

Individuals with Persistent Greater Trochanteric Pain Syndrome Exhibit Impaired Pain Modulation, as well as Poorer Physical and Psychological Health, Compared with Pain-Free Individuals: A Cross-Sectional Study

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1 Multimodal nature of GTPS

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3 1 **Individuals with persistent greater trochanteric pain syndrome exhibit impaired pain**
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5 2 **modulation, as well as poorer physical and psychological health than pain free**
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7 3 **individuals: a cross sectional study**

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9
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52
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55 21 declare.

1 Multimodal nature of GTPS

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3 **Abstract**

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6 **Objectives:** To compare physical, sensory and psychosocial factors between individuals with
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26 greater trochanteric pain syndrome and controls, and to explore factors associated with pain
27 and disability.

28 **Design:** Cross-sectional study.

29 **Setting:** General community.

30 **Subjects:** Patients with persistent, clinically diagnosed greater trochanteric pain syndrome
31 and healthy controls.

32 **Methods:** Participants completed tests of thermal and pressure pain threshold; conditioned
33 pain modulation; temporal summation; muscle strength, physical function, physical activity,
34 psychological factors and health related quality of. Standardised mean differences between
35 groups were calculated, and multiple linear regression identified factors associated with pain
36 and disability.

37 **Results:** Forty patients (95% female, average (standard deviation) age 51 (9) years), and 58
38 controls (95% female, age 53 (11) years) were included. Heat pain threshold, temporal
39 summation and pain catastrophizing were not different between groups. Compared to
40 controls, patients displayed significantly poorer quality of life (standardized mean difference
41 -2.66), lower pressure pain threshold locally (-1.47, remotely (-0.57)), poorer health status (-
42 1.22), impaired physical function (range 0.64 to 1.20), less conditioned pain modulation (-
43 1.01), weaker hip abductor/extensor strength (-1.01 and -0.59), higher depression (0.72) and
44 anxiety (0.61) levels, lower cold pain threshold locally (-0.47, (remotely (-0.39)) and less
45 time spent in (vigorous) physical activity (-0.43 to -0.39). 26% of pain and disability was
46 explained by depression, hip abductor strength and time to complete stairs.

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3 47 **Conclusions:** Patients with greater trochanteric pain syndrome exhibited poorer health
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5 48 related quality of life, physical impairments, widespread hyperalgesia, and greater
6
7 49 psychological distress than healthy controls. Physical and psychological factors were
8
9 50 associated with pain and disability.
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13 51 **Key words:** Tendinopathy, musculoskeletal pain, chronic pain.
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For Review Only

1 Multimodal nature of GTPS

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3 **54 Introduction**

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6 **55** Greater trochanteric pain syndrome (GTPS) presents as lateral hip pain on activities that load
7
8 **56** the structures at the greater trochanter. Most common in middle-aged females, it is the most
9
10 **57** prevalent lower limb tendinopathy to present to primary care (4.22 per 1000 per year) (1).

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12
13 **58** GTPS often persists, and high levels of pain and disability and poor quality of life are
14
15 **59** reported (2). Pain self-efficacy, anxiety and depression are associated with other persistent
16
17 **60** musculoskeletal conditions (3, 4) and tendinopathies (5), however, the presence of
18
19 **61** psychological factors in persistent GTPS when compared to controls has not been studied.
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26 **63** There is evidence of local and widespread mechanical and thermal hyperalgesia in upper limb
27
28 **64** tendon studies, with discrepancies seen in lower limb studies (6-9). These lower limb studies
29
30 **65** are limited by low sample size and high methodological heterogeneity including testing
31
32 **66** methods, sites of assessment and equipment (7). Currently, there is one cross-sectional study
33
34 **67** available in GTPS that reports local and widespread mechanical hyperalgesia in GTPS (n =
35
36 **68** 18) compared to controls (n = 18) (8). Altered endogenous pain inhibitory mechanisms have
37
38 **69** been reported in several chronic musculoskeletal conditions like osteoarthritis (10), low back
39
40 **70** pain (11, 12), Achilles tendinopathy (9), and recently in GTPS (13). The latter study reported
41
42 **71** a negative condition pain modulation in 34.7% of GTPS participants, although there was no
43
44 **72** comparator group included. Investigation of a more comprehensive battery of sensory tests in
45
46 **73** people with persistent greater trochanteric pain is warranted.
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52 **74** The gluteal muscles are crucial for functions like walking and stair climbing (14). Hip
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54 **75** abductor weakness is observed unilaterally (15-17) and bilaterally (15, 16) in GTPS, but hip
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56 **76** extensor muscle strength has received limited attention.
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1 Multimodal nature of GTPS

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3 78 Our primary aim was to quantify differences in physical, sensory, and psychosocial outcome
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5 79 measures in participants with GTPS compared to pain-free controls. Based on the current
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7 80 literature, we hypothesized that impaired physical strength and function, mechanical
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9 81 hyperalgesia and psychological distress would be found in persistent GTPS compared to
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11 82 pain-free controls. Our secondary aim was to identify factors associated with pain and
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13 83 disability in participants with GTPS. We hypothesized that pain and disability would be
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15 84 explained by multidimensional patient factors.
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24 87 **Methods**

25 88 Study design

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28 89 This cross-sectional study compared individuals with GTPS and age and sex matched
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30 90 controls. Reporting follows the Strengthening the Reporting of Observational studies in
31
32 91 Epidemiology (STROBE) guidelines for cross-sectional studies (18). Ethical approval was
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34 92 granted by The University of Queensland Human Research Ethics Committee (approval
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36 93 #2015000219). All participants provided verbal and written consent.
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47 96 Setting

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49 97 Between 16 May 2017 and 11 September 2018, participants were recruited from the Brisbane
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51 98 metropolitan area via newsletters and social media. A three-stage eligibility screening process
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53 99 was adopted: online screening, telephone interview and physical screening. Physical
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55 100 screening was performed by a registered post-graduate qualified musculoskeletal
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57 101 physiotherapist with >20 years clinical experience and baseline measures were conducted
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1 Multimodal nature of GTPS

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3 102 during one session of approximately 2.5 hours in a sound and temperature controlled room at

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5 103 The University of Queensland.

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14 106 Participants

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17 107 Volunteers were aged 18-70 years. Individuals with GTPS were eligible if they experienced

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19 108 lateral hip pain rated $\geq 2/10$ on an 11-point Numeric Rating Scale (NRS) (0 = no pain; 10 =

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21 109 worst pain imaginable) at its worst in the past week; pain duration ≥ 3 months; pain on

22
23 110 palpation of the tendon insertion on the greater trochanter (19), plus reproduction of

24
25 111 trochanteric pain on at least one of the following clinical tests: (1) 30s single leg stance, (2)

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27 112 the Hip FADER test, (3) static muscle test in the FADER position, (4) the FABER test, (5)

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29 113 Ober's test, (6) a static muscle contraction in the Ober's test position (19). GTPS participants

30
31 114 were excluded if they experienced groin pain on quadrant testing $> 3/10$ PNRs, received a

32
33 115 corticosteroid injection in the previous six months, experienced major trauma in the past 12

34
35 116 months, or had lower limb or back pain that was worse than their hip pain, required treatment

36
37 117 or prevented usual work or leisure activities in the previous six months. Controls were

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39 118 excluded if they had lateral hip pain or other areas of pain requiring treatment or preventing

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41 119 work or leisure activities in the preceding six months. Pregnancy, systemic inflammatory or

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43 120 neurological disorders, uncontrolled diabetes, and fibromyalgia were general exclusion

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45 121 criteria.

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54 124 Outcome measures

1 Multimodal nature of GTPS

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3 125 Data collection was performed by one researcher (MP) not blinded to the condition of the
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5 126 participants.

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11 128 *Pain and disability*

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14 129 Average pain, worst pain and pain during activity in the past week were rated using a PNRs.

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16 130 Pain and disability was measured using the Victorian Institute of Sports Assessment – GTPS

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18 131 (VISA-G) questionnaire (20), consisting of eight items. Scores range from 0 to 100, with

19
20 132 higher scores indicating less pain and better function. The VISA-G demonstrates good test-retest

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22 133 reliability (ICC 0.827; 95% CI 0.638-0.923), internal consistency (Cronbach's alpha 0.809; 95% CI

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24 134 0.709-0.934) and construct validity, compared to the Harris Hip Score and the Oswestry Disability

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26 135 Index (20).

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33 137 *Quantitative sensory testing*

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36 138 Somatosensory profiles were assessed unilaterally at a local hip site (the most painful spot in

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38 139 GTPS; 1-2cm posterior to the greater trochanter in controls) and a remote site (the lateral

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40 140 elbow, side randomly allocated by a coin toss). In participants with bilateral symptoms, the

41
42 141 most affected side was measured. The order of quantitative sensory tests (QSTs) was

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44 142 standardized as follows.

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51 144 Pain thresholds were determined by asking participants to 'press a button at the first onset of

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53 145 pain'. Cold pain threshold (CPT) and heat pain threshold (HPT) were assessed using a

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55 146 Thermotest Analyser (Somedic AB, Farsta, Sweden). From a baseline temperature of 32°C,

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57 147 incremental increases/decreases in temperature (1°C /s) were applied and tests were

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1 Multimodal nature of GTPS

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3 148 terminated when the participant pressed the button or if upper (50°C) or lower (5°C) cut-off
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5 149 temperatures were reached. Pressure pain threshold (PPT) was assessed by placing a 1cm²
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7 150 probe of a handheld pressure algometer (Somedic, Sweden) on the skin and gradually
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9 151 increasing the pressure at a rate of 30kPa/s, until the participant pressed the button. A
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11 152 maximum pressure of 900 kPa could be applied. Average pain thresholds were calculated
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13 153 from three consecutive measurements with 30-second rest intervals.
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20 155 Temporal summation was measured as the difference in perceived intensity (PNRS) between
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22 156 a single pinprick stimuli (256 mN pinprick) and the average of 10 repetitive pinprick stimuli
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24 157 applied within an area of 1cm² at 1/s. Five series were applied with 30-second rest intervals.
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31 159 Conditioned pain modulation (CPM) was assessed by immersing the contralateral hand in a
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33 160 cold-water bucket (conditioning stimulus) and measurement of PPT over the lateral hip (test
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35 161 stimulus) before, during and immediately after immersion of the hand (21). The starting
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37 162 water temperature was 10°C (range 9.5°C – 10.5°C). Water temperature was adjusted by
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39 163 adding warm or cold water until a pain intensity of 4-6/10 on PNRS was reported. The
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41 164 highest PPT score recorded during or immediately post immersion of the hand was subtracted
42
43 165 from the PPT score pre-immersion to calculate the CPM response. A positive CPM response
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45 166 (increase) reflects a hypo-algesic response, whereas a negative response (decrease) reflects a
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47 167 hyper-algesic response.
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55 169 *Strength and Physical measures*
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3 170 Hip abductor and extensor muscle strength were measured using a handheld dynamometer
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5 171 (Nicholas, Lafayette, IN47903 USA) (Figure 1). The center of the dynamometer was placed 5
6
7 172 cm proximal to the lateral malleolus for testing hip abductor strength, and in line with the
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10 173 posterior aspect of the thigh, 5 cm proximal from the kneecap for testing hip extensor
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12 174 strength (22). One practice and three experimental trials of maximal voluntary effort were
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14 175 conducted with 30-second rest intervals. Strength was reported as torque standardized to
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17 176 body weight (Nm/kg).

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23 178 >>Insert Figure 1<<

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29 180 Physical function was measured through balance (Star Excursion Balance Test (SEBT)) (23)
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31 181 and time to complete a 20-meter walk test (20MWT), five times sit to stand test (STS), and a
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33 182 flight of stairs. For the SEBT, participants were asked to maintain single leg stance while
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35 183 maximally reaching with the contralateral leg in anterior, posterolateral, and posteromedial
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37 184 directions (24). The 20MWT and flight of stairs were performed on a 10-meter course and a
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39 185 set of 11 stairs that participants were asked to respectively complete/ ascend and descend as
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41 186 fast as they were able to, without running (25). STS was performed from a seated position,
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43 187 with arms across the chest, and participants stood up and down five times as quickly as
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45 188 possible (26). One practice trial and two testing trials with 3-minute rests were performed,
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47 189 and the fastest trial was used for analysis.

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55 191 Physical activity time was determined with the Active Australia Survey (27). Participants
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57 192 reported minutes spent in walking, and performing moderate, and vigorous activity during the
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3 193 previous week. Total physical activity was calculated as the sum of minutes spent in these
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5 194 activities.
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11 196 *Self-reported psychosocial outcomes and health related quality of life*
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14 197 Quality of life was measured with the EuroQoL questionnaire (28). Participants rated their
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16 198 current level of disability (severe, moderate or none) in five dimensions (mobility, self-care,
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18 199 usual activities, pain/discomfort, anxiety/depression). Responses were transformed into a
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21 200 single index score ranging from 0 to 1, with higher scores reflecting greater quality of life
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23 201 (28). Health status was measured on a visual analogue scale of the EuroQol, ranging from 0
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25 202 (worst health you can imagine), to 100 (best health you can imagine). The EuroQol has
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27 203 demonstrated moderate validity and reliability (29, 30).
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34 205 Pain catastrophizing was quantified with the self-reported Pain Catastrophizing Scale (PCS),
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36 206 that has high reliability (Cronbach's alpha = 0.91) and moderate construct validity compared
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38 207 to the Inventory of Negative Thoughts in Response to Pain (31). Participants indicated the
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40 208 degree to which they experience each of 13 thoughts or feelings when in pain on a 5-point
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42 209 scale, ranging from 0 (not at all), to 4 (all the time) (32). Total scores range from 0-52, higher
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44 210 scores indicating higher levels of pain catastrophizing (32). A total score ≥ 30 was defined as
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46 211 clinically relevant (32).
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54 213 Anxiety and depression were measured with the Hospital Anxiety and Depression Scale
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56 214 (HADS) (33). Total anxiety and depression scores ranged from 0-21, higher scores indicating
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58 215 higher levels of anxiety and depression. Cases of anxiety and depression were defined by a
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1 Multimodal nature of GTPS

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3 216 total score ≥ 8 (33). The HADS has good reliability (Cronbach's alpha 0.82 and 0.83) and
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5 217 validity (33).

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11 219 Fear of movement (kinesiophobia) was measured with the Tampa Scale of Kinesiophobia
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13 220 (TSK) (34), asking participants to rate their agreement on a 4-point Likert scale, ranging from
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15 221 1 (strongly disagree), to 4 (strongly agree). Total scores range from 17 to 68, with higher
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17 222 scores indicating greater kinesiophobia. High fear was defined as a total score >37 , low fear
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19 223 as a total score ≤ 37 (34). The TSK has reported good reliability (Cronbach's alpha 0.74 -
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21 224 0.87) and validity (35).
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29 226 Pain self-efficacy was measured with the Pain Self-Efficacy Questionnaire (PSEQ), a
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31 227 questionnaire used to assess confidence in performing activities while in pain (36).

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33 228 Participants rate how confidently they can perform activities described on a 7-point Likert
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35 229 scale, ranging from 0 (not at all confident), to 6 (completely confident). Total scores range
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37 230 from 0 to 60, where higher scores reflect stronger self-efficacy beliefs (36). Scores $<40/60$
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39 231 were identified as participants having "less sustainable gains," as opposed to scores ≥ 40
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41 232 identifying participants that "could maintain functional gains" (36). The PSEQ is shown to be
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43 233 a valid and reliable measure (37).
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53 236 Study Size

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56 237 Sample size calculations were done a-priori with G*Power (Universitat Dusseldorf) v3.1(38),
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58 238 based on values of the remote PPT measure in lateral elbow tendinopathy (39). Based on a
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1 Multimodal nature of GTPS
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3 239 moderate effect size of 0.67 (39), power of 0.8, alpha of 0.05, and a 2:1 allocation ratio, we
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5 240 estimated a total sample size of 36 GTPS and 72 control participants.
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14 243 Statistical Method
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17 244 Statistical analyses were performed in SPSS version 25.0 (IBM, New York, NY, USA).
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19 245 Normality was assessed visually (histograms, quantile-quantile plots).
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25 247 Differences between GTPS and controls were assessed using parametric tests for continuous
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27 248 outcome measures (independent t-tests) and non-parametric tests for ordinal and nominal data
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29 249 (Mann-Whitney U test, Chi-square test). CPM efficacy was analysed using ANCOVA,
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31 250 including baseline hip PPT, water temperature and pain ratings of the conditioning stimulus
32
33 251 prior to PPT testing as covariates. Significance was determined with the Benjamini-Hochberg
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35 252 procedure to control for possible false positives caused by multiple comparisons (40). The
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37 253 false discovery rate was set at 0.10 (10%).
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45 255 Standardized mean differences (SMDs) and 95% confidence intervals (CI) were calculated to
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47 256 facilitate comparison for outcomes with different measurement units (RevMan V5.0; random
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49 257 effect model). Effect sizes were considered as: 0.2 small, 0.6 moderate, 1.2 large and ≥ 2.0
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51 258 very large (41).
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1 Multimodal nature of GTPS

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3 260 Correlations between pain intensity, number of pain regions and all outcome measures were
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5 261 calculated to evaluate the degree of association of these commonly regarded co-factors in
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7 262 presentation of musculoskeletal pain. Pearson correlation coefficients of (negative) 0.0 to 0.3
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9 263 were regarded as negligible, 0.30 to 0.50 low, 0.5 to 0.7 moderate, 0.7 – 0.9 high, and 0.9 to
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11 264 1.0 very high.

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18 266 Multiple linear regression analysis ('Enter' method) was performed with variables that were
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20 267 (a) continuous, (b) significantly impaired compared to controls (variables with highest effect
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22 268 sizes were chosen if they measured similar constructs), (c) significantly correlated with
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24 269 VISA-G. Symptom duration and pain intensity during activity were considered possible
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26 270 confounders. Independent variables were sequentially excluded from the model based on
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28 271 magnitude of significance. Multicollinearity reflected by a VIF of <2 was considered
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30 272 respectable.

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38 275 **Results**

39
40 276 Forty participants with GTPS and 58 controls were recruited (Figure 2). GTPS and controls
41
42 277 were comparable in age and sex, the majority being female (Table 1). GTPS participants had
43
44 278 a significantly greater BMI, waist girth and hip circumference compared to controls (Table
45
46 279 1). Within the GTPS group, 35% had a normal BMI, 32.5% were classified overweight,
47
48 280 17.5% class I obesity, 7.5% class II obesity, and 7.5% class III obesity compared to 3.4%
49
50 281 underweight, 63.8% normal, 22.4% overweight and 10.3% class I obesity in controls ($p < 0.01$,
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52 282 Table 1)(42).

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59 284 >>Insert Figure 2<<

1 Multimodal nature of GTPS
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5 286 >>Insert Table 1<<
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11 289 Outcome measures
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14 290 Sensory, physical and psychological outcomes, and mean differences (95% CI) are presented
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16 291 in Table 2 and Supplementary Material 1 outlines significant p-values.
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22 293 >>Insert Table 2<<
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27 295 *Quantitative Sensory Testing*
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30 296 Compared to controls, GTPS displayed large differences in local PPT and small differences
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32 297 in remote PPT. Small differences in local and remote CPT (GTPS displaying cold
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34 298 hyperalgesia) were noted. HPT and temporal summation did not differ between groups.
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37 299 CPM was measured for 39 GTPS and 41 controls (Figure 3). One GTPS and three control
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39 300 participants did not consent to CPM testing, three controls could not be measured due to time
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41 301 constraints or skin condition, and nine controls reached >900kPa during PPT or CPM testing.
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44 302 Moderate differences were found between groups, with GTPS displaying smaller changes in
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46 303 PPT (Table 2, Figure 4).
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49 304 Low associations were found for worst pain and local HPT ($r = -0.37$, $p = 0.02$; as was
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51 305 average pain), local temporal summation ($r = 0.48$, $p < 0.01$) and local PPT ($r = -0.37$, $p =$
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53 306 0.02). No significant associations were found between the number of pain regions and any of
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56 307 the QST measures including temporal summation and CPM.
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1 Multimodal nature of GTPS

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3 309 >>Insert Figure 3 and Figure 4<<

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9 311 *Strength and Physical measures*

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12 312 GTPS showed large differences in STS performance and moderate differences for unilateral

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14 313 hip abductor strength, 20MWT, flight of stairs, and SEBT performance (all directions)

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16 314 compared to controls. A small reduction in hip extensor strength was observed (Table 2,

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18
19 315 Figure 4).

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22 316 Significant but small group differences were found for total physical activity time and

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24 317 vigorous physical activity in the previous week (Table 2, Figure 4).

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27 318 Low associations were found for worst pain and SEBT posteromedial ($r = -0.35$, $p = 0.04$; as

28
29 319 was average pain), flight of stairs ($r = 0.47$, $p < 0.01$; as was average pain $r = 0.41$, $p = 0.01$),

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31 320 STS ($r = 0.41$, $p = < 0.01$), and extensor strength ($r = -0.36$, $p = 0.03$). No significant

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33 321 associations were found between the number of pain regions and any strength or physical

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35 322 measures.

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42 324 *Self-reported psychological distress and quality of life*

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45 325 Compared to controls, GTPS displayed large differences in quality of life, health status and

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47 326 moderate differences in anxiety and depression scores. No significant group differences were

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49 327 found for pain catastrophisation (Table 2, Figure 4). Within the GTPS group, 25% were

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51 328 classified with anxiety, 5% with depression, compared to 5.2% and 3.4% of controls

52
53 329 respectively. (Table 2). Within the GTPS group, 87.5% were able to ‘maintain functional

54
55 330 gains’ (PSEQ scores), whereas 57.5% had a high degree of kinesiophobia (Table 2). These

56
57 331 measures were not collected in the control group.

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3 332 Low associations were found for worst pain and anxiety ($r = -0.33$, $p = 0.04$), health status (r
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5 333 $= -0.48$, $p < 0.001$; as was average pain $r = -0.49$, $p < 0.001$), and for the number of pain sites
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7 334 and pain catastrophising ($r = 0.43$, $p < 0.01$). High associations were found for worst pain and
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9 335 quality of life ($r = -0.75$, $p < 0.001$; as was average pain $r = -0.73$, $p < 0.001$).

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16 337 *Factors associated with pain and disability (VISA-G)*

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19 338 The final multivariate regression model explained 26% of the variance of VISA-G. Cases
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21 339 with evidence of marginal significance were retained in the final model. Based on the non-
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23 340 standardised coefficients, one unit increase in depression on the HADS is likely to decrease
24
25 341 VISA-G by 1.67 units, one N.m.kg⁻¹ increase in abductor strength is likely to increase VISA-
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27 342 G by 12.64 units, and one second increase in time to complete stairs is likely to decrease
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29 343 VISA-G by 0.53 units (Supplementary Material 2).

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36 37 346 **Discussion**

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39 347 This study aimed to quantify differences in physical, sensory, and psychosocial outcome
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41 348 measures in participants with GTPS compared to pain-free controls, and to explore the factors
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43 349 associated with pain and disability. Large effects were found for health-related quality of life,
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45 350 hip PPT, and STS; moderate effects for CPM, hip abductor strength, all other functional
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47 351 measures, anxiety and depression; small effects for elbow PPT, hip and elbow CPT, hip
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49 352 extensor strength and physical activity time. Notably we did not find any differences in
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51 353 temporal summation of pain between groups. VISA-G scores were explained by a
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53 354 combination of depression, hip abductor strength and time to complete stairs.

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1 Multimodal nature of GTPS

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3 356 This study found evidence of widespread mechanical and cold hyperalgesia. The degree of
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5 357 impairment in PPT was greater at the local tendon (SMD -1.49) than the elbow (SMD -0.58),
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7 358 and small for local and remote CPT (SMD -0.47 and -0.39). Previous literature reported
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9 359 evidence of *local* mechanical and thermal hyperalgesia in some, but not all lower
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11 360 tendinopathy studies (7-9, 43). *Widespread* mechanical and cold hyperalgesia have been
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13 361 reported in Achilles and lateral elbow tendinopathy (9, 39), but not in other studies (43). A
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15 362 recent cross-sectional study in persistent GTPS reported significant group differences in PPT
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17 363 locally, bilaterally and remotely, inferring primary and secondary mechanical hyperalgesia in
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19 364 GTPS (8). Comparison of our study results with previous literature shows inconsistencies in
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21 365 findings. High quality methodological studies with a larger sample size that explore the
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23 366 involvement of pain sensitivity in persistent tendinopathies like GTPS are warranted.
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32 368 CPM is an established paradigm used to study endogenous pain inhibitory mechanisms. It is
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34 369 thought to reflect the efficacy of the diffuse noxious inhibitory control system (DNIC) (44), a
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36 370 spinal-medullary-spinal pathway that triggers pain inhibition when two painful stimuli are
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38 371 applied simultaneously (45). In humans, CPM may reflect peripheral neural mechanisms,
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40 372 such as chronic inflammation and hyper-excitability (46) as well as higher cortical centres,
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42 373 which are also affected by age, sex, menstruation cycle, and psychological features (45). We
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44 374 found moderate differences in CPM efficacy, possibly reflecting alterations in DNIC,
45
46 375 however we did not find evidence of altered facilitatory ascending mechanisms in GTPS (i.e.,
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48 376 temporal summation was not different between groups). We could speculate that persistent
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50 377 pain causes ongoing activation of pain inhibitory mechanisms, leaving patients unable to
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52 378 further activate these systems, resulting in a ceiling effect. This has been previously proposed
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54 379 in other persistent pain conditions (47).
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6 381 The presence of widespread pain sites is often considered linked with central nervous system
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8 382 sensitization. We did not find this in our cohort, which is consistent with a study of knee
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10 383 osteoarthritis (48), but not others. A recent cross-sectional study including 49 participants
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12 384 with GTPS reported significant associations of widespread pain distribution with less CPM
13
14 385 and increased temporal summation (13). The association between widespread pain and less
15
16 386 CPM has also been reported in low back pain (11, 49). It might be that a subgroup of
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18 387 individuals who have GTPS and widespread pain may be more likely to experience central
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20 388 nervous system sensitization. Future research should further assess if subgroups of
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22 389 individuals with different severity of GTPS vary according to their pain distribution. This
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24 390 may lead to improved patient specific pain management.
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32 392 The VISA-G is a self-reported questionnaire concerning pain and functional disability
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34 393 specifically designed for GTPS (20). Linear regression revealed a strong association between
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36 394 VISA-G and depression, implying depression levels to be an indicator of severity of self-
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38 395 reported pain and disability. High quality evidence shows depression levels to be associated
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40 396 with many other chronic musculoskeletal pain conditions (50, 51), and reported depression to
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42 397 be a possible moderator in the relationship with chronic pain (52). Further, positive
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44 398 behaviours like resilience, optimism and pain acceptance are thought to positively affect
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46 399 chronic pain (53, 54). Thus, the interpretation of self-reported pain and disability
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48 400 questionnaires, such as VISA-G, should take this association with levels of depression into
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1 Multimodal nature of GTPS

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3 403 The limitations of this study include the unblinded assessor, although a standardized protocol
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5 404 was rigorously followed. Only 80% of the calculated sample size for controls was recruited
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7 405 due to time constraints. Further, our population was highly educated (>65% of both groups
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9 406 had at least graduated from University or polytechnic) and predominantly female, which
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11 407 should be taken into account when generalizing findings. QST requires operator skill,
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13 408 however, members of this research lab have considerable experience in QST studies. Future
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15 409 research should aim to identify the prognostic significance of physical, sensory and
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17 410 psychological characteristics on pain and disability in persistent GTPS before targeted
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19 411 treatments can be developed. In addition, the impact of social factors and environment should
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21 412 be further investigated to understand the patient characteristics and prognosis of individuals
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23 413 with GTPS.
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31 32 415 **Conclusions**

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35 416 This study shows that compared to controls, people with persistent GTPS exhibit impaired
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37 417 health related quality of life, physical strength and functioning, widespread hyperalgesia, and
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39 418 altered psychological factors. No differences were seen in heat hyperalgesia, temporal
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41 419 summation or pain catastrophizing. Self-reported pain and disability was associated with
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43 420 depression, hip abductor strength and time to complete stairs. The connections between
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45 421 biopsychological features and persistent pain in GTPS should be considered in order to and
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47 422 inform management approaches.
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51 52 423 53 54 424 **Acknowledgments and Conflict of Interest**

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5 428 have no conflicts of interest to declare.
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For Review Only

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Tables

Table 1. Participant characteristics of the GTPS and the control group. Data represent mean (SD) for each group unless otherwise indicated, with group mean differences (95% CI; p-value). Significant group differences are indicated by *.

	GTPS group n = 40	Control group n = 58	Group difference
Age years	51 (9)	53 (11)	-1.2 (-5.5, 3.1; p=0.59)
Sex female n, (%)*	38 (95%)	55 (95%)	p = 0.97
Height cm	165.7 (6.8)	165.7 (5.7)	0 (-0.0, 0.0; 1.0)
Body mass kg	78.3 (18.5)	66.2 (12.8)	12 (5.7, 18.3; p<0.001*)
Body Mass Index kg/m ²	28.5 (6.2)	24.0 (4.1)	4.4 (2.3, 6.5; p<0.001*)
Underweight (BMI <18.5)	0%	3.4%	p <0.01*†
Normal (18.5–24.9)	35%	63.8%	
Overweight (25.0–29.9)	32.5%	22.4%	
Obese class I (30.0–34.9)	17.5%	10.3%	
Obese class II (35.0–39.9)	7.5%	-	
Obese class III (≥40)	7.5%	-	
Waist girth cm	94.7 (14.0)	84.12 (13.3)	10.6 (5.1, 16.2; p<0.001*)
Hip circumference cm	110.5 (13.9)	101.4 (10.2)	9.1 (4.3, 14.0; p<0.001*)
Highest education†			p = 0.28
Less than 3y high school n, (%)	1 (2.5)	1 (1.7%)	
3y or more high school n, (%)	5 (12.5%)	2 (8.6%)	
Some tertiary training n, (%)	8 (20%)	9 (15.5%)	
Graduated from University or polytechnic n, (%)	11 (27.5%)	19 (32.8%)	
Any post-graduate study n, (%)	15 (37.5%)	24 (41.4%)	
Work status†			p = 0.91
Employed for wages n, (%)	26 (65%)	35 (60.3%)	
Self-employed n, (%)	4 (10%)	3 (5.2%)	
Out of work n, (%)	1 (2.5%)	2 (3.4%)	
A homemaker n, (%)	3 (7.5%)	1 (1.7%)	
Student n, (%)	6 (15%)	4 (6.9%)	

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Retired n, (%)	0	13 (22.4%)	
Hip pain interference with sleep quality			
Not at all n, (%)	4 (10%)	-	-
Occasionally n, (%)	9 (22.5%)	-	-
Some of the time n, (%)	16 (40%)	-	-
Most of the time n, (%)	7 (17.5%)	-	-
All of the time n, (%)	4 (10%)	-	-
Duration of symptoms months, median (IQR)	18 (15)	-	-
Unilateral n, (%)	28 (70%)	-	-
VISA-G (0-100)	63 (11)	-	-
Pain severity in past week (PNRS 0-10)			
Average, median (IQR)	4 (3)	-	-
Worst, median (IQR)	7 (3)	-	-
During activity, median (IQR)	5 (4)	-	-
Number of pain regions, median (IQR)‡	3 (2)		

Abbreviations: BMI, body mass index; GT, gluteal tendinopathy; IQR, interquartile range; PNRS, pain numeric rating scale;

SD, standard deviation; VISA-G, Victorian Institute of Sports Assessment – Gluteal tendinopathy; 3y, 3 years.

*significant p level set on $p = 0.05$

†Group differences calculated with the χ^2 test.

‡Number of pain regions recorded with The Nordic Musculoskeletal Questionnaire (55).

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Table 2. Mean (SD) for quantitative sensory testing, strength and physical tests, psychological self-reported outcome measures, and quality of life in the GTPS and control groups, with group mean differences (95% CI; p-value).

	GTPS group n = 40	Control group n = 58	Group differences
QST measures			
Cold pain threshold hip °C	10 (7.52)	7.02 (5.24)	2.97 (0.41, 5.53; 0.03*)
Cold pain threshold elbow °C	10.40 (7.77)	7.79 (5.85)	2.60 (0.13, 5.53; 0.08*)
Heat pain threshold hip °C	45.09 (2.84)	46.09 (2.76)	-1.00 (-2.14, 0.14; 0.09)
Heat pain threshold elbow °C	46.05 (3.59)	46.82 (2.80)	-0.78 (-2.06, 0.50; 0.23)
Pressure pain threshold hip kPa	203.25 (71.99)	395.88 (155.59)	-192.63 (-245, -140.26; <0.001*)
Pressure pain threshold elbow kPa	317.83 (133.81)	396.48 (134.96)	-78.66 (-133.53, -23.79; <0.01*)
Temporal summation hip /10 PNRS	1.33 (1.01)	1.16 (1.33)	-0.17 (-0.67 to 0.34; 0.51)
Temporal summation elbow /10 PNRS	0.58 (0.69)	0.73 (1.08)	0.15 (-0.21 to 0.50; 0.42)
Conditioned pain modulation hip kPa†	48.96 (51.48)	117.98 (79.31)	-59.79 (-98.22, -21.36; <0.01*)
Strength and physical measures			
Hip abductor strength N.m.kg ⁻¹	0.70 (0.25)	1.00 (0.31)	-0.30 (-0.42, -0.18; <0.001*)
Hip extensor strength N.m.kg ⁻¹	0.42 (0.20)	0.58 (0.30)	-0.16 (-0.27, -0.05; <0.01*)
Star Excursion Balance Test			
Anterior	0.52 (0.07)	0.58 (0.07)	-0.05 (-0.08, -0.03; <0.001*)
Posterolateral	0.78 (0.12)	0.86 (0.13)	-0.08 (-0.13, -0.03; <0.01*)
Posteromedial	0.66 (0.13)	0.77 (0.14)	-0.11 (-0.16, -0.05; <0.001*)
Sit to stand test s	11.98 (3.15)	8.76 (2.23)	3.22 (2.15, 4.30; <0.001*)
20 meter walk test s	9.84 (2.87)	7.42 (1.26)	2.42 (1.58, 3.27; <0.001*)
Flight of stairs test s	20.94 (5.47)	16.93 (3.64)	4.01 (2.18, 5.84; <0.001*)
Total physical activity min/week	465.38 (472.25)	677.16 (502.27)	211.78 (11.76, 411.80; 0.04*)
Vigorous physical activity min/week	98.25 (163.13)	166.98 (182.09)	68.73 (-2.54, 140.01; 0.06*)
Psychosocial self-reported outcome measures			
Pain catastrophizing scale			

Multimodal nature of GTPS

Total score /52	7.23 (6.56)	5.55 (7.0)	1.67 (-1.10, 4.45; 0.23)
Clinical level n, (%)‡	1 (2.5%)	1 (1.7%)	p = 0.79
Non clinical level n, (%)‡	39 (97.5%)	57 (98.3%)	

Hospital Anxiety and Depression

Scale: Anxiety	5.38 (3.43)	3.43 (2.96)	1.94 (0.66, 3.23; <0.01*)
Total score /21	10 (25%)	3 (5.2%)	p<0.01
Cases n, (%)‡	30 (75%)	55 (94.8%)	
Non-cases n, (%)‡			

Hospital Anxiety and Depression

Scale: Depression	3.15 (2.476)	1.52 (2.096)	1.63 (0.71, 2.55; 0.001*)
Total score /21	2 (5%)	2 (3.4%)	p = 0.70
Cases n, (%)‡	38 (95%)	56 (96.6%)	
Non-cases n (%)‡			

Pain self-efficacy

Total score /60	49.58 (8.258)	-	-
Less sustainable gains n, (%)	5 (12.5%)	-	-
Maintenance of function n, (%)	35 (87.5%)	-	-

Tampa Scale of Kinesiophobia

Total score /68	35.93 (4.599)	-	-
High degree of kinesiophobia n, (%)	23 (57.5%)	-	-
Low degree of kinesiophobia n, (%)	17 (42.5%)		

EQ-5D-3L

Index score /1	0.72 (0.14)	0.98 (0.06)	-0.26 (-0.30, -0.22; <0.001*)
Self-reported health /100 VAS	68.68 (15.50)	84.21 (10.16)	-15.53 (-20.67, -10.39; <0.001*)

Abbreviations: GT, gluteal tendinopathy; PNRS, pain numeric rating scale SD, standard deviation; VAS, visual analogue scale.

*Significance calculated with the Benjamini-Hochberg procedure (Supplementary Material 1).

‡Group differences calculated with an ANCOVA with GT n = 39 and HC n = 41.

‡Group differences calculated with the χ^2 test.

1 Multimodal nature of GTPS

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3 **Figure legends**

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6 **Figure 1.** Positioning of the participant during measurements of hip abductor muscle strength
7 (upper image) and hip extensor muscle strength (lower image). Hip abductor muscle strength
8 was measured with the test knee extended and the hip at 10° abduction and 0° flexion, and
9 the opposite leg flexed at the hip (45°) and knee (90°). Hip extensor strength was measured
10 with both hips in 30° flexion and both knees in 45° flexion. In both tests, the pelvis was
11 stabilized with a seatbelt and towel, strapped to the plinth, and the participant held the side(s)
12 of the plinth with both hands.
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23 **Figure 2.** Flowchart of recruitment.

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26 **Figure 3.** Individual data points of the greater trochanteric pain syndrome (GTPS) group
27 (blue colour scheme; n =39) and control group (grey colour scheme; n = 41) and the group
28 average (black line) for the pressure pain threshold (PPT) measure pre conditioning stimulus
29 and the PPT max (maximum of PPT during/after).
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36 **Figure 4.** Forest plot including standardized mean differences (SMD) and 95% confidence
37 intervals (CI) for all outcome measures. Quantitative sensory testing on the hip and elbow
38 (cold pain threshold (CPT), heat pain threshold (HPT), pressure pain threshold (PPT) and
39 conditioned pain modulation (CPM)); strength (abductor and extensor), physical function
40 (star excursion balance test (SEBT), time to complete 20 meter walk test, sit to stand, flight
41 of stairs) and physical activity (Active Australia Survey (AAS)); psychological outcome
42 measures (the Hospital Anxiety and Depression Scale (HADS)), and the Pain Catastrophizing
43 Scale (PCS)); health related quality of life.
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Multimodal nature of GTPS

Figures

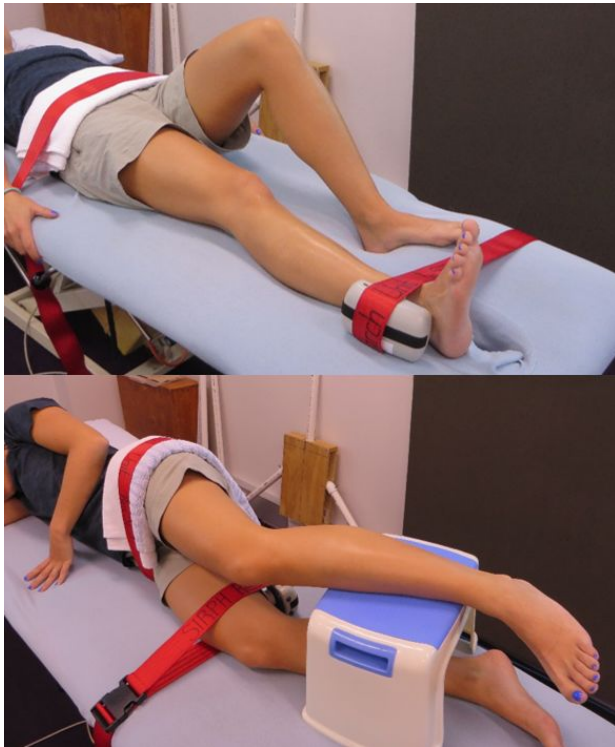


Figure 1.

view Only

Multimodal nature of GTPS

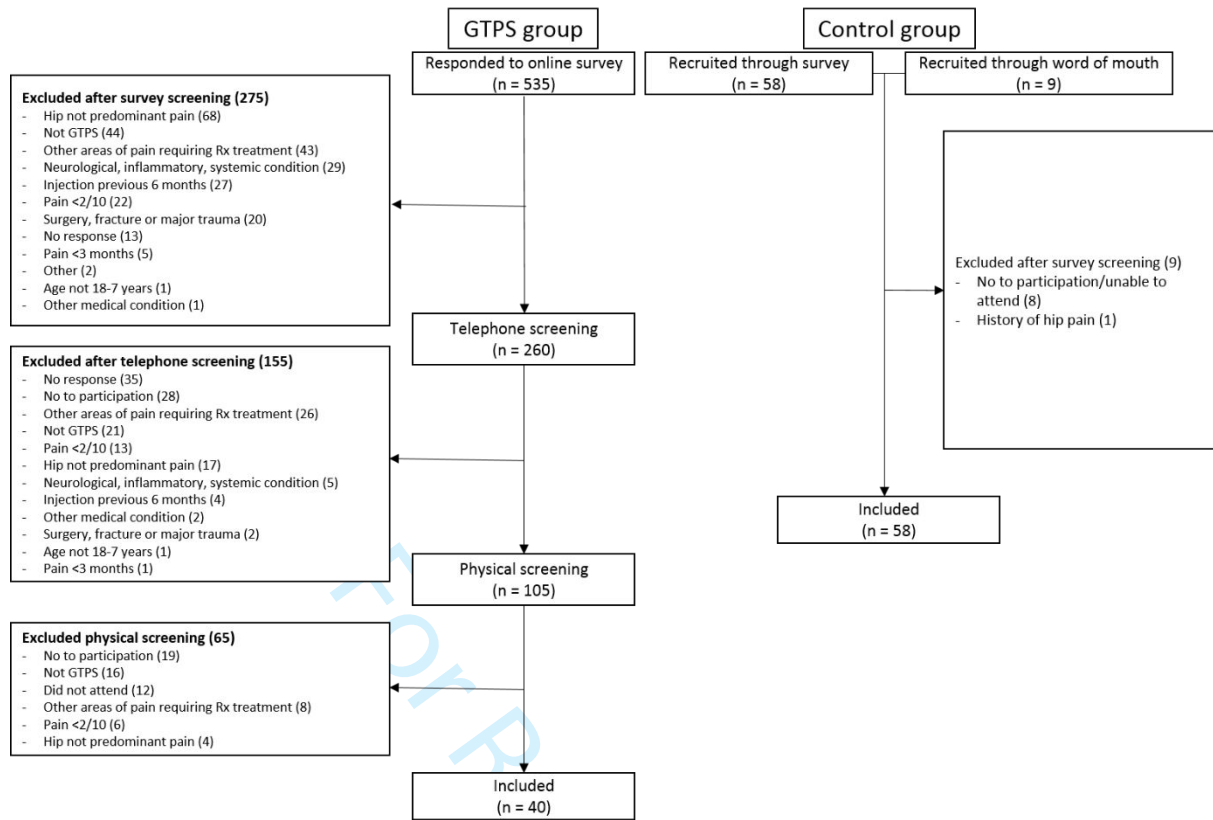


Figure 2.

Multimodal nature of GTPS

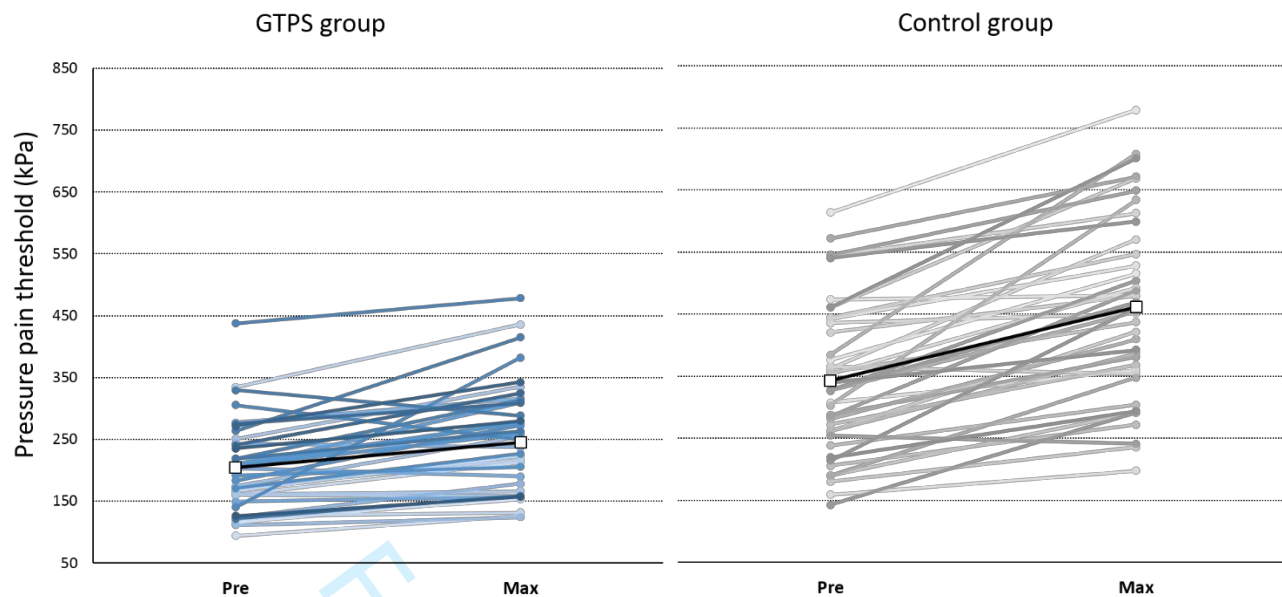


Figure 3.

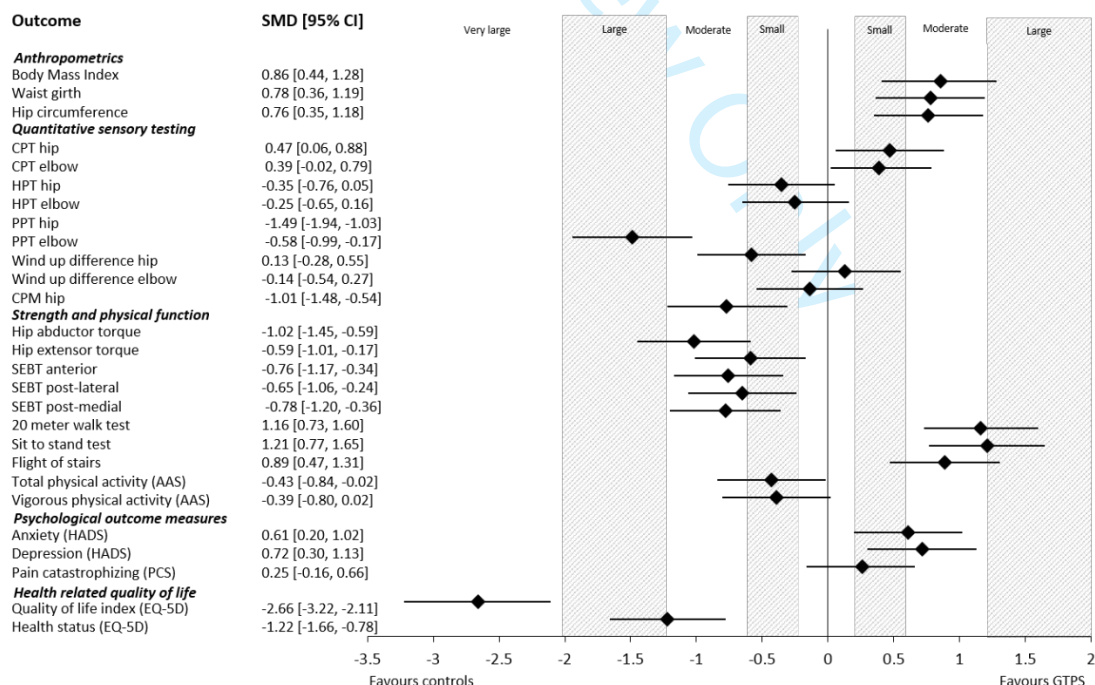


Figure 4.