Title: "How does acute pain influence biomechanics and quadriceps function in individuals with patellofemoral pain?"

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Word count: 3193 words manuscript
Word count abstract: 228

number of tables*:* 4
Number of figures: 1
number of references: 33

Key words: patellofemoral pain, knee, PFP, AKP, inhibition, quadriceps, strength, pain

Abstract

Objectives:

Beside pathophysiological factors, pain is believed to play a crucial role in the progression of patellofemoral pain (PFP). However, the isolated effect of pain on biomechanics and quadriceps function has not been investigated in PFP. Thus, this study aimed to investigate the effect of pain on quadriceps function and lower limb biomechanics in individuals with PFP.

Methods

Twenty-one individuals with PFP (11 males and 10 females, age: 29.76 ±6.36 years, height: 1.74 ± 0.09m, mass: 70.12 ±8.56kg) were measured at two different occasions: when not and when experiencing acute pain. Peak quadriceps torque (concentric, eccentric and isometric) and arthrogenic muscle inhibition (AMI) was assessed. Three-dimensional motion analysis and surface electromyography of the quadriceps and hamstrings muscles were collected during running, a single-leg-squat and step-down task. The normality was assessed using the Shapiro-Wilk test and a MANOVA was performed at the 95% confidence interval.

Results

AMI increased significantly in acute pain. The net muscle activation of the knee extensors and flexors decreased during running in acute pain. The lower limb biomechanics and the quadriceps torque did not change in acute pain.

Discussion:

It appears that even if individuals with PFP experience pain they can still deliver maximal quadriceps contractions and maintain their moving patterns without biomechanical changes. However, the overall reduced activation of the quadriceps and the increased AMI indicate the presence of quadriceps inhibition in acute pain.

Key words: patellofemoral pain, knee, PFP, AKP, inhibition, quadriceps, strength, pain

1. Introduction

Patellofemoral pain (PFP) is commonly diagnosed in individuals with knee injuries and often affects younger and active populations [1]. Follow-up studies showed that the majority of individuals with PFP still suffered from pain and dysfunction, despite initially received treatment and education; Lankhorst et al. reported an unfavourable recovery at 5 to 8 years of 57% of individuals with PFP [2] and Stathopulu & Baildam found that 91% of patients still suffered from PFP 4-18 years after their initial presentation at a hospital [3]. Thus, the long-term prognosis of PFP is still poor, which raises the question whether the pathophysiological factors that cause PFP are understood and addressed in treatments sufficiently. Currently, pathophysiological factors associated with PFP can be compared with a complex mosaic where various anatomical, biomechanical, psychological and social factors are interconnected to each other and are likely to contribute to pain [4]. Long-term studies showed that individuals with PFP with greater durations of pain and worse pain were more likely to develop an unfavourable outcome and a more progressive pathology [5, 6]. Thus, it is believed that pain might play a role in the aetiology and progression of PFP [7].

Previous studies have reported a link between PFP and lower limb muscle weakness and inhibition, knee instability, and functional performance [8-10]. However, all studies either correlated the pain intensity to specific factors or based their findings on the comparison of the pain intensity before and after a treatment. The only studies that investigated the direct influence of acute knee pain on muscular function and lower limb biomechanics analysed the effect of artificially induced knee pain [11-14]. These studies demonstrate a link of pain to several factors, such as alterations of lower limb biomechanics, muscular coordination, quadriceps strength and arthrogenic muscle inhibition (AMI). AMI describes an ongoing reflex response which results in an inability to completely contract a muscle voluntarily, despite no structural damage to the muscle or innervating nerve [15, 16]. AMI is closely linked to knee pain, because it is caused by altered afferent input originating from mechanoreceptors and nociceptors, which reflexively reduce the efferent quadriceps alpha motor-neuron output [16, 17]. However, the isolated effect of pain in individuals with PFP has not been investigated.

Individuals with PFP commonly show altered movement patterns and aberrant muscle function [4], but it remains unclear whether these changes are consequence of pain or are causal factors in the development of PFP. It also remains unknown to what extent acute pain would influence the functional performance and muscular function in individuals with PFP. A better

understanding of the influence of pain in individuals with PFP would provide further insights into PFP that might help to optimise management and treatment of PFP. Therefore, this study aimed to investigate the direct effect of acute PFP on quadriceps strength and AMI, quadriceps and hamstrings co-contraction and hip and knee biomechanics.

2. Methods

The study was approved by the University of Salford Research and Governance Committee (HSR 15-143) and the trial was registered at ClinicalTrials.gov (NCT02914574). The informed consent was obtained from each participant. Posters and flyers at fitness centres, gyms, and sports clubs in Manchester and Salford were used to recruit participants with PFP and without PFP.

2.1. Participants

The inclusion and exclusion criteria, as well as the clinical assessment were developed based on current recommendations [18]. The inclusion criteria for participants with PFP were: (1) aged 18-45 years (to exclude patients with knee or patellar osteoarthritis); (2) antero- or retro-patellar pain with at least two of these activities: ascending or descending stairs or ramps, squatting, kneeling, prolonged sitting, hopping/ jumping, isometric quadriceps contraction or running (3) duration of current PFP symptoms >1 month

The exclusion criteria were: (1) any history of previous lower limb surgery or patella instability and dislocation, (2) lower limb deformities or any history of traumatic, inflammatory or infectious pathology in the lower extremities or any internal derangements, (3) not able to perform running, squatting and the step-down task during the measurement. (4) Those who failed to satisfy the above listed inclusion criteria.

Since there is no definite clinical test to diagnose PFP, further clinical assessment were carried out, which involved the Clarke's test, a palpation test of the patellar edges and a single leg squat task to investigate the pain region [18]. These three tests have been chosen based on the current recommendations and have shown to provide limited to good diagnostic evidence [18]. All clinical assessments were performed by the same experienced musculoskeletal

physiotherapist. All participants were fitted with standard running shoes (New Balance, model M639SA UK), to control the interface of the shoe and the surface.

The participants were asked to attend the first appointment whilst not experiencing pain and the second appointment whilst experiencing acute pain. This order was set to ensure, that the participants had time to raise questions and concerns during the first visit, before they performed the exercises that triggered their acute PFP. Both measurement sessions were scheduled within one week. The participants were instructed to perform exercises before the second appointment which they were familiar with and were sure would trigger their acute PFP. Since the participants performed the exercises independently between the first and second assessment, the researchers were unable to control the exercises. However, the researcher documented the form of exercises the participants had chosen; Twelve participants chose running and 9 participants chose eccentric quadriceps exercises (in particular lunges and squats) to trigger the acute PFP. The pain intensity was reported but participants were not instructed to self-inflict their acute pain up to a specific pain intensity level. Instead the participants were instructed to self-inflict the pain to the extent that they experienced as their familiar acute PFP. To ensure that they were not fatigued they were asked to not perform the painful activity at least 5 hours before coming to the second appointment and were advised to rest before arriving at the gait laboratory.

2.2. 3D movement analysis

Three-dimensional motion data were collected with ten Qualisys OQUS7 cameras (Qualisys AB, Sweden) at a sampling rate of 250Hz. Three force plates (BP600900, Advanced Mechanical Technology, Inc. USA) were used to collect the force data at a sampling rate of 1500Hz. The calibrated anatomical system technique (CAST) model, which included anatomical landmarks (markers on anatomical bony landmarks) and anatomical frames (segment mounted marker clusters), was used in the biomechanical modelling and analysis [19]. Retroflective markers were placed, with double sided hypoallergic tape to the following anatomical landmarks of both lower limbs of the participant: the anterior superior iliac spine (ASIS), the posterior superior iliac spine (PSIS), the iliac crest, the greater trochanter, the medial and lateral femoral epicondyle, the medial and lateral malleoli, the posterior calcanei, and the head of the first, second and fifth metatarsals. The anatomical frames were rigid clusters

of 4 nonorthogonal markers and were positioned over the lateral shank, and the lateral thigh of the limbs (Figure 1) [19].

For the electrode placement of the surface Electromyography (sEMG), the skin was shaved, abraded and cleaned with isopropyl alcohol. The sEMG electrodes (Noraxon Dual Electrodes, 2cm spacing) were placed on the vastus medialis, vastus lateralis, biceps femoris and semitendinosus muscle in accordance with the SENIAM guidelines [20]. The sEMG data were collected with the Noraxon Telemyo system at a sampling rate of 1500Hz. The sEMG data were synchronised to the kinematic and kinetic data.

All participants were measured at one occasion without acute pain or only very light pain and at the second occasion while the participant experienced acute pain. The participants were asked on both occasions to rate their pain intensity using the numeric pain rating scale (NPRS) after performing the biomechanical tasks. To investigate whether the application of the 3D markers and bandages modified the pain, each participant was asked to rank his/her pain intensity with and without the applied bandages and markers. Each subject was asked at both occasions to perform a static trial and to run on a 15m walkway at a self-selected speed. Running speed was measured and reported by using Brower timing lights (Draper, UT). The participant was asked to perform a single leg squat and a step-down test while holding his/her arms folded across his/her chest. Both tasks were demonstrated and explained by the researcher. Each task was performed until five successful trials were collected. Unsuccessful trials were ones whereby less than three markers per segment were visible or a partial/double foot contact with one of the force platforms happened.

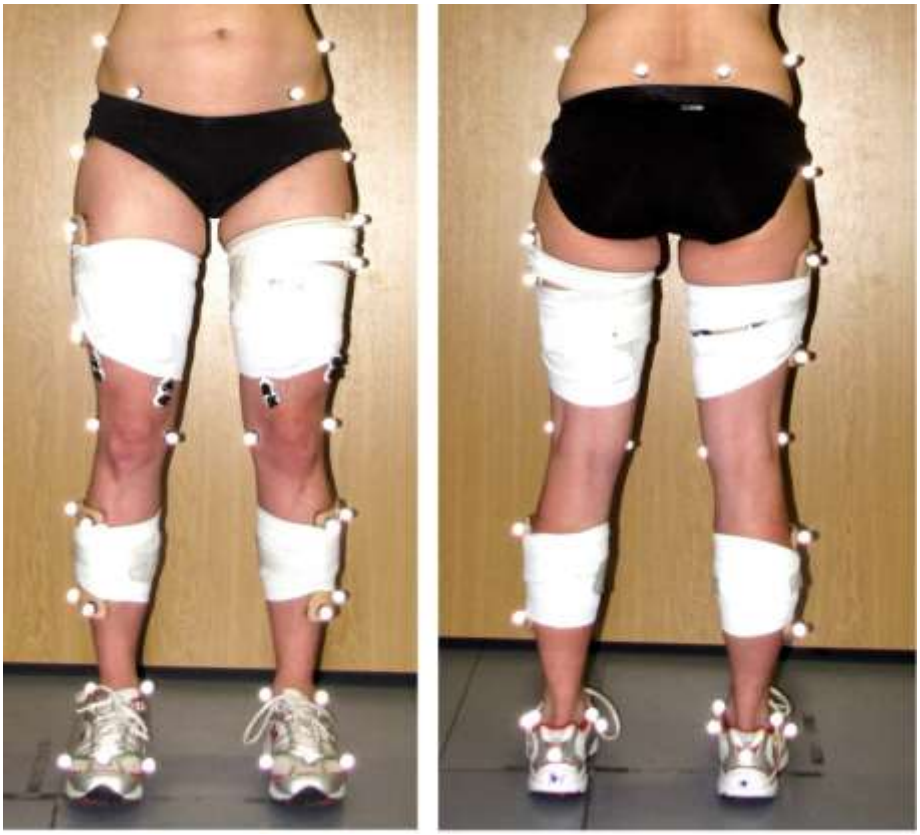

Figure 1: The placement of the markers and the sEMG electrodes

2.3. Quadriceps strength and inhibition analysis

At both occasions each subject was asked to perform three times the following knee extensor strength tests: an isometric, an eccentric and a concentric test. The peak torque was measured with an isokinetic dynamometer (Kin-Com, Chattanooga, USA). Participants were positioned in 90° hip flexion and 60° knee flexion in an isokinetic dynamometer and secured to the test chair with a chest and pelvic belt. The Kin-Com shin pad was attached 1 cm proximal to the malleoli of the ankle (Figure 2). The isokinetic knee extensor torque measurements were tested at the angular velocity of 60 degrees/second. The participants were advised to keep their arms across their chest.

The muscular inhibition of the quadriceps was assessed, during a maximal voluntary isometric contraction (MVIC) of the quadriceps with the interpolated twitch technique, using a single twitch with a pulse duration of 200 ms and a stimulus amplitude of 125mA (DS7AH Digitimer Ltd, Hertfordshire, England). Two electrodes (proximal: 50×130 mm, distal: 7.5×100 mm) (Axelgaard, Fallbrook, Ca, USA) were placed on the quadriceps muscle at one-third and two-

thirds from the distance between the anterior superior iliac spine and the upper border of the patella [21].

Prior to the test a warm-up session of 4 submaximal isometric and isokinetic quadriceps contractions were performed. The submaximal testing at around 50% of the participants MVIC was chosen to ensure that the participant was warmed up and familiarised with the measurement without feeling fatigued. After the warm-up a familiarisation of the stimulation sensation was made with several test stimuli. Prior to the isometric MVIC two single twitches of 125 mA were triggered by the assessor on the relaxed quadriceps. During the MVIC attempt two single pulses of 200µs duration, 200Volt and 125 mA were triggered by the investigator when the MVIC force had plateaued on the monitor. The strength data and AMI data of each participant was exported from the Kin-Com to asci-files and loaded into Excel. The peak concentric, eccentric and isometric torque was determined for each file. AMI was quantified by calculating the difference between the stimulus-evoked torque during MVIC (ITT in Nm) to the stimulus-evoked torque at rest (RTT in Nm) and expressed in %: activation deficit (AD) at 100% MVIC from the ratio: AD = (ITT/RTT) x 100. An inhibition of 0% means that the subject was able to fully recruit the muscle without showing any signs of inhibition.

Figure 2: Knee extensor strength and quadriceps arthrogenic muscle inhibition measurement

2.4. Processing of 3D motion data

The kinematic and kinetic outcomes were calculated using a 6 degrees of freedom model in Visual3D (Version 5, C-motion Inc., USA). The pelvis, thigh, shank, foot and virtual foot segments were defined and 4 tracking markers were used for each segment. Ankle and knee joint centers were calculated as midpoints between the malleoli and femoral epicondyles respectively and the hip joint center was calculated using the regression model of Bell et al. [22] based on the ASIS and PSIS markers. The global coordinate system was defined as *x* for the forward/ backward, *z* the vertical and y the left/ right (medial/ lateral) axis. Marker motion data and the analogue data from the force plate were filtered with a 4th order lowpass Butterworth filter with cut-off frequencies of 12Hz. The joint moments were calculated using three dimensional inverse dynamics and normalised to body mass. The kinematic and kinetic data were normalised to 100% of a single leg squat, a step-down task and the stance phase in running, whereby the stance phase was sub-grouped in early (0-24% of stance phase), mid (25-62%) and late-stance phase (63%-100%) [23]. The peaks of the hip and knee flexion, adduction and internal rotation angles and the moments were calculated for the single leg squat, step-down task and the early, mid and late-stance phase. Furthermore, the average knee angular velocity was calculated for the eccentric phase during the single leg squat and step-down task.

2.5. Processing of sEMG data

The sEMG data was band-pass filtered at 20-500 Hz and rectified by using a root mean square over a 75 ms window for the running task and 300 ms for the single leg squat and step-down task [24]. Co-contraction ratios were (CCR) calculated by using the formula of Heiden et al.:

If agonist mean EMG > antagonistic mean EMG:

CCR= 1- antagonistic mean EMG/agonist mean EMG

If agonist mean EMG < antagonistic mean EMG:

CCR= agonist mean EMG/ antagonistic mean EMG -1 [25]

The peak quadriceps torque was determined for each file and AMI was calculated during the isometric contraction.

2.6. Statistical analysis

The statistical analysis was performed using SPSS (v. 20, IBM, USA) and Excel 2013 (Microsoft, USA). The normality was assessed by applying the Shapiro-Wilk test and by the investigation of the normal q-q plots. The Wilcoxon rank test was used with a significance level set at $p<0.05$ to investigate the ordinal data (pain scale).

Kinematic and kinetic variables, quadriceps strength, quadriceps AMI and co-contraction ratios were compared between the two conditions: with and without acute pain using a one way repeated measures MANOVA. The standard error of mean (SEM) was calculated using the following formula: SEM = SD/√sample size. The effect size for each variable was calculated using the Cohen d to give an indication of the magnitude of the effect of acute pain (>0.8 large effect, 0.5 moderate effect, <0.3 small effect) [26].

3. Results

Twenty-one individuals with PFP (11 males and 10 females, age: 29.76 ±6.36 years, height: 1.74 ± 0.09m, mass: 70.12 ±8.56kg) participated in the study. The running speed without and with pain was not significantly different (p=0.608) (without pain: 3.32±0.71m/s, with pain: 3.4 ±0.15m/s).

The application of the bandage and the markers did not result in significant changes in pain under both test conditions (NPRS: baseline pain: without marker application: 1.29±1.95; with application: 1.17±1.95,p=0.582, acute pain: without application: 3.88±1.92; with application: 3.86±1.96,p=0.902). Pain was significantly increased when participants performed the tasks with acute pain (with and without pain: p=0.0001). A clinically significant change in pain has been described as 1.74 points, thus the pain increase by 2.59 represents a clinical meaningful increase in pain [27].

Only during the late-stance phase in running the external knee flexion moment significantly decreased with a moderate effect size in acute pain (p=0.042) (Table 2). Although the change was not significant a moderate effect size indicated also a reduction of the external knee flexion moment during the mid-stance phase.

The net activation of the knee extensors and flexors decreased significantly during the early and mid-stance phase with medium to large effect sizes (quadriceps: 32.2% reduction, $p=0.025$, hamstrings: 11.4% reduction, $p=0.008$) in acute pain (Table 3).

The peak isometric, concentric and eccentric torque did not change with or without acute pain (Table 4). However, the AMI increased significantly in acute pain with a moderate effect size (6.56% increase, $p=0.035$) (Table 4).

Table 1: The lower extremity kinematics during the single leg squat task and the step-down task with and without acute pain (*indicated the results were significantly different.)

The kinematic variables (º) during the single leg squat and step-down task		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion angle	75.7	15.6	3.4	76.9	16.4	3.6	0.813	0.08
	Hip adduction angle	14.5	7	1.5	13.6	7.6	1.7	0.697	0.08
	Hip internal rotation angle	1.9	7.5	1.6	0.7	7.8	1.7	0.607	0.16
	Knee flexion angle	81.1	9.3	2	81.9	10.7	2.3	0.786	0.08
	Knee adduction angle	5.3	4.7	1	4.2	4.5	1	0.460	0.24
	Knee internal rotation angle	-2.5	6.3	1.4	-1.5	5.9	1.3	0.575	0.16
Step-down task	Hip flexion angle	71.8	18.2	4	74.5	15	3.3	0.608	0.16
	Hip adduction angle	16.4	6.7	1.5	15.7	6.7	1.5	0.717	0.10
	Hip internal rotation angle	2.2	6.8	1.5	0.6	7.6	1.7	0.485	0.22
	Knee flexion angle	89.4	14	3.1	90.3	13	2.8	0.842	0.07
	Knee adduction angle	5.4	4.4	1	4.5	4.6	1	0.508	0.2
	Knee internal rotation angle	-1.1	6.5	1.4	-1.1	6.1	1.3	0.977	0
Early-stance phase	Hip flexion angle	36.5	5.9	1.3	36.8	5.5	1.2	0.835	0.05
	Hip adduction angle	7.1	4.6	1	6.7	4.8	1.1	0.746	0.09
	Hip internal rotation angle	2.9	7.9	1.7	3.4	7.4	1.6	0.895	0.07
	Knee flexion angle	30.6	3.9	0.9	31.6	4	0.9	0.460	0.25
	Knee adduction angle	2.2	3.4	0.7	2.5	3.9	0.8	0.779	0.08
	Knee internal rotation angle	-4.8	5.9	1.3	-3.9	5.2	1.1	0.373	0.18
Mid-stance phase	Hip flexion angle	34.6	6.5	1.4	34.9	5.9	1.3	0.946	0.05
	Hip adduction angle	11.5	4.8	1	10.1	5.3	1.2	0.387	0.28
	Hip internal rotation angle	-0.1	7.5	1.6	-0.9	8.7	1.9	0.908	0.10
	Knee flexion angle	43.3	5	1.1	44.6	5	1.1	0.824	0.26
	Knee adduction angle	1.7	3.3	0.7	0.9	4.8	1	0.784	0.19
	Knee internal rotation angle	1	6.3	1.4	1.2	5.5	1.2	0.783	0.03
Late-stance phase	Hip flexion angle	21.1	5.7	1.2	21	5.2	1.1	0.856	0.18
	Hip adduction angle	7.2	5	1.1	7	4.9	1.1	0.279	0.04
	Hip internal rotation angle	1.1	7.4	1.6	0.2	9.2	2	0.594	0.11
	Knee flexion angle	40.9	4	0.9	41.7	4.6	1	0.441	0.19
	Knee adduction angle	1.2	2.7	0.6	1.1	3.8	0.8	0.514	0.03
	Knee internal rotation angle	0	7.1	1.5	0.6	5.4	1.2	0.651	0.10

Table 2: The lower extremity kinetics during the single leg squat task and the step-down task with and without acute pain (*indicated the results were significantly different.)

The kinetic variables (Nm/kg) during the single leg squat and step-down task		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Hip flexion moment	1.29	0.55	0.12	1.34	0.55	0.12	0.790	0.09
	Hip adduction moment	0.95	0.28	0.06	0.91	0.2	0.04	0.636	0.16
	Hip internal rotation moment	-0.14	0.05	0.01	-0.15	0.07	0.02	0.619	0.16
	Knee flexion moment	1.74	0.41	0.09	1.67	0.28	0.06	0.556	0.20
	Knee adduction moment	0.33	0.12	0.03	0.3	0.11	0.02	0.421	0.26
	Knee internal rotation moment	0.4	0.09	0.02	0.37	0.09	0.02	0.350	0.33
Step-down task	Hip flexion moment	1.49	0.72	0.16	1.58	0.69	0.15	0.690	0.13
	Hip adduction moment	1.13	0.27	0.06	1.06	0.2	0.04	0.387	0.29
	Hip internal rotation moment	-0.1	0.07	0.02	-0.12	0.06	0.01	0.405	0.31
	Knee flexion moment	1.74	0.35	0.08	1.69	0.29	0.06	0.594	0.16
	Knee adduction moment	0.39	0.18	0.04	0.35	0.14	0.03	0.475	0.25
	Knee internal rotation moment	0.4	0.09	0.02	0.37	0.09	0.02	0.252	0.33
Early-stance phase	Hip flexion moment	2.03	0.42	0.09	1.99	0.4	0.09	0.545	0.10
	Hip adduction moment	1.24	0.45	0.1	1.08	0.33	0.07	0.396	0.41
	Hip internal rotation moment	0.05	0.12	0.03	0.06	0.09	0.02	0.946	0.09
	Knee flexion moment	1.42	0.48	0.11	1.38	0.33	0.07	0.060	0.10
	Knee adduction moment	0.52	0.28	0.06	0.45	0.26	0.06	0.576	0.26
	Knee internal rotation moment	0.22	0.1	0.02	0.2	0.11	0.02	0.648	0.19
Mid-stance phase	Hip flexion moment	0.94	0.59	0.13	0.87	0.42	0.09	0.986	0.14
	Hip adduction moment	1.95	0.42	0.09	1.82	0.47	0.1	0.710	0.29
	Hip internal rotation moment	-0.26	0.17	0.04	-0.26	0.17	0.04	0.523	0
	Knee flexion moment	2.89	0.72	0.16	2.48	0.77	0.17	0.078	0.55
	Knee adduction moment	0.55	0.29	0.06	0.5	0.3	0.07	0.918	0.17
	Knee internal rotation moment	0.44	0.14	0.03	0.41	0.15	0.03	0.764	0.21
Late-stance phase	Hip flexion moment	-0.03	0.28	0.06	0.02	0.26	0.06	0.540	0.19
	Hip adduction moment	1.43	0.42	0.09	1.37	0.46	0.1	0.680	0.14
	Hip internal rotation moment	0.02	0.03	0.01	0.02	0.04	0.01	0.778	0
	Knee flexion moment	1.96	0.51	0.11	1.68	0.51	0.11	0.042*	0.55
	Knee adduction moment	0.36	0.21	0.05	0.33	0.21	0.05	0.742	0.14
	Knee internal rotation moment	0.25	0.11	0.02	0.23	0.11	0.02	0.600	0.19

Table 3: Co-contraction ratio, net activation of the knee flexors and knee extensors during the stance phase in running, the single leg squat task and the step-down task with and without acute pain, (*indicated the results were significantly different.)

		Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
		Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Single leg squat	Co-contraction ratio (knee ext: knee flx.)	0.6	0.28	0.07	0.65	0.19	0.05	0.331	0.20
	Net activation knee extensors in %	74.97	36.65	8.64	52.95	35.32	8.32	0.177	0.61
	Net activation knee flexors in %	28.81	16.93	3.99	18.83	14.78	3.48	0.075	0.63
Step-down task	Co-contraction ratio (knee ext: knee flx.)	0.58	0.29	0.07	0.63	0.23	0.05	0.688	0.19
	Net activation knee extensors in %	72.43	30.6	7.21	52.81	36.72	8.66	0.283	0.58
	Net activation knee flexors in %	30.55	20.7	4.88	19.29	14.74	3.47	0.183	0.63
Early-stance phase	Co-contraction ratio (knee ext: knee flx.)	0.66	0.15	0.04	0.72	0.13	0.03	0.558	0.43
	Net activation knee extensors in %	134.49	67	15.79	102.29	59.11	13.93	0.025*	0.51
	Net activation knee flexors in %	38.26	17.91	4.22	26.86	17.99	4.24	0.008*	0.64
Mid-stance phase	Co-contraction ratio (knee ext: knee flx.)	0.32	0.24	0.06	0.41	0.25	0.06	0.882	0.37
	Net activation knee extensors in %	81.74	41.9	9.88	63.16	35.75	8.43	0.010*	0.48
	Net activation knee flexors in %	50.21	21.43	5.05	33.29	19.61	4.62	0.002*	0.82
Late-stance phase	Co-contraction ratio (knee ext: knee flx.)	-0.44	0.47	0.11	-0.33	0.44	0.1	0.117	0.24
	Net activation knee extensors in %	6.76	5.67	1.34	8.9	16.29	3.84	0.928	0.18
	Net activation knee flexors in %	20.03	15.55	3.67	14.05	10.98	2.59	0.096	0.44

Table 4: Strength, AMI, time to peak, rate to force development and the break phenomenon with and without acute pain. (*indicated the results were significantly different.)

	Without pain			With acute pain			P value: (T-test, sig 2-tailed)	Effect size
	Mean	SD	Std. Error Mean	Mean	SD	Std. Error Mean		
Isometric quadriceps strength (Nm/kg*100)	2.86	0.76	0.17	2.90	1.26	0.27	0.889	0.04
Eccentric quadriceps strength (Nm/kg*100)	3.14	1.40	0.30	2.74	0.69	0.15	0.249	0.36
Concentric quadriceps strength (Nm/kg*100)	1.74	0.71	0.15	1.88	0.57	0.12	0.480	0.22
AMI in %	10.58	9.33	2.04	17.14	12.71	2.77	0.035*	0.59

4. Discussion

To the authors' knowledge, this is the first study to investigate the direct influence of acute pain on hip and knee biomechanics, quadriceps and hamstrings activation and quadriceps strength and AMI in individuals with PFP. This study showed that despite acute pain, hip and knee kinematics were not significantly changed. However, the external knee flexion moment was slightly decreased in acute pain during the mid- and late-stance phase in running, which is in accordance with previous studies demonstrating that artificially induced knee pain resulted in a decreased knee flexion moment [11, 12]. A reduced knee flexion moment is believed to be caused by the quadriceps avoidance strategy, which is a compensatory strategy to decrease joint loading and thereby joint pain [28]. This assumption could be supported by the findings

of a significantly increased quadriceps inhibition, decreased quadriceps activation and the slight decrease in the knee flexor moment. The simultaneously reduced activation of the quadriceps and hamstrings muscles has been previously described in individuals with artificial induced pain [12, 13].

A balanced co-contraction of the quadriceps and hamstrings activation might assist in knee joint stabilisation in the frontal plane due to increased joint compression [29]. Thus, the overall reduced co-contraction of the quadriceps and hamstrings muscles might result in knee instability during the loading response and thus also might be responsible for the development of pain and the greater reduction and variability of the knee flexion moment [12, 13]. However, the reduced quadriceps muscle activation could also be a compensatory strategy to reduce patellofemoral joint reaction forces during painful activities, which has been described in literature as the quadriceps avoidance strategy.

The quadriceps avoidance strategy is believed to be often caused by quadriceps inhibition [12, 13, 30]. Rice et al. described that the inhibitory response of the quadriceps occurs partially due to spinal reflex inhibition of the alpha-motor-neuron (MN) [31]. This reflex inhibition is modulated by the pre- and postsynaptic mechanism and elicited by abnormal afferents from a painful or damaged joint [21, 32]. Thereby the painful or damaged joint causes a decreased motor drive to muscles and thus a limited muscle's potential to generate force [21]. Studies which investigated the association of pain to AMI found that it was significantly associated to knee pain [16, 21, 33] and that already 1 point increase on the visual analogue pain scale (VAS) caused an increase in AMI of 1.6% [21]. These findings are in accordance with the results of this study, where the pain increase of 1 on the NPRS caused an increase of 2.1% AMI. Thus, AMI appears to play an important role in the injury cycle of knee pain.

Previous studies suggested an increase of the voluntary antagonist neural drive to overcome any inhibitory contractions [30, 33]. In contrary, this study showed that pain caused a decrease of the antagonistic muscles and thus indicates that not only the quadriceps, but also the hamstrings muscles might be inhibited due to pain [14]. This suggests that pain suppressed the motor output globally. But despite the significant altered muscle activation of the quadriceps and the hamstrings muscle, no significant biomechanical changes or differences in the maximal voluntary quadriceps contraction could be identified. Knee pain may be caused by a number of structures, such as the infrapatellar fat pad with its nociceptive innervations [34]. Previous studies have shown that knee pain, that was artificially induced in the quadriceps muscle or the

infrapatellar fat pad altered the coordination of the quadriceps muscle [12, 13, 35]. These studies showed that pain caused a reduced activation and altered activation timing of the quadriceps muscle, which is in accordance to our findings.

In contrary to our findings, previous studies have shown that pain also resulted in a decrease of quadriceps strength [14, 33, 36]. However, these results were shown in healthy individuals with artificially induced knee pain. Individuals with PFP experience knee pain frequently and thus might show a different physical reaction to pain. Furthermore, in comparison to strength results of individuals with PFP in previous studies the participants in this study appeared to belong to a strong subgroup of individuals with PFP. Selfe et al. described three subgroups of patients with PFP; a "strong subgroup" with high quadriceps and hip abductor strength scores, a "weak and tight subgroup" with weak quadriceps and hip abductor muscles and low muscle flexibility and a "weak and pronated foot subgroup" with weak quadriceps and hip abductor muscles, greater patellar mobility and an increased foot pronation [37]. The strong subgroup had quadriceps torque scores of 1.65 ±0.53 Nm/kg in comparison with the weak groups with quadriceps torque values of 0.84 ±0.32 Nm/kg and 0.82 ±0.32Nm/kg. The group of individuals with PFP who participated in this study were highly active and had an isometric quadriceps strength score of: 2.86 ±0.76 Nm/kg without acute pain and with acute pain of 2.9 ±1.26 Nm/kg. These results demonstrate that participants with PFP that participated in this study were stronger than previously reported in literature. The good training status of the participants with PFP might have enabled them to deliver maximal quadriceps contractions and maintain their moving patterns without biomechanical changes even when they experienced more pain and had a presence of AMI. However, research on strong individuals with PFP is still lacking and thus further research is needed to confirm these findings [37].

2. Clinical implications

These results indicate that quadriceps AMI appears to be a crucial factor in acute PFP. AMI is present in a wide range of knee joint pathologies and described as a reflexive "shut-down" of the quadriceps muscle [16]. Immediately after knee injuries a decreased voluntary quadriceps activation is believed to be a protective mechanism to prevent further injuries [38]. However, quadriceps AMI may persist for a long time after the original injury and can lead to posttraumatic weakness and muscle atrophy [39]. Thereby it can become a limitation during rehabilitation [16, 39]. Thus, it is important for clinicians to identify AMI and to devise a

strategy to overcome this impairment [40]. Traditional strengthening exercises have demonstrated no effect on quadriceps AMI [38]. Although treatments, such as transcutaneous electrical nerve stimulation (TENS) have shown to have strong effects to reduce AMI they are not implemented in recommended physical interventions [38, 41]. Thus, a successful identification of AMI in individuals with PFP might be an important for clinicians to be able to apply an adequate treatment scheme.

5. Limitations

One limitation of this study was that pain caused by activities could not be monitored and standardised. The participants performed their familiar functional activities to reproduce the pain condition, which was not quantified and controlled. This study aimed to reproduce the acute PFP that these individuals experience during their familiar and functional and sports activities. Thus, the test procedure did not allow us to reproduce the individual familiar sport environment of each participant and to monitor and standardise the painful activities.

It is important to note that the participants wore a pair of standard training shoes to control the shoe-surface interface and to minimise the influence of footwear in the study. The standard training shoes might have negatively influenced the comfort during running and thereby might have influenced their biomechanical performances.

6. Conclusions

To the authors knowledge this was the first study investigating the effect of acute pain on lower limb biomechanics, AMI and strength. Acute PFP pain caused a decrease of muscular activity of the quadriceps and hamstrings muscles and resulted in an increase of AMI of the quadriceps. However, acute pain did not alter biomechanical changes or quadriceps torque. These findings show that AMI appears to be an important factor that is linked to pain in individuals with PFP, which needs to be addressed appropriately in the treatment scheme.

2. References

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