



Aalborg Universitet

AALBORG UNIVERSITY
DENMARK

Local hyperalgesia, normal endogenous modulation with pain report beyond its origin
a pilot study prompting further exploration into plantar fasciopathy

Riel, Henrik; Plinsinga, Melanie L; Mellor, Rebecca; Boudreau, Shellie A; Vuvan, Viana; Vicenzino, Bill

Published in:
Scandinavian Journal of Pain

DOI (link to publication from Publisher):
[10.1515/sjpain-2019-0109](https://doi.org/10.1515/sjpain-2019-0109)

Publication date:
2020

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

[Link to publication from Aalborg University](#)

Citation for published version (APA):
Riel, H., Plinsinga, M. L., Mellor, R., Boudreau, S. A., Vuvan, V., & Vicenzino, B. (2020). Local hyperalgesia, normal endogenous modulation with pain report beyond its origin: a pilot study prompting further exploration into plantar fasciopathy. *Scandinavian Journal of Pain*, 20(2), 375-385. Advance online publication. <https://doi.org/10.1515/sjpain-2019-0109>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

Original experimental

Henrik Riel*, Melanie L. Plinsinga, Rebecca Mellor, Shellie A. Boudreau, Viana Vuvan and Bill Vicenzino

Local hyperalgesia, normal endogenous modulation with pain report beyond its origin: a pilot study prompting further exploration into plantar fasciopathy

<https://doi.org/10.1515/sjpain-2019-0109>

Received August 1, 2019; revised August 29, 2019; accepted August 31, 2019; previously published online September 21, 2019

Abstract

Background and aims: Persistent tendinopathies were previously considered solely as peripheral conditions affecting the local tendinous tissue until quantitative sensory testing identified involvement of altered pain processing. In similar fashion, pain in patients with persistent plantar fasciopathy may also involve more than local tissue. The aim of this pilot study was to investigate potential differences in conditioned pain modulation and pressure and thermal pain thresholds, between individuals with PF and healthy pain-free controls, as a precursor to a larger-scale study.

Methods: We assessed 16 individuals with plantar fasciopathy and 11 pain-free controls. Plantar fasciopathy diagnosis was: palpation pain of the medial calcaneal tubercle or the proximal plantar fascia, duration ≥ 3 months, pain intensity $\geq 2/10$, and ultrasound-measured plantar fascia thickness ≥ 4 mm. Quantitative sensory tests were performed locally at the plantar heel and remotely on the ipsilateral elbow. Assessments included pain thresholds for pressure, heat and cold, and conditioned pain modulation measured as change in local resting pressure pain threshold with cold water hand immersion. Participants rated pain intensity at pain threshold. Additionally, the area and distribution of plantar fasciopathy pain was drawn on a digital body chart of the lower limbs. Descriptive analyses

were performed and between-group differences/effects expressed as standardised mean differences (d).

Results: There was no conditioned pain modulation difference between participants with plantar fasciopathy and controls ($d = 0.1$). Largest effects were on local pressure pain threshold and reported pain intensity on pressure pain threshold ($d > 1.8$) followed by pain intensity for heat and cold pain thresholds ($d = 0.3$ – 1.5). According to the digital body chart, pain area extended beyond the plantar heel.

Conclusions: The unlikelihood of a difference in conditioned pain modulation yet a pain area extending beyond the plantar heel provide a basis for exploring altered pain processing in a larger-scale study.

Implications: This was the first study to investigate the presence of altered pain processing in individuals with plantar fasciopathy using a conditioned pain modulation paradigm and thermal pain thresholds. We found no indication of an altered pain processing based on these measures, however, patients rated pain higher on thresholds compared to controls which may be important to clinical practice and warrants further exploration in the future.

Keywords: plantar fasciopathy; conditioned pain modulation; pressure pain threshold; thermal pain threshold; pain distribution; pain experience on pain threshold.

1 Introduction

Plantar fasciopathy (formerly known as plantar fasciitis) is one of the most common musculoskeletal conditions with a lifetime prevalence of 10% and has the second highest prevalence and incidence rate among lower extremity tendinopathies [1–4]. The condition is characterised by severe and sharp heel pain. Patients often report pain during their first steps in the morning or after inactivity which improves with ambulation and worsens during the day [5].

Historically, tendinopathies have been considered peripheral conditions only involving the tendons. Recent evidence challenges this notion and suggests that altered pain

*Corresponding author: Henrik Riel, MSc, Center for General Practice at Aalborg University, Fyrkildevvej 7, Aalborg East, Denmark, Phone: +45 30201570, E-mail: hriel@dcm.aau.dk

Melanie L. Plinsinga, Rebecca Mellor, Viana Vuvan and Bill Vicenzino: The University of Queensland, School of Health and Rehabilitation Sciences: Physiotherapy: Sports Injury Rehabilitation and Prevention for Health, St. Lucia QLD, Australia

Shellie A. Boudreau: Center for Sensory-Motor Interaction (SMI), Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Fredrik Bajers Vej 7D, Aalborg East, Denmark

processing may contribute to persistent pain in tendinopathy which is similar to findings in other chronic pain conditions [6–12]. Three recent studies comparing individuals with plantar fasciopathy and healthy controls found conflicting evidence; two studies found local and widespread mechanical hyperalgesia whereas one did not find any differences [13–15]. These inconsistent reports prompt further investigation of pain processing, especially as all three studies assessed mechanical hyperalgesia using pressure pain thresholds (PPT). PPT assessment is only one of many quantitative sensory testing (QST) approaches that provide information about somatosensory function as different tests assess different primary afferent fibres [16, 17]. For example, additional gains in information about somatosensory function and pain processing can be achieved using thermal pain thresholds and conditioned pain modulation (CPM) tests. PPT tests and cold pain involve the A δ and C fibers whereas heat pain is believed to primarily access C fibers with less involvement of A δ fibers [16, 17]. CPM tests assess differences in PPT from before to during or after a remote painful stimulus and if PPT is not increased during or after the painful stimulus, the endogenous pain inhibition has been affected negatively [18]. These additional QST tests will likely provide further clarity on any altered pain processing in plantar fasciopathy and may even direct future treatment options as CPM has been found to be associated with the effect of pharmacological interventions in neuropathy [16]. In addition to QSTs, asking patients to draw their pain on body charts may provide further insight into the pain features of a chronic condition [19]. Persistent musculoskeletal conditions tend to occur with spreading area of pain, but digital pain drawings by patients with bilateral patellofemoral pain have revealed that pain may also present in symmetrical pain patterns which suggests the involvement of central neuronal mechanisms [19, 20]. Whether this is also a feature of PF remains unknown.

The aim of this pilot study was to explore thermal pain thresholds and conditioned pain modulation, in addition to pressure pain thresholds, in individuals with plantar fasciopathy compared with healthy pain-free controls and to explore pain area and distribution. This pilot study was conducted to inform planning of a larger-scale hypothesis-testing study.

2 Methods

2.1 Study design

This study was designed as a cross-sectional pilot study in which a single assessor conducted QSTs of cold, heat

and pressure pain thresholds in individuals with plantar fasciopathy (PF group) and healthy pain-free individuals (control group). In order to provide some control over known covariates of QSTs (e.g. sex and age), we attempted to match controls to recruited participants with PF on the basis of sex and age. Reporting of this study follows the STROBE statement: guidelines for reporting observational studies [21]. Ethical approval was granted by the Medical Research Ethics Committee of the University of Queensland, and all participants provided written informed consent prior to participation. The study was conducted in accordance with the Declaration of Helsinki [22].

2.2 Setting

The study was conducted at the University of Queensland, Brisbane, Australia. Participants were recruited from June 1st 2017 to July 21st 2017 through public advertisements in the local community and social media (Facebook). Potentially eligible participants who had completed an online questionnaire then underwent a telephone interview to further determine eligibility, and those who matched the criteria were invited to attend a physical examination at the University of Queensland during which eligibility was confirmed with clinical diagnostic tests. The assessor responsible for confirming inclusion, including performing ultrasound measurements, and data collection was a registered physiotherapist with 6 years of experience in treating patients with musculoskeletal disorders.

2.3 Participants

The inclusion criteria of the individuals with plantar fasciopathy were: (i) plantar heel pain for at least 3 months before enrolment; (ii) average heel pain intensity of ≥ 2 on an 11-point numerical rating scale (NRS, 0 is no pain, 10 is worst pain imaginable) during the previous week [23]; (iii) thickness of the plantar fascia of 4.0 mm or greater as measured by ultrasonography [24] and; (iv) pain on palpation of the medial calcaneal tubercle or the proximal plantar fascia. The exclusion criteria were: (i) below 18 years of age; (ii) history of inflammatory systemic diseases [23]; (iii) prior heel surgery; (iv) pregnancy; (v) pain medication 24 h prior to examination; (vi) corticosteroid injection for plantar fasciopathy within the previous 6 months and; (vii) other musculoskeletal injuries for which treatment was sought within the previous 6 months. Controls were selected on the same criteria with the exception that they were not to have any history of heel pain or other lower limb pain.

2.4 Outcomes

The study outcomes included: (i) PPT measured in kPa of the two groups (plantar fasciopathy and controls); (ii) CPM measured in kPa. The CPM effect was defined as the change in pressure pain threshold (PPT) from before cold water immersion of the hand to when PPT was re-tested during immersion. (iii) cold pain threshold (CPT) measured in °C; (iv) heat pain threshold (HPT) measured in °C; (v) rating of perceived pain on pain thresholds measured on an 11-point NRS and; (vi) water temperature during cold water immersion measured in °C. All pain threshold tests were measured locally at the plantar heel (most tender point in patients and antero-medially in controls) and at a distant site of the lateral elbow.

2.5 Pressure pain thresholds

Pressure pain thresholds were assessed using a hand-held algometer (Somedic, Hörby, Sweden) with a 1 cm² probe. PPT testing at the plantar surface of the heel in patients with PF has been found to have a good intra-rater reliability (ICC = 0.75–0.92) [15]. The probe was placed perpendicular to the skin and pressure was applied at a rate of 30 kPa/s. The participants were instructed to push the button of a hand-held switch when they first felt the sensation of pressure change to a sensation of pain and the test was terminated. A maximum pressure of 1,200 kPa was applied. If any participant reached this level of pressure the assessor would terminate the test. Due to a possible ceiling effect of the pressure pain threshold at the plantar aspect of the heel in the control group, as found during preliminary testing, the soleus muscle was chosen as an additional test site in this group.

2.6 Conditioned pain modulation

Investigating CPM is used to explore the efficacy of the endogenous pain inhibition [25]. The test stimulus was PPT and the conditioning stimulus was immersion of the hand into cold water. After the PPT measurement under the heel was assessed as described above, the contralateral hand to the test side was immersed in circulating cold water with a starting temperature of 12–14 °C [6, 18, 26]. After 30 s of immersion, the participant was asked to rate the perceived pain in the hand on an 11-point NRS (ranging from 0 which was no pain to 10 which was the worst pain imaginable). The water temperature was either increased or decreased by adding warm water or ice until

the participant rated their hand pain within a range of 4–6 out of 10 and then the PPT testing was performed at the plantar surface of the heel. The participant was instructed to rate the hand pain again if they felt it had changed and the temperature would be adjusted to keep them within the range of 4–6 out of 10 throughout the immersion of the hand in the cold water. After the PPT test, the hand was removed from the water. As soon as possible (no later than 30 s after removal of the hand out of the cold water), an additional PPT measurement was performed. In the control group, PPTs of the soleus were tested immediately after the hand was removed from the water and before the PPTs under the heel were re-tested. In cases where control participants did not experience pain before a pressure under the heel of 1,200 kPa was reached, the before and after immersion PPT measurements of the soleus would be used to measure CPM. The PPTs were assessed over the soleus muscle at 40% of the length from the medial malleolus to the medial knee joint line.

2.7 Thermal pain thresholds

The cold pain thresholds were measured using the ThermoTest system (Somedic, Farsta, Sweden) [7]. The thermode was placed on the skin at the test sites and from a temperature of 32 °C the temperature of the thermode decreased at a rate of 1 °C/s. The participant was instructed to push the button of a hand-held switch when they first experienced the onset of pain and the test was terminated. If the participant did not experience pain the test was terminated when the minimum cut-off temperature of 5 °C was reached. The heat pain thresholds were investigated using the same ThermoTest system as with CPT and used the same starting temperature of 32 °C. The temperature of the thermode increased until participants first experienced pain or when the maximum cut-off temperature of 50 °C was reached.

2.8 Pain area and distribution

To assess the area and distribution of pain, plantar fasciopathy participants completed pain drawings on a detailed body chart of the foot soles as well as the whole body front and back views on a personal computer tablet (Samsung Galaxy note 10.1, 2014 Edition) using the Navigate Pain app (Aalborg University, Denmark) [27, 28]. All pain drawings of the feet were visually assessed by an experienced assessor (SAB) for the presence of symmetrical pain. Symmetrical pain drawings are defined as mirrored images of

the left and right foot and to a high extent cover the same anatomical areas. The total area drawn, expressed as the total number of pixels, were automatically extracted. A visual assessment of each pain drawing was performed to determine the locations of pain and recorded as local versus widespread (i.e. pain spreading beyond the plantar heel region) as well as unilateral versus bilateral pain. Further, the total number of independent non-contiguous pain sites was also recorded. All drawings were exported offline to create an overlay image detailing plantar fasciopathy pain distribution on the foot soles.

2.9 Procedure

After eligibility had been confirmed the plantar fasciopathy group completed the Foot Function Index questionnaire (FFI) to assess the severity of the condition. The FFI is a self-report questionnaire, ranging from 0 (no pain, disability or activity limitation) to 100 (worst pain and disability), that assesses multiple dimensions of foot function [29].

For participants who presented with bilateral plantar fasciopathy, the self-reported most affected side was the test side and for the controls the test side was randomised by the flip of a coin. By way of palpation the most tender spot at the plantar heel was used for the test site while the antero-medial aspect of the plantar heel was used as the test site for controls. The ipsilateral elbow was used as the remote test site in both groups. When testing was performed on the elbow (measured first), the participant lay supine on the examination table and then lay prone when testing was performed at the plantar heel (measured second). All tests were repeated three times with 30 s of rest in between and mean values were used for all analyses. After each test, the participants were asked to rate the level of perceived pain at its first onset on an 11-point NRS [30].

2.10 Sample size

As this was a pilot study, no formal sample size calculation was performed [31, 32]. We aimed to include 20 participants in each group.

2.11 Statistical methods

Data normality was assessed using Q-Q plots. Descriptive statistics were reported using mean and standard

deviation (SD) or median and interquartile range (IQR), frequency counts (%) and effect sizes (d). Interpretation of effect sizes ranged from *very small* ($d=0.01$) to *huge* ($d=2.0$) [30]. Due to the nature of a pilot study, no hypothesis testing was performed [32]. Between-group differences were reported as mean differences (95% confidence intervals (CI)) and were adjusted for sex to account for potential sex influences [17].

A *post-hoc* evaluation of differences in total pain area between heel pain participants who had local versus widespread pain was analysed with Mann-Whitney U -tests (with 95% confidence limit). Associations between pain area and mean pain during the past week and symptom duration were investigated using Spearman's rank correlation coefficient and associations between mean pain during the past week and PPT under the heel and CPM effect were explored using Pearson's correlation coefficient. STATA ver. 14 was used for all analyses.

3 Results

The time-frame of the study limited recruitment and an eligible sample of 16 in the PF group and 11 in the control group was achieved at the end of recruitment. Of the 366 individuals who completed the online questionnaire advertised on Facebook, 106 were eligible for telephone screening. Of these, 33 individuals were eligible for clinical examination. One was ineligible due to a plantar fascia thickness <4 mm as determined by ultrasonography, and 16 did not attend their appointment. This resulted in 16 individuals with PF being included (see flow chart in supplementary material). Twelve potential participants of the control group either responded to an online questionnaire or contacted the assessor directly. One had musculoskeletal pain and was excluded on that basis which resulted in the inclusion of 11 pain-free participants in the control group. Clinical and demographic characteristics were similar in the groups in terms of age, height and weekly sports participation ($p > 0.05$), but BMI was higher in the PF group compared with the control group (mean difference: 6.6 kg/m^2 , 95% CI: 2.7–10.5, $p = 0.002$) and the proportion of females was higher in the PF group (12/16 vs. 6/11) (Table 1). Two participants had taken days off work (1 and 5 days) due to their heel pain. One participant in the control group reached 1,200 kPa during all PPT tests under the heel. For this participant the PPT measures of the soleus were used in the analysis of CPM effect as they were repeated from pre to post cold water immersion.

Table 1: participant characteristics (mean (SD) or count).

	PF group (n = 16)	Control group (n = 11)
Sex, females (%)	12 (75%)	6 (56%)
Age (years)	47.0 (9.4)	45.7 (12.8)
Height (cm)	169.9 (10.1)	172.0 (6.4)
Mass (kg)	84.6 (18.3)	67.5 (9.9)
BMI (kg/m ²)	29.3 (6.0)	22.7 (2.5)
Weekly sports participation (minutes)	247.5 (183.8)	283.2 (225.3)
Symptom duration ^a (months)	8.5 (6–14.5)	N/A
Pain during past week (0–10 NRS)	4.6 (1.4)	N/A
FFI (/100)	74.8 (29.5)	N/A
Sought treatment (%)	13 (81%)	N/A
Bilateral pf (%)	7 (44%)	N/A

pf = plantar fasciopathy; BMI = body mass index; FFI = foot function index; NRS = numerical rating scale.

^amedian (inter-quartile range).

Table 2: Results of quantitative sensory testing.

	PF group (n = 16)	Control group (n = 11)	Mean difference adjusted for sex (95% CI)	Effect size (<i>d</i>)
Heel				
CPM effect (kPa)	93.0 (121.7)	103.6 (114.8)	-21.5 (-119.6 to 76.7)	0.1
PPT before immersion (kPa)	380.0 (225.9)	810.9 (246.6)	-406.6 (-598.6 to -214.6) ^a	1.8
Pain rating (NRS)	3.7 (1.7)	1.1 (0.5)	2.6 (1.5–3.6) ^a	2.1
CPT (°C)	9.0 (3.6)	8.5 (5.0)	0.7 (-2.9 to 4.2)	0.1
Pain rating (NRS)	1.9 (2.0)	0.5 (0.8)	1.3 (-0.1 to 2.6)	0.9
HPT (°C)	49.3 (2.0)	49.6 (0.6)	-0.2 (-1.5 to 1.1)	0.2
Pain rating (NRS)	1.4 (2.2)	0.9 (1.3)	0.3 (-1.3 to 1.9)	0.3
Pain rating of PPT during immersion (NRS)	4.0 (1.5)	1.3 (0.8)	2.7 (1.6–3.8) ^a	2.3
PPT after immersion (NRS)	428.9 (185.5)	827.3 (243.6)	-379.3 (-553.2 to -205.4)	1.8
Pain rating of PPT after immersion (NRS)	4.1 (1.8)	1.4 (0.9)	2.6 (1.4–3.8) ^a	1.9
Elbow				
PPT (kPa)	376.4 (203.8)	508.4 (200.5)	-109.3 (-274.3 to 55.7)	0.7
Pain rating (NRS)	3.1 (1.7)	1.6 (0.8)	1.5 (0.3–2.7) ^a	1.1
CPT (°C)	8.0 (5.1)	6.0 (2.7)	2.2 (-1.4 to 5.8)	0.5
Pain rating (NRS)	0.9 (1.3)	0.2 (0.4)	0.6 (-0.3 to 1.5)	0.7
HPT (°C)	46.0 (2.4)	47.3 (2.4)	-0.9 (-2.8 to 1.0)	0.5
Pain rating (NRS)	4.3 (2.3)	1.7 (0.8)	2.6 (1.0–4.1) ^a	1.5

Data presented as mean (SD).

Mean differences adjusted for sex.

CPM = conditioned pain modulation; PPT = pressure pain threshold; CPT = cold pain threshold; HPT = heat pain threshold; NRS = numerical rating scale.

^aStatistical significance.

3.1 Outcomes

The PF group demonstrated lower PPTs at the plantar heel with a very large effect size ($d=1.8$) and on the elbow with a medium effect size ($d=0.7$) (Table 2, Figs. 1 and 2). There was no between-group difference for CPM (mean difference = -21.5 kPa, 95% CI: -119.6 to 76.7) (Table 2, Fig. 1). The median relative change in PPT under the heel during immersion expressed as percentage of pre-immersion PPT

was 20% in the PF group and 16% in the control group. Small mean differences were seen for the thermal thresholds with effect sizes ranging from very small to medium (CPT $d=0.1$ to $d=0.5$; HPT $d=0.2$ to $d=0.5$). Not all participants experienced an onset of pain within the pre-determined temperature limits (i.e. 5–50 °C). In the PF group, nine participants did not reach the CPT on the elbow and five did not reach it under the heel, and one did not reach the HPT on the elbow and twelve did not reach the HPT

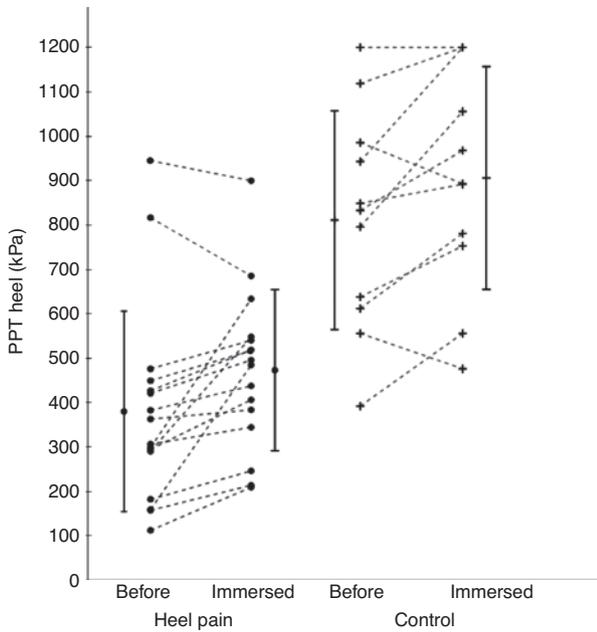


Fig. 1: Individual participant data of pressure pain thresholds under the heel before and during immersion of the hand to test the conditioned pain modulation. Means and standard deviations are shown as dots with error bars.

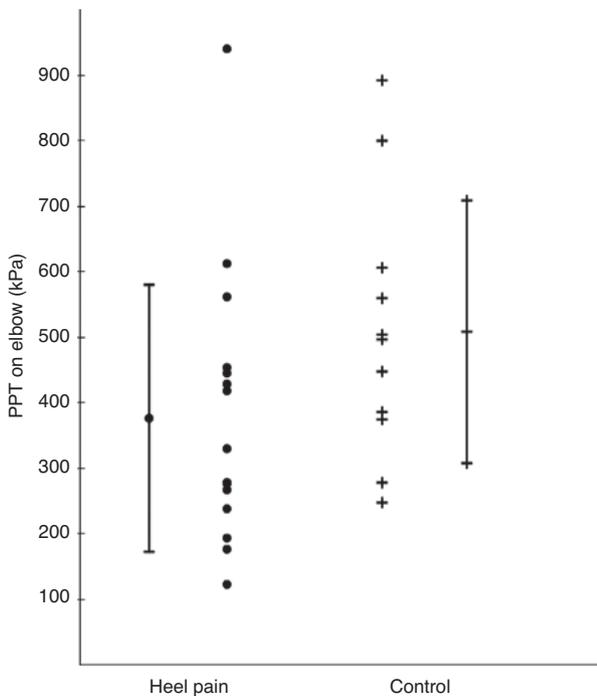


Fig. 2: Individual participant data of pressure pain thresholds on the lateral elbow. Means and standard deviations are shown as dots with error bars.

under the heel. In the control group, eight participants did not reach the CPT on the elbow and six did not reach it under the heel, and all reached the HPT on the elbow but

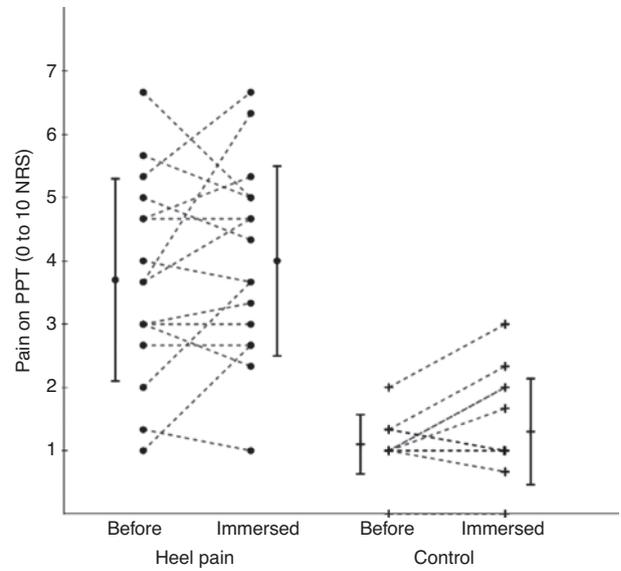


Fig. 3: Individual participant data of perceived pain under the heel on pain onset during pressure pain thresholds under the heel before and during immersion of the hand. Means and standard deviations are shown as dots with error bars.

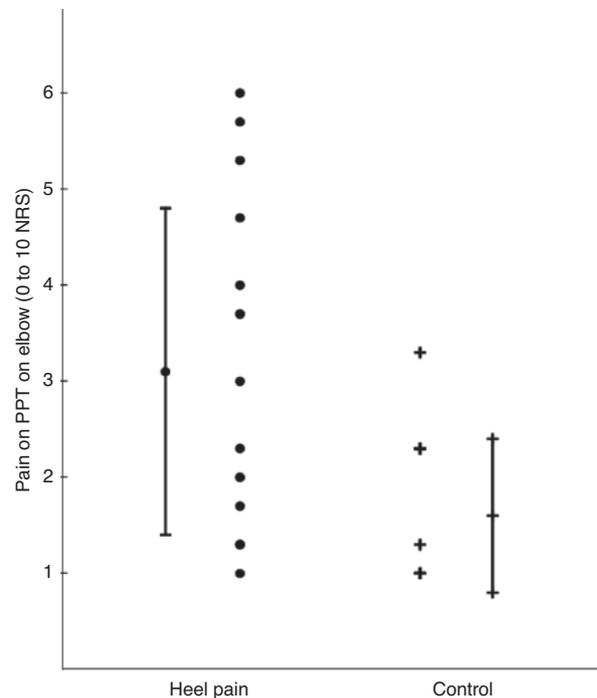


Fig. 4: Individual participant data of pain ratings on pain onset during pressure pain thresholds on the lateral elbow. Means and standard deviations are shown as dots with error bars.

five did not reach the HPT under the heel. Perceived pain on pain onset was higher for the PF group compared to the control group during all PPT measurements and effect sizes ranged from large to huge (Figs. 3 and 4). Differences

in perceived pain on thermal pain thresholds were observed, however, the effect sizes ranged from small to very large (Table 2). The water temperature at the time of PPT testing during cold water immersion was on average $14.3 (\pm 3.0) ^\circ\text{C}$ in the PF group and $12.1 (\pm 2.9) ^\circ\text{C}$ in the control group (mean difference: $2.2 ^\circ\text{C}$, 95% CI: -0.3 to 4.7 , $d=0.8$). We found no association between pain during the past week and PPT under the heel ($r = -0.327$, $p = 0.216$) or CPM ($r = 0.208$, $p = 0.438$).

3.2 Pain drawings

A superimposed overlay of the original pain drawings from the test side drawings is presented in Fig. 5. Six out of seven individuals with bilateral pain presented with a symmetrical plantar pain distribution. Half of the individuals showed widespread pain which extended beyond the plantar heel. In total, three out of nine with unilateral pain and five out of seven of those with bilateral plantar fasciopathy reported pain on the anterior and/or posterior lower limb body charts (Fig. 6).

The total area of plantar heel pain, but not pain sites, was greater for individuals presenting with widespread pain (mean rank=11.88) as compared to those with

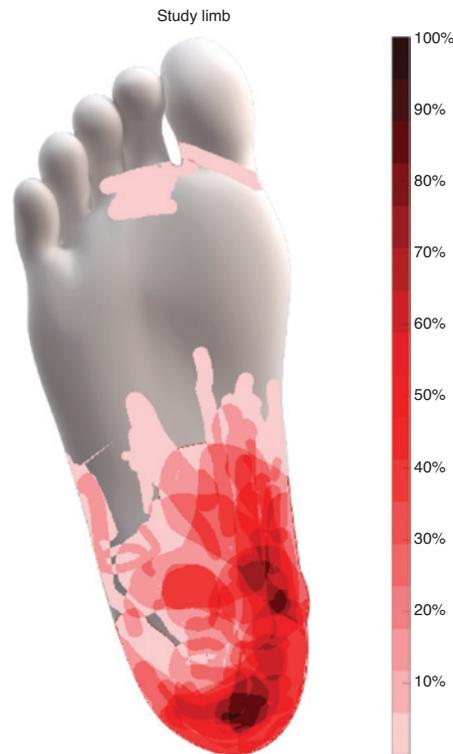


Fig. 5: An overlay made by superimposing the 16 original pain drawings from individuals with PF. The darker areas indicate a higher degree of overlap between drawings and the common pain locations.

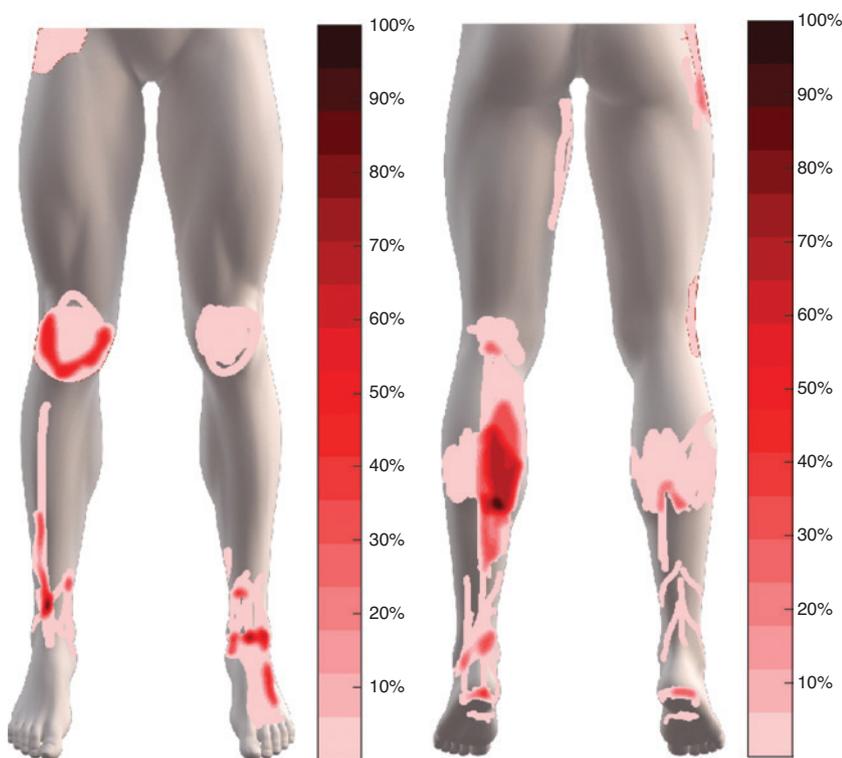


Fig. 6: An overlay made by superimposing the 8 original pain drawings from individuals with PF who drew pain on the lower limb body charts. The darker areas indicate a higher degree of overlap between drawings and the common pain locations.

localised heel pain ((mean rank = 5.15) $U = 59.00$, $z = 2.836$, $p = 0.005$). The total area of plantar heel pain was not related to the mean pain or the duration of reported pain ($p = 0.351$).

3.3 Adverse events

No adverse events were observed.

4 Discussion

4.1 Key results

This was the first study to investigate the presence of altered pain processing using thermal pain thresholds and a CPM paradigm in individuals with plantar fasciopathy. Despite the study being a pilot with small numbers, the findings indicate that it is unlikely that endogenous inhibitory pain modulation as tested with our CPM protocol is different in individuals with plantar fasciopathy when compared to pain-free controls. Individuals with plantar fasciopathy demonstrated localised mechanical hyperalgesia at the plantar heel and rated pain higher at local and remote test sites compared with the controls. Altogether, these findings warrant further research in pain processing in plantar fasciopathy to confirm differences between individuals with plantar fasciopathy and pain-free controls.

4.2 Interpretation

Two recent studies of pressure pain hypersensitivity found widespread pain in individuals with unilateral PF compared with healthy individuals [13, 14]. However, individuals with plantar fasciopathy reported higher pain ratings than those of the present study (5.7 and 6.3 NRS vs. 4.6 NRS, respectively). In one of the studies [13], individuals with plantar fasciopathy reported considerably longer symptom durations to that of the present study (18.4 vs. 8.5 months, respectively). Indeed, higher pain ratings and longer symptom duration may reflect greater condition severity. Thus, it is a possibility that condition severity of the individuals with plantar fasciopathy in the present study were less and this may have contributed to the lack of a clear indication of widespread mechanical hypersensitivity. The control group did show slightly higher pressure pain thresholds (PPTs) on the elbow than the PF group ($d = 0.7$)

but also seemingly higher than those of pain-free controls in other similar studies [33–35]. Therefore, any potential difference between individuals with plantar fasciopathy and pain-free controls at the remote site in the present study could be the result of unusually high PPTs among controls rather than low PPTs in the PF group. A lack of a between-group difference is in line with findings by Plinsinga et al. [33] where no remote pressure pain hyperalgesia was found in Achilles or patellar tendinopathy. Together with the results of the present study, there is now conflicting evidence regarding altered pain processing in both Achilles tendinopathy and plantar fasciopathy [33]. Future larger-scale studies should include additional quantitative sensory tests to either confirm or dismiss the role of altered pain processing in persistent plantar fasciopathy.

If reduced endogenous inhibition was present, it could be assumed that the PF group would have had lower CPM, defined as a smaller increase in PPT during the cold water immersion, than the controls as seen in Achilles tendinopathy by Tompra et al. [6], still, it appears unlikely that there is a difference between individuals with PF and controls ($d = 0.1$). Based on our findings and using a two-sided 5% significance level and a power of 80%, a sample size of 3,914 participants would be required to find a significant difference. This implies that when using our CPM procedure, it is highly unlikely that further research into CPM of plantar fasciopathy is warranted.

We found lower PPTs under the heel in the PF group compared with the control group which is contrary to the findings of Saban et al. [15]. In the present study, PPT was assessed over the most tender location in contrast to the study by Saban et al. where PPTs were assessed over multiple standardised sections of the heel. It can be argued that using the most sensitive area for PPT assessments would give the most precise reflection of pain sensitivity rather than standardised sections of the plantar heel should the measure be adopted in the clinic.

Pain ratings on all pain thresholds were higher among individuals with plantar fasciopathy which indicates that their perception of pain is more intense than that of pain-free individuals. Similar findings have been seen in carpal tunnel syndrome where no altered pain processing was found when patients were compared to matched controls but ratings of pain were higher at remote sites [35]. There might be other factors that contribute to these higher pain ratings, for example, kinesiophobia, anxiety, and pain catastrophizing that can influence pain perception and have been found to be higher in individuals with plantar fasciopathy compared with healthy controls [36]. We did not record these pain related measures and recommend future research to include them.

Patients with plantar fasciopathy indicated the area and location of their pain covered a much larger area than clinical dogma and text-book presentations. The text-book presentation is on the antero-medial aspect of the calcaneus, whereas in our study pain extended to cover the entire plantar heel region and half of the proximal arch of the foot [37]. This fits with the idea that the association between the perception of pain and tissue integrity is less clear [38]. Another possibility might be that the plantar fascia is not the only structure contributing to the pain experience.

Six out of seven individuals with bilateral pain had symmetrical pain patterns, that is pain was expressed in the same locations of both feet. Similar findings have been seen in other chronic pain conditions such as patellofemoral pain and rheumatoid arthritis [20, 39]. It is unclear whether the severity of a chronic condition is associated with symmetrical or asymmetrical patterns [39], however, bilateral pain is also associated with poorer prognosis and longer symptom duration compared with unilateral pain which should be considered in clinical practice [19, 40].

4.3 Limitations

This study is not without limitations. First, despite advertisement on social media and handing out flyers, we were not able to recruit the planned sample size within the time frame of the study. Further, 16/33 patients with plantar fasciopathy cancelled their appointment which should be accounted for in a future larger scale study. Second, the thermosystem did not allow for temperatures lower than 5 °C or higher than 50 °C and several participants of both groups did not reach their CPT or HPT within these temperatures. Third, the assessor was not blinded to group allocation, largely due to resource implications and PPT being applied to the most tender spot at the plantar heel in the PF group. Fourth, as we used a target pain rating rather than a target water temperature, the immersion times were not the same between participants which could potentially have influenced the stimulus received, however, this applied to both groups and is not likely to have affected the between-group comparisons.

4.4 Generalisability

The participants of the PF group are comparable to those of previous studies in terms of age and had a higher BMI compared with the controls. A high BMI has been found to be associated with plantar fasciopathy [41].

4.5 Conclusions

Although the recent findings of widespread hyperalgesia in plantar fasciopathy support altered pain processing as a feature, we were unable to substantiate this in our study. We did not find that individuals with plantar fasciopathy had reduced endogenous inhibition compared to healthy controls and could not draw firm conclusions of lower remote pain thresholds. We did observe higher perceived pain on pain threshold and a pain area that extended beyond the antero-medial aspect of the plantar heel, which in conjunction with recent findings of widespread hyperalgesia provide rationale for exploring altered pain processing in a larger-scale study.

Acknowledgements: We would like to acknowledge Gearoid Cleary for his role in the execution of the study.

Authors' statements

Research funding: The study was internally funded by the Center for General Practice at Aalborg University.

Conflict of interest: Authors state no conflict of interest.

Informed consent: Informed consent has been obtained from all individuals included in this study.

Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies and was performed in accordance with the tenets of the Helsinki Declaration, and has been approved by the Medical Research Ethics Committee of the University of Queensland.

References

- [1] Taunton JE, Ryan MB, Clement DB, McKenzie DC, Lloyd-Smith DR, Zumbo BD. A retrospective case-control analysis of 2002 running injuries. *Br J Sports Med* 2002;36:95–101.
- [2] Albers IS, Zwerver J, Diercks RL, Dekker JH, Van den Akker-Scheek I. Incidence and prevalence of lower extremity tendinopathy in a Dutch general practice population: a cross sectional study. *BMC Musculoskelet Disord* 2016;17:16.
- [3] Riel H, Cotchett M, Delahunt E, Rathleff MS, Vicenzino B, Weir A, Landorf KB. Is 'plantar heel pain' a more appropriate term than 'plantar fasciitis'? Time to move on. *Br J Sport Med* 2017;51:1576–7.
- [4] Landorf KB. Plantar heel pain and plantar fasciitis. *BMJ Clin Evid* 2015.
- [5] Goff JD, Crawford R. Diagnosis and treatment of plantar fasciitis. *Am Fam Physician* 2011;84:676–82.
- [6] Tompra N, van Dieën JH, Coppieters MW. Central pain processing is altered in people with Achilles tendinopathy. *Br J Sports Med* 2016;50:1004–7.
- [7] Coombes BK, Bisset L, Vicenzino B. Cold hyperalgesia associated with poorer prognosis in lateral epicondylalgia. *Clin J Pain* 2015;31:30–5.

- [8] Heales LJ, Lim ECW, Hodges PW, Vicenzino B, Vicenzino B. Sensory and motor deficits exist on the non-injured side of patients with unilateral tendon pain and disability—implications for central nervous system involvement: a systematic review with meta-analysis. *Br J Sports Med* 2014;48:1400–6.
- [9] Skou ST, Graven-Nielsen T, Rasmussen S, Simonsen OH, Laursen MB, Arendt-Nielsen L. Widespread sensitization in patients with chronic pain after revision total knee arthroplasty. *Pain* 2013;154:1588–94.
- [10] Vaegter HB, Handberg G, Graven-Nielsen T. Similarities between exercise-induced hypoalgesia and conditioned pain modulation in humans. *Pain* 2014;155:158–67.
- [11] Lannersten L, Kosek E, Kosek E. Dysfunction of endogenous pain inhibition during exercise with painful muscles in patients with shoulder myalgia and fibromyalgia. *Pain* 2010;151:77–86.
- [12] Plinsinga ML, Brink MS, Vicenzino B, Van Wilgen CP. Evidence of nervous system sensitization in commonly presenting and persistent painful tendinopathies: a systematic review. *J Orthop Sports Phys Ther* 2015;45:864–75.
- [13] Plaza-Manzano G, Ríos-León M, Martín-Casas P, Arendt-Nielsen L, Fernández-de-las-Peñas C, Ortega-Santiago R. Widespread pressure pain hypersensitivity in musculoskeletal and nerve trunk areas as sign of altered nociceptive processing in unilateral plantar heel pain. *J Pain* 2019;20:60–67.
- [14] Fernández-Lao C, Galiano-Castillo N, Cantarero-Villanueva I, Martín-Martín L, Prados-Olleta N, Arroyo-Morales M. Analysis of pressure pain hypersensitivity, ultrasound image, and quality of life in patients with chronic plantar pain: A preliminary study. *Pain Med (United States)* 2016;17:1530–41.
- [15] Saban B, Masharawi Y. Pain threshold tests in patients with heel pain syndrome. *Foot Ankle Int* 2016;37:730–6.
- [16] Backonja MM, Attal N, Baron R, Bouhassira D, Drangholt M, Dyck PJ, Edwards RR, Freeman R, Gracely R, Haanpaa MH, Hansson P, Hatem SM, Krumova EK, Jensen TS, Maier C, Mick G, Rice AS, Rolke R, Treede R-D, Serra J, et al. Value of quantitative sensory testing in neurological and pain disorders: NeuPSIG consensus. *Pain* 2013;154:1807–19.
- [17] Rolke R, Baron R, Maier C, Tölle TR, Treede R-D, Beyer A, Binder A, Birbaumer N, Birklein F, Bötefür IC, Braune S, Flor H, Häge V, Klug R, Landwehrmeyer GB, Magerl W, Maihöfner C, Rolko C, Schaub C, Scherens A, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. *Pain* 2006;123:231–43.
- [18] Vaegter HB, Handberg G, Graven-Nielsen T. Hypoalgesia after exercise and the cold pressor test is reduced in chronic musculoskeletal pain patients with high pain sensitivity. *Clin J Pain* 2016;32:58–69.
- [19] Boudreau SA, Royo AC, Matthews M, Graven-Nielsen T, Kama-vuako EN, Slabaugh G, Thorborg K, Vicenzino B, Rathleff MS. Distinct patterns of variation in the distribution of knee pain. *Sci Rep* 2018;8:16522.
- [20] Boudreau SA, Kamavuako EN, Rathleff MS. Distribution and symmetrical patellofemoral pain patterns as revealed by high-resolution 3D body mapping: a cross-sectional study. *BMC Musculoskelet Disord* 2017;18:160.
- [21] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453–7.
- [22] World Medical Association Declaration of Helsinki. *JAMA* 2013;310:2191.
- [23] McMillan AM, Landorf KB, Gilheany MF, Bird AR, Morrow AD, Menz HB. Ultrasound guided corticosteroid injection for plantar fasciitis: randomised controlled trial. *BMJ* 2012;344:e3260.
- [24] Skovdal Rathleff M, Moelgaard C, Lykkegaard Olesen J. Intra- and interobserver reliability of quantitative ultrasound measurement of the plantar fascia. *J Clin Ultrasound* 2011;39:128–34.
- [25] Pud D, Granovsky Y, Yarnitsky D. The methodology of experimentally induced diffuse noxious inhibitory control (DNIC)-like effect in humans. *Pain* 2009;144:16–9.
- [26] Soon B, Vicenzino B, Schmid AB, Coppieters MW. Facilitatory and inhibitory pain mechanisms are altered in patients with carpal tunnel syndrome. *PLoS One* 2017;12:e0183252.
- [27] Boudreau SA, Badsberg S, Christensen SW, Egsgaard LL. Digital pain drawings: Assessing touch-screen technology and 3D body schemas. *Clin J Pain* 2016;32:139–45.
- [28] Boudreau SA, Spence R, Vasov G, Egsgaard LL. Feature extraction APP for pain profiles. *Biosyst Biorobotics* 2014;7:853–4.
- [29] Budiman-Mak E, Conrad KJ, Roach KE. The foot function index: a measure of foot pain and disability. *J Clin Epidemiol* 1991;44:561–70.
- [30] Kelly KG, Cook T, Backonja M-M. Pain ratings at the thresholds are necessary for interpretation of quantitative sensory testing. *Muscle Nerve* 2005;32:179–84.
- [31] Billingham SAM, Whitehead AL, Julious SA. An audit of sample sizes for pilot and feasibility trials being undertaken in the United Kingdom registered in the United Kingdom Clinical Research Network database. *BMC Med Res Methodol* 2013;13:104.
- [32] Eldridge SM, Chan CL, Campbell MJ, Bond CM, Hopewell S, Thabane L, Lancaster G. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016;355:i5239.
- [33] Plinsinga ML, van Wilgen CP, Brink MS, Vuvan V, Stephenson A, Heales LJ, Mellor R, Coombes BK, Vicenzino B. Patellar and Achilles tendinopathies are predominantly peripheral pain states: a blinded case control study of somatosensory and psychological profiles. *Br J Sports Med* 2018;52:284–91.
- [34] Bisset L, Carty M, Smith A. Unilateral lateral epicondylalgia demonstrates a pro-nociceptive pain profile: a case control observational study. *Clin J Pain* 2018;34:954–59.
- [35] Schmid AB, Soon BT, Wasner G, Coppieters MW. Can widespread hypersensitivity in carpal tunnel syndrome be substantiated if neck and arm pain are absent? *Eur J Pain* 2012;16:217–28.
- [36] Cotchett M, Lennecke A, Medica VG, Whittaker GA, Bonanno DR. The association between pain catastrophising and kinesiophobia with pain and function in people with plantar heel pain. *Foot* 2017;32:8–14.
- [37] Martin RL, Davenport TE, Reischl SF, McPoil TG, Matheson JW, Wukich DK, McDonough CM. Heel Pain – Plantar Fasciitis: Revision 2014. *J Orthop Sport Phys Ther* 2014;44:A1–33.

- [38] Moseley GL. Reconceptualising pain according to modern pain science. *Phys Ther Rev* 2007;12:169–78.
- [39] Zangger P, Keystone EC, Bogoch ER. Asymmetry of small joint involvement in rheumatoid arthritis: prevalence and tendency towards symmetry over time. *Joint Bone Spine* 2005;72:241–7.
- [40] Hansen L, Krogh TP, Ellingsen T, Bolvig L, Fredberg U. Long-term prognosis of plantar fasciitis: A 5- to 15-year follow-up study of 174 patients with ultrasound examination. *Orthop J Sport Med* 2018;6:232596711875798.
- [41] van Leeuwen KDB, Rogers J, Winzenberg T, van Middelkoop M. Higher body mass index is associated with plantar fasciopathy/'plantar fasciitis': systematic review and meta-analysis of various clinical and imaging risk factors. *Br J Sports Med* 2016;50:972–81.

Supplementary Material: The online version of this article offers supplementary material (<https://doi.org/10.1515/sjpain-2019-0109>).