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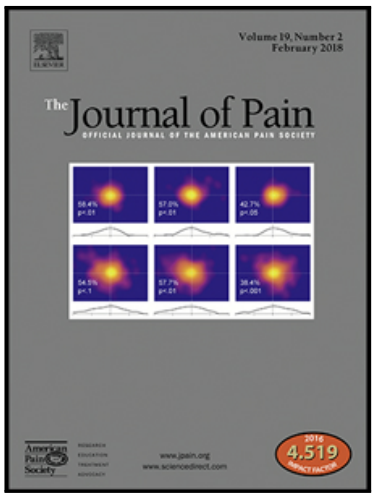

Widespread Pressure Pain Hypersensitivity in Musculoskeletal and Nerve Trunk Areas as Sign of Altered Nociceptive Processing in Unilateral Plantar Heel Pain

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Highlights

- Patients with plantar heel pain exhibit widespread pressure hypersensitivity
- Pressure hypersensitivity was present in musculoskeletal points and nerve trunks
- Nerve trunk sensitivity was associated with pain intensity and related-disability.

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Widespread Pressure Pain Hypersensitivity in Musculoskeletal and Nerve Trunk Areas as Sign of Altered Nociceptive Processing in Unilateral Plantar Heel Pain

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Short title: Pressure pain sensitivity in plantar heel pain

Abstract

Our aim was to investigate the differences in pressure sensitivity over musculoskeletal and nerve symptomatic and distant areas between individuals with plantar heel pain and healthy subjects, and to determine the relationship between sensitivity to pressure pain, foot pain, and fascia thickness. Thirty-five patients with unilateral chronic plantar heel pain and 35 matched healthy controls participated. Pressure pain thresholds (PPTs) were bilaterally assessed over several nerve trunks (median, radial, ulnar, common peroneal, tibial and sural nerve trunks) and musculoskeletal structures (calcaneus, medial gastrocnemius, tibialis anterior, second metacarpal) by an assessor blinded to the subject's condition. Pain was assessed with a numerical pain rate scale (NPRS, 0-10), impact of foot pain was assessed with the Foot Function Index (FFI), and plantar fascia thickness was measured via ultrasound imaging. The ANCOVA revealed lower widespread and bilateral PPTs over both nerve trunks and musculoskeletal structures in individuals with plantar heel pain ($P<0.001$). Female showed lower PPT than men in almost all points ($P<0.001$). PPT over peripheral nerve trunks of the lower extremity were significantly associated with the intensity of pain at first step on the morning and with foot function disability scale of the FFI ($P<0.05$). This study found widespread pressure pain hypersensitivity over both nerve trunks and musculoskeletal structures in individuals with unilateral chronic plantar heel pain, suggesting the presence of a central altered central nociceptive pain processing. Pressure hypersensitivity over nerve trunks on the lower extremity was associated with higher pain intensity and related-disability.

Key words: Plantar heel pain, pressure pain, sensitization.

Perspective

This study found widespread pressure hypersensitivity over both nerve trunks and musculoskeletal structures in individuals with unilateral chronic plantar heel pain, as manifestation of a central altered central nociceptive pain processing

Widespread Pressure Pain Hypersensitivity in Musculoskeletal and Nerve Trunk Areas as Sign of Altered Nociceptive Processing in Unilateral Plantar Heel Pain

Introduction

Plantar heel pain is a foot condition commonly treated by healthcare providers[16]. Subjects with this condition report insidious sharp pain under the plantar surface of the heel, usually spreading from the medial border of the plantar fascia to its insertion at the medial tuberosity of the calcaneus[1]. The pain increases in the morning with the first step after getting out of bed, after prolonged periods of inactivity and/or at the beginning of a workout[3]. Due to the presence of degenerative changes and the absence of inflammation in the plantar fascia[14], it has been proposed that the proper term for this pain condition is plantar fasciopathy[22] or plantar heel pain[15]. Its prevalence ranges from 4% to 7% in the general population[7,11] and from 8% to 15% in athletic people[25].

The aetiology of plantar heel pain is commonly associated to an increased plantar fascia thickness[15]; however, it is possible that these patients also exhibit an altered pain processing[21]. Two studies have investigated nociceptive processing in this population by assessing sensitivity to pressure pain; although the results have been controversial[23,24]. Rose et al observed that individuals with plantar heel pain exhibited higher sensitivity to pressure pain over the medial

calcaneal and over the medial plantar nerves,[23] whereas Saban and Masharawi did not find such differences in pressure pain thresholds over the calcaneus between patients and controls[24]. Both studies investigated mechanical pain sensitivity over the symptomatic area[24] or innervated-segments[23], mainly reflecting the presence of peripheral, but not central, pain hyperalgesia. To determine the presence of central hyperalgesia, it is needed the assessment of widespread pressure hyperalgesia. The only study investigating an altered central pain processing in this condition found that individuals with plantar heel pain showed widespread pressure pain hyperalgesia in some distant pain-free areas compared to healthy people[9]. However, this study did not include assessment of sensitivity to pressure pain over nerve trunk structures and did not include body mass index as a covariate[9]. To further determine the presence of altered central pain processing in patients with plantar heel pain, more studies assessing both local and distant sensitivity to pressure pain including musculoskeletal and nerve trunk areas are needed. Therefore, the aims of this study were: 1, to investigate the differences in sensitivity to pressure pain over symptomatic and distant pain-free musculoskeletal structures and nerve trunk areas between individuals with unilateral chronic plantar heel pain and healthy controls; and 2, to determine the relationship pressure sensitivity over nerve trunks and musculoskeletal structures, foot pain, and fascia thickness in patients with unilateral chronic plantar heel pain.

Methods

Participants

Consecutive individuals presenting to a physical therapy clinic in Madrid (Spain) with a primary report of heel pain from January 2017 and February 2018 were screened for eligible inclusion criteria. For patients to be eligible, they had to meet the following: 1, clinical

diagnosis of plantar heel pain following the clinical practice guidelines from the Orthopaedic Section of the American Physical Therapy Association, i.e., insidious onset of sharp pain on the plantar heel surface upon weight bearing after a period of non-weight bearing, heel pain increasing in the morning with the first step after waking up and pain with palpation of the proximal insertion of the plantar fascia[15]; 2, plantar heel pain for more than 3 months; 3, unilateral symptoms; and, 4, aged 18 years or older

Patients were excluded if any of the following criteria were present: 1, a history of surgery to the lower extremity; 2, presented with 2 or more positive neurologic signs consistent with nerve root compression; 3, other causes of heel pain, e.g., tarsal tunnel syndrome, diabetes mellitus, arthritis of the foot/ankle, rheumatoid arthritis, peripheral neuropathy, or 4, had received treatment for the heel within the previous 6 weeks.

Additionally, age- and gender-matched healthy controls with no history of lower extremity pain recruited from the general population by local announcements were also included. Exclusion criteria were the same than for the patient group. The study design was approved by local Ethics Committee ((URJC 051220160022017). All participants signed an informed consent prior to their inclusion in the study.

Pain and Function Variables

Demographic data included pain history, aggravating and relieving factors, age, gender, height and weight (body mass index, kg/cm^2). A 11-points numerical point rate scale (NPRS; 0: no pain; 10: maximum pain) was used to determine the pain at first step on the morning, the mean intensity of pain, and the worst level of pain experienced the preceding week[12]. The impact of foot pain on self-reported function was assessed with the Foot Function Index (FFI)[4]. The FFI is the most used foot-specific self-measure for the foot[5]. It consists of 23

self-reported items divided into 3 subcategories: pain (9-items), disability (9-items), and activity limitation (5-items). The patient scored each question on a scale from 0 (no pain or difficulty) to 10 (worst pain or so difficult it requires help). The FFI has been shown to be valid, reliable and sensitive to change in various populations with a variety of disorders, including plantar heel pain[13]. Subscales scores range from 0% to 100%, with higher scores indicating lower levels of function and worse foot health-related quality of life[4]. The FFI total score is derived by calculating the mean of the 3 subscale scores.

Pressure Pain Sensitivity

Pressure pain threshold (PPT), defined as the minimal amount of pressure where a sensation of pressure first changes to pain, was assessed with an electronic algometer (Somedic, Farsta, Sweden). The algometer was calibrated prior to data collection. The pressure was applied perpendicularly to each point at a rate of approximately 30kPa/s. Participants were instructed to press the "stop-button" of the algometer as soon as the pressure resulted in pain. The mean of 3 trials on each point was calculated and used for the analysis. A 30 sec resting period was allowed between trials for avoiding temporal summation[17].

Participants were asked to avoid any analgesic or muscle relaxant 24 hours prior to the examination. PPTs were bilaterally assessed over some musculoskeletal structures and nerve trunks by an experienced assessor blinded to the subjects' condition. The musculoskeletal structures included the symptomatic area (calcaneus bone: origin of the plantar fascia), two segmental-related areas (mid-point of muscle belly of the medial gastrocnemius and upper one third of muscle belly of the tibialis anterior muscle) and a distant pain-free non-related area (second metacarpal space). Xiong et al found intra-rater reliability ranging from 0.74 to 0.97 for PPT measurements in these areas[28]. Saban and Masharawi reported that the smallest real difference between patients with plantar heel pain and healthy controls for PPTs over the

calcaneus bone ranged from 98 to 161 kPa[24], whereas Walton et al found that the minimal detectable change for PPT over the tibialis anterior muscle in patients with acute neck pain was 98 kPa[27].

Peripheral nerve trunks nerves were identified by manual palpation and marked with a wax pencil as follows. For the upper extremity, the median nerve was located in the cubital fossa medial to and immediately adjacent to the tendon of biceps; the ulnar nerve was located in the groove between the medial epicondyle and the olecranon, and the radial nerve was marked where it passes through the lateral inter-muscular septum between the medial and lateral heads of triceps to enter the mid to lower third of the humerus. For the lower extremity, the common peroneal nerve was marked where it passes behind the head of the fibula as it winds forwards around its neck; the tibial nerve was marked where it bisects the popliteal fossa, lateral to the popliteal artery; and the sural nerve was marked at the posterior and lateral to the myotendinous junction of the Achilles tendon. The reliability of PPT assessment over these nerve trunks has been found to range from moderate to high[10].

Ultrasonographic Variables

An ultrasonographic (US) assessment to obtain quantitative measurements of the plantar fascia was conducted. An ultrasound device (MyLab^{TM} 25Gold, Esaote Medical Systems, Genova, Italy) and a 12 MHz linear probe were used. Participants were placed in prone, with their feet hanging over the edge of the examination table. The probe was placed over the plantar portion of the heel to get a view of the long axis of the plantar fascia[6]. The focus was individually adjusted to the depth of the fascia of each subject. The thickness of the sagittal view of the plantar fascia was bilaterally assessed into the following 2 areas: 1, at its proximal end, near its insertion into the calcaneus; and, 2, at the middle point of the fascia, 1cm from the origin (**Fig. 1**).

Sample size determination

The sample size calculation was based on detecting between-groups differences of 130 kPa on pressure pain thresholds[24], assuming a standard deviation of 150 kPa, a 2-tailed test, an alpha level (α) of 0.05 and a desired power (β) of 90%. The estimated desired sample size was calculated to be at least 29 participants per group. A percentage of 15% drop-out was expected, so 35 patients were included in each group.

Statistical Analysis

Data were analysed with the SPSS statistical package (21.0 Version). Results are expressed as mean, standard deviation (SD) or 95% confidence interval (95%CI). The Kolmogorov-Smirnov test revealed that all data showed normal distribution (P>0.05). Demographic characteristics of both groups were compared using unpaired Student t-test and χ^2 tests of independence. A 2-way analysis of covariance (ANCOVA) with side (affected/non-affected, dominant/non-dominant) as within-subject factor, group (plantar heel pain or controls) as between-subjects factor, and gender, age and BMI as covariates was used to determine differences in US assessments. A multilevel ANCOVA was also applied to detect differences in PPTs with side (affected/non-affected or dominant/non-dominant) as within-subject factor, group (plantar heel pain or controls) as the between-subject factor, and gender, age and BMI as covariates. Post-hoc comparisons were conducted with the Bonferroni test. Finally, the Pearson correlation (r) test was used to analyse the association between demographic features, PPTs, pain, and fascia thickness in the patient group. For the correlation analysis, the statistical analysis was conducted at a 95% confidence level, but for the ANCOVA, a Bonferroni-corrected alpha of 0.005 (10 points of PPT assessment) was considered significant. The standardized mean difference (SMD) was calculated by dividing the between-group difference by the pooled standard deviation to enable comparison of effect sizes. Values

were considered as trivial when range from 0.0 to 0.2, small from 0.2 to 0.49, moderate from 0.5 to 0.79, and large when greater than 0.8.

Results

Demographic and clinical data of the patients

Forty-five individuals with plantar heel pain were screened for eligible criteria. Ten (22%) individuals were excluded for the following reasons: bilateral symptoms (n=4), previous surgery (n=3), steroid injection (n=3). Finally, 35 patients (55% women, mean age: 42±10 years) and 35 sex- and age-matched healthy controls (55% women, mean age: 41±11 years) were included. **Table 1** shows clinical and demographic data of the groups. No differences in demographic variables existed between both groups, except for weight and BMI (P=0.04): individuals with plantar heel pain showed higher weight and BMI than healthy controls. Additionally, individuals with plantar heel pain showed higher impact of foot pain on self-reported function (P<0.001).

Ultrasonographic Assessment

The ANCOVA revealed significant differences between both groups and sides for the calcaneus (group: F=118.149, P<0.001; side: F=20.745, P<0.001) and fascia (group: F=56.249; P<0.001; side: F=16.018; P<0.001) points. Additionally, a significant group *

side interaction was also observed (calcaneus: F=29.286, P<0.001; fascia: F=10.723, P<0.001): patients with plantar heel pain showed an increase of fascia thickness in both points (origin and the middle point) on the affected side as compared to the non-affected side and healthy controls bilaterally (P<0.01, **table 1**). No significant effects of gender (F=1.118; P=0.294), age (F=1.170; P=0.301) or BMI (F=0.015; P=0.903) was observed.

Pressure Pain Sensitivity over Musculoskeletal Structures

The ANCOVA revealed significant differences between groups, but not between sides, for PPTs over the calcaneus bone (group: F=43.380, P<0.001; side: F=0.344, P=0.559), medial gastrocnemius (group: F=74.316, P<0.001; side: F=2.431, P=0.121), tibialis anterior muscle (group: F=110.809, P<0.001; side: F=0.002, P=0.965) or second metacarpal (group: F=60.115, P<0.001; side: F=0.195, P=0.659). No significant group * side interaction was either found for PPTs over the calcaneus bone (F=0.164, P=0.686), medial gastrocnemius (F=0.672, P=0.411), tibialis anterior (F=2.330, P=0.129), or second metacarpal (F=1.892, P=0.171): individuals with plantar heel pain exhibited bilateral lower widespread PPTs than healthy controls (P<0.001). A significant effect of gender (F=12.96; P<0.001) but not age (F=1.431; P=0.236) or BMI (F=0.337; P=0.563) was observed: women exhibited lower PPTs than men in all points (P<0.001). **Table 2** summarizes PPT over musculoskeletal structures for both sides within each group.

Pressure Pain Sensitivity over Nerve Trunk Structures in the Upper Extremity

The ANCOVA revealed significant differences between groups, but not between sides, for PPTs over the median (group: F=22.170, P<0.001; side: F=0.618, P=0.433), radial (group: F=9.840, P=0.002; side: F=1.318, P=0.253), and ulnar (group: F=19.251,

P<0.001; side: F=0.066, P=0.798) nerve trunks. No significant interaction between side and group for PPTs over the median (F=0.312, P=0.577), radial (F=0.003, P=0.959), and ulnar (F=0.970, P=0.326) nerves: subjects with plantar heel pain showed bilateral lower PPTs over the upper extremity peripheral nerve trunks than healthy controls (P<0.001). A significant effect of gender (F=4.318; P=0.004), but not age (F=1.549; P=0.218) or BMI (F=0.165; P=0.686) was observed: women exhibited lower PPTs than men in all points (P<0.001). **Table 3** summarizes PPT over upper extremity nerve trunks for both sides within each group.

Pressure Pain Sensitivity over Nerve Trunk Structures in the Lower Extremity

The ANCOVA also found significant differences between groups, but not between sides, for PPTs over the common peroneal (group: F=31.994, P<0.001; side: F=0.047, P=0.829), tibial (group: F=31.997, P<0.001; side: F=0.609, P=0.437), and sural (group: F=32.383, P<0.001; side: F=0.500, P=0.481) nerve trunks. No significant interaction between side and group for PPTs over the common peroneal (F=2.519, P=0.115), tibial (F=0.219, P=0.641) and sural (F=0.122, P=0.727) nerves: with plantar heel pain showed bilateral lower PPTs over the lower extremity peripheral nerve trunks than healthy controls (P<0.001). In this case, no significant effect of gender (F=1.630; P=0.206), age (F=1.298; P=0.259) or BMI (F=0.153; P=0.697) was found. **Table 4** summarizes PPTs over lower extremity nerve trunks for both sides within each group.

Inter-measure Comparisons of Effect Size

Large effects were observed between patients with plantar heel pain and healthy controls comparisons for PPTs over the calcaneus bone (SMD: 1.12, 95%CI 1.04-1.20), medial gastrocnemius (SMD: 1.45, 1.32-1.58), tibialis anterior muscle (SMD: 1.88, 1.64-2.12) and

second metacarpal (SMD: 1.42, 1.30-1.54). Similarly, large effects were also observed for between-groups differences in PPTs over the nerve trunks of the lower extremity: common peroneal (SMD: 1.12, 1.06-1.18), tibial (SMD: 1.01, 0.91-1.11) and sural (SMD: 1.51, 1.35-1.66) nerves. In addition, moderate between-groups differences were also observed for PPTs over nerve trunks of the upper extremity: median (SMD: 0.71, 0.65-0.77), radial (SMD: 0.62, 0.54-0.70), or ulnar (SMD: 0.59, 0.55-0.63) nerves.

Pressure pain sensitivity, pain, and fascia thickness

Within the group of patients with plantar heel pain, we observed significant negative moderate associations between PPT over peripheral nerve trunks of the lower extremity with the pain intensity at first step on the morning ($-0.391<r<-0.351$, $P<0.05$) and with the disability scale of the FFI ($-0.460<r<-0.347$, $P<0.05$): the higher the intensity of pain at first step on the morning or the higher the impact of foot pain on self-reported function, the lower the PPTs over the peripheral nerve trunks of the lower extremity. No significant association between PPT with demographic data (age, height, weight, BMI), pain intensity, duration of symptoms, disability, or fascial thickness was found.

Discussion

This study found widespread pressure hypersensitivity over nerve trunks and musculoskeletal structures in unilateral chronic plantar heel pain patients, suggesting the presence of central altered nociceptive processing. The pressure pain hypersensitivity over the nerve trunks of the lower extremity was associated with higher pain intensity and related-disability.

In this study, PPT was significantly decreased bilaterally over local (calcaneus), related segment (medial gastrocnemius or tibialis anterior) and distant pain-free (second metacarpal) points, suggesting the presence of widespread pressure pain hyperalgesia over musculoskeletal structures in subjects with unilateral chronic plantar heel pain. The presence of widespread pressure pain hypersensitivity is a potential manifestation of an altered central pain processing as structures away from the site of pain were assumed non-symptomatic and considered normal. The between-groups PPT differences ranged from 70kPa (second metacarpal) to 153.2kPa (calcaneus bone). Although no available data exists on minimal detectable changes for all assessed points in our study, these values are closed to those determined for the calcaneus bone[24], the tibialis anterior and cervical spine[27], suggesting that real differences existed between patients and controls.

The topic of central sensitization and widespread pain hyperalgesia in individuals with chronic plantar heel pain has been previously suggested by Fernández-Lao et al[9]. That study also found widespread pressure hyperalgesia in a small sample of individuals with plantar heel pain; however, there are some differences with the current one. First, we controlled for BMI as covariate, an important variable to consider in this population since plantar heel pain patients are usually more obese than healthy people. In addition, since PPTs are lower in older people[8] and females[20], we also included age and gender as covariates. In agreement with the study conducted by Fernández-Lao et al[9] we observed a significant effect of gender showing that women exhibited higher pressure sensitivity, i.e., lower PPTs, than men (particularly in the nerve trunks); but not a significant effect of age, probably due to narrow confidence intervals of the sample. Second, we assessed mechanical sensitivity over

nerve trunks which was not analyzed in this previous study[9]. In fact, our study observed the presence of widespread pressure hyperalgesia over nerve trunks in patients with plantar heel pain. There is just one published study investigating PPTs over nerve trunks in individuals with plantar heel pain; however, this study only evaluated two nerve trunks related to foot innervation, e.g., medial calcaneal and medial plantar nerves[23]. When assessing pressure pain sensitivity over nerve trunks innervating the musculoskeletal structures in and over the heel region bypasses a possible primary hyperalgesia, but PPTs assessment from extra-segmental areas most likely represent a general increased central gain. One could argue that assessments over the nerve trunks innervating the heel region represent an increased segmental central gain and that PPT assessments from distant structures more represent generalized increased central gain[29]. Since plantar heel pain is considered a musculoskeletal pain condition, the presence of widespread decreased PPT over nerve trunks of the upper and lower extremities further support a central altered nociceptive pain processing[29].

In the current study, pressure pain sensitivity over the nerve trunks of the lower extremity, but not other variables including plantar fascia thickness was associated with the intensity of pain or related-disability. These findings further support a potential role of peripheral input from nerve tissues, at least from the lower extremity, on pain and function in this musculoskeletal condition. Since neural tissues are highly sensitivity to compressive forces, repetitive minor traumas due to inappropriate walking patterns, the use of inappropriate shoes, or minor compressive forces due to an increase in fascia thickness could irritative nerve nociceptors. In fact, it is possible that in some patients with signs and symptoms compatible with plantar

heel pain, but without an increase in plantar fascia thickness, the neural tissues of the feet can play an etiological role in the symptomatology[2]. In such cases, differential diagnosis would be crucial since treatment may be different depending on a more neural or more musculoskeletal origin of plantar heel pain. The role of nerve trunk tissues in plantar heel pain deserves future studies.

The presence of widespread pressure pain sensitivity is considered a manifestation of central sensitization. It has been proposed that central sensitization is associated to long-lasting nociceptive inputs from peripheral tissues, in this case the plantar fascia[21]. It is interesting to note that the increased in plantar fascia thickness, a common finding observed in people with plantar heel pain, was not associated with widespread pressure pain hypersensitivity. These findings would suggest that nociception from other tissues, and not just from the plantar fascia, can be involved in this process in this population. In fact, the role of different tissues on specific tendinopathies could explain the discussion if tendinopathies are mainly peripheral, or also central, conditions. A systematic review concluded that central sensitization is present in tendinopathies of the shoulder and the elbow, but evidence on the lower extremity was scarce[18]. In fact, this systematic review did not find any study including individuals with Achilles tendinopathy and no mention to plantar fascia tendinopathy was reported[18]. A recent study has observed that patients with Patellar or Achilles tendinopathy do not exhibit widespread sensory changes when compared to controls, suggesting that these two tendinopathies are mainly peripheral[19]. Therefore, it seems that each tendinopathy should be different and the discrepancies in relation to peripheral or central processing observed between different tendinopathies can simply reflect differences on nociceptive mechanisms, tendon physical demands, or the

involvement of other structures rather than just the tendon (i.e., muscle or nerve). Based on available literature, it seems that plantar heel pain exhibit not just peripheral, but also, central sensitization. Further studies including other quantitative sensory tests are needed to further confirm this process in patients with plantar heel pain.

Finally, some limitations of the current study should be considered. First, the cross-sectional design does not permit to determine any cause and effect relationship. Second, patients included in the study seek for physical treatment, which could limit the extrapolation of the results to the general population with plantar heel pain. Third, we have only tested sensitivity to pressure pain, a static outcome of nociceptive gain. The inclusion of dynamic outcomes such as wind-up or nociceptive withdrawn reflex would help to further determine the presence of central sensitization in individuals with plantar heel pain. Further, the assessment of other components of the sensitization process, e.g., conditioned pain modulation, should be also included in studies as it has been recently investigated in Achilles tendinopathy[26].

Conclusions

Patients with unilateral plantar chronic heel pain exhibited widespread pressure pain hypersensitivity when assessed over nerve trunks and musculoskeletal structures, suggesting an altered central nociceptive processing. Pressure pain hypersensitivity over the nerve trunks of the lower extremity was associated with higher pain intensity and related-disability.

Legend of Figure

Figure 1: Ultrasound measurement of the plantar fascia in a patient with plantar heel pain.

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Table 1: Demographic and clinical variables of patients with plantar heel pain and healthy controls

	Plantar Heel Pain (n=35)	**Healthy Controls (n=35)**
Gender (male/female)	18/17	18/17
Age (years)	41.7 (37.5, 45.9)	40.0 (35.9, 44.1)
Height (cm)	170.0 (166.6, 173.4)	171.9 (168.2, 175.6)
Weight (kg)	74.6 (69.7, 79.5)	68.0 (63.3, 72.7)
Body Mass Index (kg/cm^2)*	28.6 (21.8, 35.4)	22.9 (21.7, 24.1)
Affected side (left/right)	18/17	-----
Duration of Pain (months)	18.4 (11.7, 25.1)	-----
Mean Intensity of Foot Pain (NPRS, 0-10)	5.7 (5.0, 6.4)	-----
Pain Intensity with First Step (NPRS, 0-10)	6.1 (5.4, 6.8)	-----
Worst Intensity of Foot Pain (NPRS, 0-10)	7.6 (6.9, 8.3)	-----

Plantar fascia thickness at calcaneal insertion (cm)*		
Affected side / Dominant side	0.48 (0.46-0.50)	0.31 (0.29-0.33)
Non-affected side / Non-dominant side	0.38 (0.35-0.41)	0.32 (0.30-0.34)
Plantar fascia thickness at the middle point (cm)*		
Affected side / Dominant side	0.40 (0.38-0.42)	0.27 (0.24-0.30)
Non-affected side / Non-dominant side	0.31 (0.28-0.34)	0.26 (0.24-0.28)
FFI (0-100)#		
Pain Scale	50.0 (43.2, 56.8)	1.2 (0.2, 2.2)
Disability Scale	37.2 (28.7, 45.7)	0.6 (0.0, 1.2)
Activity Limitation Scale	16.1 (11.4, 20.8)	0.1 (0.0, 0.2)
Total Score	41.7 (34.7, 48.7)	0.8 (0.0, 1.6)

Significant differences between patients with plantar heel pain and healthy controls

* Significant group x side interaction (ANCOVA, P<0.01)

Table 2: Differences in widespread pressure pain thresholds (kPa) between patients with plantar heel pain and healthy controls

	Symptomatic Point Calcaneus Bone*	**Distant Pain-free Point Second Metacarpal***	**Segmental-related Point Tibialis Anterior***	**Segmental-related Point Medial Gastrocnemius***
Plantar Heel Pain (n=35)				

Affected/Dominant side	280.0 (230.8, 329.2)	164.8 (151.2, 178.4)	230.5 (201.3, 259.7)	189.9 (169.9, 209.9)
Non-affected/Non-Dominant side	301.2 (253.5, 349.9)	173.5 (159.7, 187.3)	251.3 (224.3, 278.3)	197.6 (172.2, 223.0)
	Healthy Controls (n=35)			
Affected/Dominant side	429.4 (390.2, 468.6)	250.3 (221.9, 278.7)	390.1 (361.3, 418.9)	271.6 (254.0, 289.2)
Non-affected/Non-Dominant side	433.2 (397.0, 469.4)	233.3 (217.2, 249.4)	370.5 (348.4, 392.6)	296.6 (272.0, 321.2)

Values (kPa) are expressed as means (95% confidence intervals)

* Significant differences between patients and controls (ANCOVA test, P<0.001)

Table 3: Differences in pressure pain thresholds (kPa) over nerve tissues of the upper extremity between patients with plantar heel pain and healthy controls

	Median Nerve*	Ulnar Nerve*	Radial nerve*
Plantar Heel Pain (n=35)			
Affected/Dominant side	130.6 (120.2, 141.0)	130.4 (118.4, 152.4)	148.8 (133.6, 164.0)
Non-affected/Non-Dominant side	138.2 (124.0, 152.4)	140.8 (128.7, 152.9)	158.3 (142.2, 174.4)
Healthy Controls (n=35)			
Affected/Dominant side	160.4 (149.5, 171.3)	175.3 (152.8, 197.8)	175.6 (161.6, 189.6)
Non-affected/Non-Dominant side	161.7 (151.7, 171.7)	169.2 (150.3, 188.1)	186.1 (162.2, 210.0)

Values (kPa) are expressed as mean (95% confidence interval)

* Significant differences between patients and controls (ANCOVA test, P<0.001)

Table 4: Differences in pressure pain thresholds (kPa) over nerve tissues of the lower extremity between patients with plantar heel pain and healthy controls

	Sural Nerve*	Tibial Nerve*	Common Peroneal Nerve*
Plantar Heel Pain (n=35)			
Affected/Dominant side	151.6 (136.0, 167.2)	151.0 (135.1, 166.9)	161.2 (145.3, 177.1)
Non-affected/Non-Dominant side	162.2 (147.4, 177.0)	154.0 (140.3, 167.7)	178.3 (159.9, 196.7)
Healthy Controls (n=35)			
Affected/Dominant side	233.6 (211.9, 255.3)	200.8 (179.3, 222.3)	251.9 (213.8, 290.0)
Non-affected/Non-Dominant side	237.2 (211.0, 263.4)	212.7 (187.9, 237.5)	229.3 (205.8, 252.3)

Values (kPa) are expressed as mean (95% confidence interval)

* Significant differences between patients and controls (ANCOVA test, P<0.001)