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Published in:
American Journal of Physical Medicine and Rehabilitation

DOI:
[10.1097/PHM.0000000000001673](https://doi.org/10.1097/PHM.0000000000001673)

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

Publication date:
2021

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Plinsinga, M. L., Meeus, M., Brink, M. S., Heugen, N., & van Wilgen, P. (2021). Evidence of widespread mechanical hyperalgesia but not exercise induced analgesia in athletes with mild patellar tendinopathy compared to pain-free matched controls: a blinded exploratory study. *American Journal of Physical Medicine and Rehabilitation, Publish Ahead of Print*, 946-951.
<https://doi.org/10.1097/PHM.0000000000001673>

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Evidence of Widespread Mechanical Hyperalgesia but Not Exercise-Induced Analgesia in Athletes With Mild Patellar Tendinopathy Compared With Pain-Free Matched Controls

A Blinded Exploratory Study

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Nienke Heugen, MSc, and Paul van Wilgen, PhD

Objective: The aim of the study was to assess centrally induced pain processing with pressure pain thresholds bilaterally and remotely in active volleyball and basketball athletes with mild patellar tendinopathy compared with asymptomatic control athletes. Secondary objective was to explore the role of exercise-induced analgesia during a training session in athletes with patellar tendinopathy.

Design: In this exploratory study, pressure pain thresholds of 21 patellar tendinopathy athletes and 16 age- and sex-matched asymptomatic team members were measured by a blinded assessor bilaterally on the patellar tendon and unilaterally on the elbow extensor tendon with a pressure algometer before, during, and after a regular training session.

Results: Patellar tendinopathy athletes had a significantly higher average body mass index compared with asymptomatic athletes (mean difference 1.75 kg/m²; 95% confidence interval = 0.35–3.15, $P = 0.02$). At baseline, athletes with patellar tendinopathy showed lowered pressure pain thresholds in the affected knee ($P = 0.001$), unaffected knee ($P < 0.001$), and elbow ($P = 0.01$) compared with controls. No clear patterns were identified to explain between-group differences in pressure pain thresholds before, during, and after exercise.

Conclusions: This exploratory study found primary and secondary mechanical hyperalgesia in athletes with patellar tendinopathy compared with asymptomatic athletes. Further research is required on the effects of an acute exercise bout on pain thresholds in this population.

Key Words: Jumper's Knee, Patellar Tendinopathy, Pain Thresholds, Central Sensitization, Exercise-Induced Analgesia

(*Am J Phys Med Rehabil* 2021;100:946–951)

Patellar tendinopathy is one of the most prevalent injuries in athletes who engage in sports with an explosive character involving sprints and high amounts of jumping (like basketball or volleyball).^{1,2} Patellar tendinopathy is characterized by activity-induced anterior knee pain and tenderness on the patellar tendon, resulting in significant pain and disability that

What Is Known

- Although the underlying mechanism for pain in persistent tendinopathy remains unclear, altered mechanical pain processing is proposed as a contributor to persistence of pain in tendinopathies. Evidence is, however, limited, particularly in athletes with mild but persistent patellar tendinopathy. Patellar tendinopathy is commonly managed through exercise, yet evidence on the pain reducing mechanisms of exercise is lacking.

What Is New

- This study showed lower pressure pain thresholds locally, bilaterally, and remotely in athletes with mild but persistent patellar tendinopathy compared with asymptomatic athletes from the same team. No clear patterns of exercise-induced analgesia were found in this study.

persists from months to years.^{2,3} More than 50% of athletes with patellar tendinopathy are thought to end their sports career as a result of this painful condition.⁴

Evidence of absent or minimal tendon pathology in the presence of pain challenged the perspective of persistent pain in tendinopathy.⁵ One of the explanations for persistent pain might be the alterations in the pain processing itself.⁶ Besides, primary hyperalgesia or peripheral sensitization (local to the painful site), secondary hyperalgesia or central sensitization (bilateral and widespread from the painful side) is seen as signs of alterations in pain processing. Evidence on alterations in the peripheral and central nervous system has been established mostly in upper limb tendinopathies.⁶ Only four studies have been published in the nonathletic patellar tendinopathy population. Three reported primary mechanical hyperalgesia measured

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Financial disclosure statements have been obtained, and no conflicts of interest have been reported by the authors or by any individuals in control of the content of this article. Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.ajpmr.com).

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ISSN: 0894-9115

DOI: 10.1097/PHM.0000000000001673

at the most painful spot⁷ or a standardized spot^{8,9} (mixed cohorts), and one did not (standardized spot, male individuals only¹⁰). The only study assessing secondary hyperalgesia measuring widespread pressure pain threshold (PPT) did not find evidence of secondary hyperalgesia.⁹

Exercise as a treatment option for musculoskeletal conditions is effective in reducing pain and disability.¹¹ Exercise is believed to have the potential to induce acute pain-alleviating effects (also referred to as exercise-induced analgesia/hypoalgesia).¹² In chronic lower limb tendinopathies, acute hypoalgesia (decrease in experienced pain or increase in pain thresholds) in response to *isometric* exercise was reported in one study on patellar tendinopathy,^{13,14} but not in two other studies on Achilles tendinopathy and plantar fasciopathy.^{15,16} For *aerobic exercise*, acute analgesic effects are primarily reported in healthy individuals.^{17,18} Variable pain inhibition effects (hypoalgesic and hyperalgesic) are reported in chronic pain conditions like low back pain and fibromyalgia,^{17,19} suggesting alterations in endogenous pain inhibition mechanisms in these patients.²⁰ Moreover, there is no criterion standard for the optimal type, duration, and dose of exercise to induce an analgesic response, which differ per exercised muscle and population.^{18,20} The potential effect of exercise-induced analgesia is, to our knowledge, not studied in athletes with patellar tendinopathy. It is unknown whether exercise in the form of a training session that involves aerobic exercise and mechanical loading activities (loading activities like jumping being specific risk factors for patellar tendinopathy²¹) increases pain sensitivity or induces an analgesic effect in athletes with persistent patellar tendinopathy.

To gain more insight in the peripheral and central pain mechanisms in persistent patellar tendinopathy, the primary objective of this study was to assess PPTs bilaterally and remotely in active volleyball and basketball athletes with mild patellar tendinopathy compared with matched asymptomatic control athletes. Our secondary objective was to explore the role of exercise-induced analgesia during a training session in athletes with patellar tendinopathy.

MATERIAL AND METHODS

Procedure

This exploratory study aimed to recruit participants previously diagnosed with mild patellar tendinopathy and asymptomatic athletes from the same teams. At the time of recruitment, symptomatic athletes were paired with an asymptomatic control athlete on age, sex, and training times/hours, as sex and age are known to influence quantitative sensory testing²² and training status to influence pain sensitivity and processing.²³

Participants were asked to refrain from nonsteroidal anti-inflammatory drugs or paracetamol 24 hours before testing and from other analgesics 1 week before testing. In addition, they were asked to refrain from nicotine or caffeine and not to be involved in moderate to vigorous physical exercise on the day of measurements.

Measurements were conducted in the regions around Groningen (the Netherlands), Ghent, and Antwerp (Belgium). All measurements were conducted during indoor volleyball and basketball training sessions. The training consisted of a typical

warm-up and training procedure, although the intensity and type of exercises were not monitored by the research team. Self-reported outcome measures were collected before the training session, and PPT measurements took place inside, on the side of the sports courts.

This study was developed according to the Declaration of Helsinki. Ethical approval was granted by the ethics committee of Human Movement Sciences Groningen on February 23, 2016, and the ethics committee of the University of Gent on September 25, 2017. This study conforms to all the strengthening the reporting of observational studies in epidemiology guidelines and reports the required information accordingly (see Supplemental Checklist, Supplemental Digital Content 1, <http://links.lww.com/PHM/B194>). All participants provided written informed consent before participation.

Participants

Participants between the ages of 18 and 65 yrs who trained at least once a week were recruited from several volleyball and basketball clubs in the Netherlands and Flanders between September 2016 and September 2017. Clubs were invited to participate to the study by mail or directly through the senior authors' network (PvW, MB, MM). None of the participants and researchers had any previous relationships. Inclusion criteria for the patellar tendinopathy group were (1) previous clinical diagnosis of patellar tendinopathy by a registered physiotherapist or sports physician; (2) patellar tendon pain and symptoms on one side for at least 3 months; (3) not receiving any treatment for the knee complaints at the time of measurements; and (4) being able to train as usual and fulfill training sessions despite the presence of knee complaints. Based on the previously mentioned inclusion criteria, the included patellar tendinopathy athletes were considered to be cases of "mild" patellar tendinopathy. Control athletes without any history of patella tendon complaints were eligible. Exclusion criteria for all athletes were previous surgery in the area of the knee or lower back; knee pain bilaterally; and a diagnosis of diabetes, epilepsy, or any neurological conditions.

Pressure Pain Threshold

Pressure pain thresholds were assessed bilaterally over the patellar tendon. A researcher palpated and marked the most *painful spot on the patellar tendon* in patellar tendinopathy participants (supine position, knee 10-degree flexion), and the same spot was marked on the *unaffected knee*. These two spots (affected and unaffected side) were also marked on their paired asymptomatic control athlete. In addition, the *elbow extensor tendon* (1–2 cm distally from the lateral epicondyle) of the dominant arm was marked as a remote site. Participants were measured in a supine position on the ground with the knees in 10-degree flexion supported by a towel for all PPT measurements (Supplementary Figure 1, Supplemental Digital Content 2, <http://links.lww.com/PHM/B195>). Pressure pain thresholds were measured with a handheld pressure algometer with an accuracy of 0.1 N/sec (Microfet, Procure; FPX 50, Wagner). Pressure was applied perpendicular to the skin with a 1-cm² probe size, and the force was gradually increased with 10.0 N/sec. Participants were asked to say "stop" at the first experience of a painful sensation; thereafter, the algometer was

released. Each spot was measured twice with at least 30 seconds of rest in between, and the PPT was calculated as the average of the two consecutive assessments. The procedure was explained and demonstrated before the PPT assessments.

Pressure pain thresholds were measured at baseline before the start of the training, during the training (after 15 mins of training), and after the training (up to 5 mins after) by another researcher blinded to the condition. Previous literature reported an adequate to moderate test-retest (intraclass correlation coefficient [ICC] = 0.6) and interrater (ICC = 0.93) reliability for PPT measurements in people with patellar tendinopathy.⁷

Self-reported Outcome Measures

Pain and Disability (Victorian Institute of Sports Assessment–Patella)

The Victorian Institute of Sports Assessment–Patella (VISA-P) is a patient self-reported scale that was used as an index for severity of pain and disability, specific for individuals with patellar tendinopathy. The Dutch translation has shown to have good test-retest reliability (ICC = 0.74) and validity.²⁴ The total score ranges from 0 to 100, with higher scores indicating less pain and disability.

Central Sensitization

Assessment of central sensitization was assessed with the Central Sensitization Inventory (CSI). The Dutch version of the CSI has a good internal consistency, discriminative power, and excellent test-retest reliability (ICC = 0.88–0.91).²⁵ The CSI consists of two parts. Part A contains 25 patient-rated items on physical symptoms, emotional distress, headache/jaw symptoms, and urological symptoms. The items are measured on a 5-point Likert scale ranging from “0” (never) to “4” (always). A score of 40 or higher has previously been used as a cutoff score, suggestive for the presence of central sensitization.²⁶ Part B of the CSI identifies the presence of seven different central sensitivity syndromes, namely, restless legs, chronic fatigue syndrome, fibromyalgia, temporomandibular joint disorder, migraine or tension headache, irritable bowel, and multiple chemical sensitivities, and 3 related disorders, namely, neck pain (whiplash), depression, and anxiety or panic attacks.²⁶

Statistical Analysis

Group differences were assessed with parametric tests for normally distributed data (independent *t* tests) and nonparametric tests for nonnormally distributed data (Mann-Whitney *U*, χ^2 test). To explore changes in PPTs before, during, and after training, changes were classified as an “increase,” “no change,” or “decrease” in PPTs by using meaningful detectable change (MDC) scores.²⁷ As no MDCs of PPTs after loading have been reported for patellar tendinopathy, MDCs from a study in patellofemoral pain were used.²⁷ Although the populations are different, Pazzinatto et al.²⁷ calculated MDCs from PPTs on the *patellar tendon* and reported an MDC of 0.6 kgf (~6.4 N) after loading in asymptomatic participants and an MDC of 1.5 kgf (~15.0 N) in symptomatic participants.²⁷ Based on the reported MDCs in Pazzinatto et al.,²⁷ an increase or decrease of 15.0 N was considered respectively a positive or negative change for the patellar tendinopathy group. An increase or decrease of 6.4 N was considered respectively a

positive or negative change for the asymptomatic control group.²⁷ SPSS (IBM SPSS Statistics, Version 25.0; IBM Corp, Armonk, NY) was used to perform statistical analyses. A priori significance was set at a *P* value of less than 0.05.

RESULTS

Thirty-two athletes with patellar tendinopathy and 29 asymptomatic control athletes were recruited. After removal of participants who did not feel pain during PPT testing on either the bilateral knee or elbow site, 21 athletes with patellar tendinopathy and 16 asymptomatic athletes were included in the analysis. Characteristics of all participants are reported in Table 1. Participants with patellar tendinopathy were significantly heavier (MD = 8.98 kg, 95% confidence interval [CI] = 1.24–16.72, *P* = 0.02) and had a greater body mass index (MD = 1.75 kg/m², 95% CI = 0.35–3.15, *P* = 0.02) compared with controls. There were no significant differences on the central sensitization inventory (Table 1).

Baseline PPTs

Patellar tendinopathy athletes showed significantly lower PPTs on the symptomatic knee (*P* = 0.01), the asymptomatic knee (*P* < 0.001), and the elbow (*P* = 0.01) compared with controls (Table 2; Fig. 1). None of the PPT measures were significantly correlated with the VISA-P or the CSI (Supplementary Table 1, Supplemental Digital Content 2, <http://links.lww.com/PHM/B195>).

Change in PPTs During and After Training

Supplementary Figure 2 (Supplemental Digital Content 2, <http://links.lww.com/PHM/B195>) displays the mean PPT scores at the three measurements sites, before, during, and after training.

Pain Pressure Thresholds During Training Compared to Baseline

No significant between-group differences *during exercise* compared with baseline were found at the *symptomatic knee* (*P* = 0.16), *asymptomatic knee* (*P* = 0.24), or *elbow* (*P* = 0.13; Supplementary Figure 3, Supplemental Digital Content 2, <http://links.lww.com/PHM/B195>).

Pain Pressure Thresholds After Training Compared to Baseline

Significant between-group differences *after exercise* compared with baseline were found on the *asymptomatic knee* (*P* = 0.02), but not on the *symptomatic knee* (*P* = 0.15) or *elbow* (*P* = 0.06; Supplementary Figure 3, Supplemental Digital Content 2, <http://links.lww.com/PHM/B195>).

DISCUSSION

This is the first study to explore mechanical pain processing in athletes with mild but persistent patellar tendinopathy by measuring PPTs bilaterally and remotely before, during, and after a volleyball or basketball training. We found lower PPTs locally, bilaterally, and remotely in athletes with patellar tendinopathy compared with asymptomatic controls at baseline, indicating signs of secondary hyperalgesia or central sensitization. No clear patterns were identified to explain differences in PPTs before, during, and after exercise.

TABLE 1. Descriptive statistics of the symptomatic patellar tendinopathy group and the asymptomatic controls

	Symptomatic Patellar Tendinopathy (<i>n</i> = 21)	Asymptomatic Controls (<i>n</i> = 16)	Group Difference
	Mean (SD)	Mean (SD)	Mean Difference (95% CI), <i>P</i>
Age	21.9 (2.8)	21.3 (3.4)	0.66 (−1.42 to 2.73), 0.53
Sex, female, <i>n</i> (%)	5 (16)	5 (11)	<i>P</i> = 0.61 ^a
Height, cm	187.0 (9.7)	183.6 (9.4)	3.39 (−3.04 to 9.82), 0.29
Weight, kg	81.7 (12.5)	72.7 (9.9)	8.98 (1.24 to 16.72), 0.02 ^c
Body mass index, kg/m ²	23.3 (2.2)	21.5 (2.0)	1.75 (0.35 to 3.15), 0.02 ^c
Times training/past week, ^b median (range)	4 (2–5)	3 (2–5)	<i>P</i> = 0.81
Hours of training/past week	6.9 (1.6)	6.7 (2.2)	0.19 (−1.07 to 1.44), 0.77
Rate of perceived exertion of training (6–20), ^b median (range)	11 (8–17)	11 (9–16)	0.993
VISA-P (0–100)	70.0 (9.7)	—	—
CSI (0–100)	21.9 (10.7)	19.1 (8.6)	1.94 (−3.89 to 9.36), 0.41

^aSex differences between groups was calculated with the χ^2 test.^bBetween-group differences were assessed with the nonparametric Mann-Whitney *U* test.^cSignificant group differences, *P* < 0.05.

To date, four studies aimed to understand mechanical pain processing in patellar tendinopathy through algometry. The majority reported primary hyperalgesia (local at the painful site) in symptomatic participants compared with asymptomatic controls, but none reported secondary hyperalgesia (bilateral and widespread from the painful side).^{7–10} The latter contradicts our finding of secondary hyperalgesia evidenced with lowered PPTs at the bilateral knee and elbow in symptomatic athletes compared with asymptomatic athletes. Differences may be explained by differences in sex distribution, with a female percentage of 26% in the symptomatic group versus 53% in the asymptomatic group in the study by Plinsinga et al.⁹ compared with 16% in the symptomatic group versus 11% in the asymptomatic group in our study. A more female-biased asymptomatic group in the study by Plinsinga et al.⁹ could have resulted in a relatively more pain-sensitive group considering female individuals tend to be more sensitive to pain

stimuli than male individuals.²² Besides sex distribution, there is a wide range of other potential confounding factors that influence chronic pain, pain hypersensitivity, and the assessment hereof including genetic, environmental, cognitive, and psychological factors.^{28–30}

Exercise is widely used as a management option for musculoskeletal conditions and has shown to provide analgesic effects in healthy and symptomatic individuals.¹⁷ A recent systematic review in people with osteoarthritis showed that there is very low-quality evidence that local PPTs increase after acute exercise (studies were a combination of aerobic and resistance exercise), but not for remotely measured PPTs.³¹ Our study is the first to look at nonspecific exercise-induced hypoalgesia in patellar tendinopathy athletes and did not reveal hypoalgesic responses in symptomatic or asymptomatic athletes. We found various effects of training on pain thresholds, some participants showing an increase and others a decrease

TABLE 2. Pain pressure thresholds before, during, and after training in the symptomatic patellar tendinopathy group and the asymptomatic controls, analyzed with the Mann-Whitney *U* test

	Symptomatic Patellar Tendinopathy (<i>n</i> = 21)	Asymptomatic Controls (<i>n</i> = 16)	Group Difference	
	Median (Range)	Median (Range)	Mann-Whitney <i>U</i>	<i>P</i>
Before training				
PPT symptomatic knee	70 (37.5–106.7)	121.4 (50.5–196.2)	280.0	<0.001 ^a
PPT asymptomatic knee	70.5 (40–125.1)	128.2 (50.5–196.2)	271.5	<0.01 ^a
PPT elbow	50.3 (29.4–76)	67.7 (26.5–116.5)	248.0	0.01 ^a
During training				
PPT symptomatic knee	55.5 (30–119)	131.8 (59–171.7)	302.5	<0.001 ^a
PPT asymptomatic knee	63.5 (38–134.9)	125.7 (55.5–171.7)	277.0	0.001 ^a
PPT elbow	54 (29.4–78.5)	68.1 (33–114)	236.0	0.04 ^a
After training				
PPT symptomatic knee	51.5 (28–120.2)	109.2 (51–186.4)	291.0	<0.001 ^a
PPT asymptomatic knee	58 (41.5–132.4)	119 (37.5–179)	263.0	<0.01 ^a
PPT elbow	60.1 (28.5–80)	62.9 (29.4–112.8)	196.0	0.40

^aSignificant group differences, *P* < 0.05.

FIGURE 1. Individual data and mean $\pm$ SD for the baseline PPTs in patellar tendinopathy group (PT, $n = 21$) and asymptomatic group (AsC, $n = 16$) on the symptomatic knee (PT: 67.8 ± 20.9 , AsC: 118.5 ± 45.9 , square), the asymptomatic knee (PT: 77.8 ± 28.4 , AsC: 120.3 ± 43.0 , diamond), and the elbow (PT: 54.8 ± 13.1 , AsC: 74.1 ± 25.8 , triangle). “Symptomatic” and “asymptomatic” knees in the asymptomatic group refer to the corresponding site of their matched symptomatic athlete.

in pain threshold after exercise. This finding may be partially explained by the removal of participants from the analysis who were unable to reproduce pain on PPT measures. These participants could have been the ones with a large hypoalgesic response. Another explanation could be the variation in training intensity between athletes. The intensity of exercise was standardized by matching participants from the same team (e.g., same volume and duration of training; Table 1), and the rate of perceived exertion was similar in symptomatic and asymptomatic athletes. Notwithstanding, intensity and free play were not controlled in this study, which are known to be associated with the efficacy of endogenous pain inhibition (dose response).^{17,18} Future research should aim to standardize and monitor the dose of loading/exercise to enable comparison of responses and to investigate the required dose of exercise needed to induce an analgesic response.

It is not known whether mechanical loading or physical exercise induces pain or leads to overall decreased pain thresholds in athletes with persistent but mild patellar tendinopathy. Interestingly, we identified symptomatic athletes with increased PPTs but also ones with decreased PPTs. Severity is thought to be a moderator for the effectiveness of exercise on pain thresholds³² and may explain the findings in this particular cohort. The VISA-P scores support the mild severity of our symptomatic athletes with a considerably higher VISA-P of 70.0/100 (representing milder symptom) compared with previous studies looking at sensory profiles in patellar tendinopathy (VISA-P range = 58.1–62.0 [100]^{7–10}). We could speculate that a subgroup of our persistent, mild patellar tendinopathy group may cope with exercise-induced pain similarly to asymptomatic individuals (e.g., a hypoalgesic response), whereas other participants with patellar tendinopathy show hyperalgesic responses. Another explanation could lie in the characteristics of our

population. Chronic pain syndromes like fibromyalgia show associations between psychological stress factors and altered endogenous central pain inhibition.^{33,34} In these populations, increased pain levels are seen even after mild exercises.¹⁹ Our symptomatic athletes did not show psychological distress, as seen in the outcome of questionnaires, and therefore, the endogenous pain inhibition may not be affected or may only be induced with moderate to vigorous exercises. Future studies should further investigate the type and dose of exercise needed to induce an hypoalgesic response in persistent but mild (patellar) tendinopathy athletes.

In the study, we added only athletes with PT still active in sports. It is known that in approximately 50% of the athletes with PT, this pain is a reason for finishing their sports activities. The population in our study were still active, so they learned how to cope with pain. In that way, this group may differ in pain characteristics or other characteristics from the total group of athletes with PT. Handheld pressure algometers were used to induce mechanical stimuli by a blinded assessor. They are reliable⁷ but are dependent on the physical capacities (strength, weight) of the assessor³⁵ and placement of the algometer. Increased pressure heightens the difficulty of maintaining a gradual increase in pressure without slipping of the tendon. Several methodological aspects may have influenced external and internal validity of our findings. In our study, pain could not be induced in some participants to a point whereby it was difficult to keep the probe on the tendon or gradually increase pressure. To guarantee reliable PPT measures,⁸ some athletes were excluded from the analysis, which ultimately resulted in a generally more sensitive population and possibly in the exclusion of participants with a stronger inhibitory response. Another limitation was that different types of algometers were used across participants, but not within subjects. Various

assessors performed the PPT measures across participants (not various within subjects); however, protocols were strictly followed. The used MDC scores used to identifying exercise-induced analgesic profiles were based previously reported data on the patellar tendon, but from a female-only population.²⁷ There is the possibility that this affected our findings, although the MDC scores were relatively low (15.0 N in symptomatic and 6.4 N in asymptomatic participants), meaning that a very small change in PPTs would have been detected. Measurements were conducted at the side of a sports court and not in a quiet room that controls for distractions like noise and temperature. This may have altered pain perceptions. A sample size calculation was not performed a priori because of the exploratory nature of the study. The small sample size may have increased the true type I error range, increasing the chance of false-positive findings.³⁶ Considering the limitations and the exploratory nature of this study, findings should be interpreted with care and in relation to this study only. There is a need for larger-scale replication studies to strengthen the body of evidence on primary and secondary hyperalgesia in persistent patellar tendinopathy, especially in athletes.

In summary, this exploratory study found primary and secondary mechanical hyperalgesia in athletes with mild but persistent patellar tendinopathy compared with asymptomatic athletes. No clear patterns of exercise-induced analgesia were found. This study contributes to the understanding of altered central pain processing in athletes with patellar tendinopathy and provides valuable data to further explore pain processing and aerobic exercise-induced analgesia in a more standardized matter in this population.

ACKNOWLEDGMENTS

The authors thank students Yijun Li, Stefano Zampese, Johan Bouma, Bart Lambrechts, and Wout Nobels for their help with data collection.

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