated separately for men and women
629 and include the dorsal and ventral view. The color grid indicates both the number and the
630 percentage of individuals that reported pain in that specific area. Darker colors represents the
631 most frequently reported area of pain.

632

633 Figure 2: Pain location analysis which shows the number of individuals reporting pain in a
634 specific body region. Darker colors represent a higher number of people reporting pain in a
635 specific body region.

636