Vastus lateralis motor unit firing rate is higher in women with patellofemoral pain

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Title: **Vastus lateralis motor unit firing rate is higher in females with patellofemoral pain**

Running head: Motor unit firing rate in patellofemoral pain

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ABSTRACT:

Objective: To compare neural drive, determined from motor unit firing rate, to the vastus medialis and lateralis in females with and without patellofemoral pain.

Design: Cross-sectional study.

Setting: University research laboratory.

Participants: Females (N=56) 19-35 years old, 36 with patellofemoral pain and 20 controls.

Interventions: Not applicable.

Main Outcome Measure(s): Participants sustained an isometric knee extension contraction at 10% of their maximal voluntary effort for 70s. Motor units (N=414) were identified using high-density surface electromyography. Average firing rate was calculated between 5 and 35s after recruitment for each motor unit. Initial firing rate was the inverse of the first three motor unit inter-spike intervals.

Results: In control participants, vastus medialis motor units discharged at higher rates than vastus lateralis (p=0.001). This was not observed in females with patellofemoral pain (p=0.78) due to a higher discharge rate of vastus lateralis compared to control participants (p=0.002). No between-group differences were observed for vastus medialis (p=0.93). Similar results were obtained for the initial motor unit firing rate.

Conclusions: These findings suggest that females with patellofemoral pain have a higher neural drive to vastus lateralis but not vastus medialis, which may be a contributor of the altered patellar kinematics observed in some studies. The different neural drive may be an adaptation to patellofemoral pain, possibly to compensate for decreased quadriceps force production, or a precursor of patellofemoral pain.

KEYWORDS: Patellofemoral pain; Motor unit; EMG; quadriceps; neural drive

ABBREVIATIONS LIST: PFP: Patellofemoral Pain; EMG: Electromyographic; VM: Vastus Medialis; VL: Vastus Lateralis; MU: Motor Unit; ES: Effect Size; CI: Confidence Interval.

INTRODUCTION:

Patellofemoral pain (PFP) is a musculoskeletal disorder characterized by anterior knee pain during activities such as stair climbing, squatting, and sitting for long time periods [1]. As lower knee extension strength is associated with PFP [2] and has been identified as a risk factor for PFP [3], altered neuromuscular function of the knee extensor muscles is considered to play a role in the development and maintenance of PFP [4]. More specifically, as the medial and lateral components of the quadriceps apply different medio-lateral forces at the patella [5–8], their unbalanced activation may alter pressure distribution across the patellofemoral joint [7] as well as patellar kinematics [8,9].

A widely investigated indicator of coordination between vasti muscle activation in PFP is the relative timing of activation of vastus medialis (VM) and lateralis (VL) muscles during movement [10–12]. Although commonly used, a systematic review identified only a trend for delayed activation of the VM relative to VL and this was largely accounted for by large and unexplained variability across studies [13]. In addition, although timing measures are easy to obtain and provide valuable information, they only permit the identification of temporal differences in muscle activation. The force exerted by a muscle is known to depend on the number and discharge rate of its active motor units [14,15]. For this reason, altered neural drive to VM and VL may be relevant for PFP. Previous studies have investigated surface electromyographic (EMG) amplitude to compare vasti muscle activation between participants with and without PFP [16–18]. However, this provides only a crude indicator of the neural drive to a muscle, as surface EMG amplitude is influenced by factors such as: adipose tissue thickness, normalization, crosstalk, motor unit action potential cancellation, and others [19], which

may differ between groups. In isometric tasks, the influence of these factors can be limited by estimating the neural drive from motor unit (MU) activity. Although motor unit activity has traditionally been assessed using intramuscular recordings, recent technological advances enable estimation of neural drive using non-invasive high-density surface electromyography [20].

The aim of this study was to compare neural drive to the vastus medialis and lateralis in females with and without PFP during a submaximal, isometric task. On the basis of theories that propose a role for unbalanced activation of the vasti muscles, we hypothesized that MU firing rate of VM would be lower in participants with PFP relative to asymptomatic controls, or VL would be higher, or both.

METHODS:

Thirty-six females with PFP and 20 asymptomatic females (control participants) were recruited for the study from the community and from local physiotherapy clinics. To be included in the PFP group, participants had to be: female, 19-35 years old, with retro- or peri-patellar knee pain of intensity equal or greater than 3/10 for at least 1 month aggravated by any of the following activities: sitting for long time periods, stair ambulation, squatting, running, kneeling or jumping. They also needed to report pain or discomfort to at least one of the following tests: patellar palpation, patellar compression, resisted knee extension with knee close to full extension, or isometric knee extension while applying pressure proximally to the patella. These criteria were similar to those used in other studies [10,17,21]; the screening was performed by a physiotherapist with more than 2 years of clinical experience in musculoskeletal assessment. Asymptomatic

88 controls must not have had any knee pain in the last 12 months. Participants were
89 excluded from either group if they had chronic neuromuscular disorders affecting the
90 legs or previously had lower-limb surgery. All participants provided written informed
91 consent before the start of the experimental session. The study was approved by the
92 institution's Clinical Research Ethics Board.
93 Body mass and height were measured, and age, time of onset of pain and
94 average pain intensity in the previous week (11-point Numerical Rating Scale) were
95 obtained by self-report for each participant. Physical activity (General Physical Activity
96 Questionnaire, GPAQ [22]) and functional limitation (Anterior Knee Pain scale [23]) were
97 evaluated using validated questionnaires. The test leg was the most painful knee. For
98 control participants, the leg was determined randomly before the testing session.
99 The protocol consisted of recording high-density surface EMG signals from both
100 vasti during a submaximal, isometric task. The electrode grids were placed according to
101 anatomical references as described previously [24]. The medial and lateral edges of VM
102 and VL were identified using ultrasound imaging[a] and were marked on the skin. VM and
103 VL innervation zones were located using a linear electrode array (16 silver bar
104 electrodes, 10-mm interelectrode distance[b]) and marked on the skin. Two electrode
105 grids (semidisposable adhesive matrix[b]) were placed on the skin so that the innervation
106 zone was aligned between the second and third column, and all the electrodes were
107 placed on the muscle of interest. Each grid comprised 64 electrodes arranged in 5
108 columns and 13 rows with an electrode missing in one of the corners, 8 mm inter-
109 electrode distance and was held in place using bi-adhesive foam. In the VM, for
110 instance, the longer dimension of the electrode grid (approximately 10 cm) spanned the

distal-medial to the proximal-lateral region of the muscle (fig. 1); for this reason, the grid placement provided EMG signals representative of different regions within each vastus muscle. Reference electrodes (2x3.5 cm; conductive hydrogel[c]) were placed on the patella and both sides of the knee.

Isometric knee extension torque was measured using an isokinetic dynamometer[d]. Participants were secured to the chair; the hip and knee angles were 85 and 45 degrees of flexion, respectively. Resistance was applied approximately 2 cm proximal to the medial malleolus. Participants performed 3 maximal voluntary contractions (MVC) of knee extension with verbal encouragement, with a rest period of at least 60s between trials. Contraction intensity was increased to maximum over approximately 1-2 s and was maintained for at least 3 s before relaxation. The peak of the torque profile was extracted from each trial. The highest torque of the three values was considered the maximal knee extension strength, and normalized to body mass. The submaximal task consisted of a single 70 s knee extension at 10% MVC. Participants were provided with real-time feedback of their knee extension torque and target.

High-density surface EMG signals were collected as monopolar recordings (128-channel EMG-USB[b]). Signals were amplified 500-1000 times, filtered (band-pass 10-750 Hz) and digitized at 2048 Hz using a 12-bit A/D converter. Knee extension torque was acquired simultaneously using the same amplifier. Butterworth filters (4^{th} order; 10-400 Hz for the EMG signals; low-pass 10 Hz for the torque) were applied to the signals before processing.

Motor unit discharges were identified separately for VM and VL using a previously described method [25] reliable between sessions [27] and valid when compared to a gold-standard, intramuscular electromyography [26]. An example of motor unit identification from surface EMG signals can be observed in figure 1. Motor unit firing patterns were reviewed visually and firing rates >30 Hz or <3 Hz were manually excluded [27]. Similar to a previous study [28], the MU template was created by averaging epochs of 40ms around each MU discharge. The peak-to-peak amplitude was calculated for each of the 13x5 channels to identify the location of each MU, i.e.: where it was represented with highest amplitude. Motor unit recruitment was identified as the first of four consecutive discharges <500 ms apart. The initial MU firing rate was calculated as the inverse of those first three MU inter-spike intervals. The neural drive was quantified two ways: as the initial firing rate at recruitment, and the average firing rate, calculated as the average firing rate between 5s and 35s after motor unit recruitment. Additional parameters used to describe the population of MUs identified were: MU recruitment threshold, calculated as the torque value coincident with the first motor unit discharge (see above); MU location, calculated as the proximal-distal coordinate of the channel with largest peak value (along the longest dimension of the electrode grid, fig.2).

Statistical analyses were performed using SPSS v. 22[e]. After logarithmic transformation of average firing rate and initial firing rate, the assumptions of normally distributed data (Shapiro-Wilk's test) and equal variances across groups (Levene's test) were met. Demographic variables and knee extension strength were compared between groups using unpaired T-tests. Differences in MU firing rates between *Groups* (PFP,

control) and *Muscles* (VM, VL) were tested using a two-way ANCOVA, separately for average firing rate and initial firing rate. To account for the effect of the MU recruitment threshold on average firing rate and initial firing rate, recruitment threshold torque was included in the model as a covariate. Effect sizes (ES) were calculated using Cohen's d, separately for each comparison. Two-way ANOVA was used to determine whether MU recruitment threshold torque or MU location differed between *Groups* or *Muscles*. Post-hoc tests were corrected for multiple comparisons using Bonferroni corrections. Statistical significance was set at $p<0.05$.

RESULTS:

When compared to controls, participants with PFP were of similar age, height, weight and physical activity but had higher BMI and lower knee extension strength (Table 1). Twenty-six participants with PFP reported bilateral symptoms. After visual inspection, a total of 414 MUs were identified and included in the analyses. The number of identifiable MUs included for each participant ranged from 2-10 (mean MU/participant=4.8; total N=96) for the VM and 1-12 (mean 4.3; N=86) for the VL of controls, and 0-8 (mean 3.0; N=104) for the VM and 0-8 (mean 3.6; N=128) for the VL of participants with PFP. No MUs were identified from the VM of one participant with PFP and from the VL of 3 participants with PFP.

An interaction effect between *Group* and *Muscle* was observed in the MU average firing rate analysis ($p<0.05$; fig.3). A higher average firing rate was observed in the PFP group compared to controls for VL (8.8±1.7 Hz vs. 8.2±1.6 Hz, $p=0.002$, ES: 0.34, 95% CI: [0.03 0.13]) but not for VM (8.9±2.0 Hz vs. 8.8±1.6 Hz, $p=0.93$, ES: 0.07,

95% CI: [-0.05 0.06]). VM had a higher average firing rate than VL in controls (8.8±1.6 Hz vs. 8.2±167 Hz, p=0.001, ES: 0.33, 95% CI: [0.04 0.15]), but no difference between the two vasti was observed in females with PFP (8.9±2.0 Hz vs. 8.8±1.7 Hz, p=0.78, ES: 0.04, 95% CI: [-0.04 0.05]). Similarly, an interaction effect between *Group* and *Muscle* was observed in the MU initial firing rate analysis (p=0.001; fig.3). A higher initial firing rate was observed in the PFP group for VL (7.4±2.1 Hz vs. 6.4±1.7 Hz, p<0.001, ES: 0.49, 95% CI: [0.07 0.21]) but not for VM (7.1±2.0 Hz vs. 7.1±1.7 Hz, p=0.55, ES: 0.03, 95% CI: [-0.09 0.05]). VM had a higher initial firing rate than VL in controls (7.1±1.7 Hz vs. 6.4±1.7 Hz, p=0.002, ES: 0.40, 95% CI: [0.05 0.20]), but no difference between the two vasti was observed in PFP (7.1±1.9 Hz vs. 7.4±2.1 Hz, p=0.17, ES: 0.17, 95% CI: [-0.11 0.02]). Neither *Muscle* nor *Group* influenced the recruitment threshold torque (p>0.2) or MU position (p>0.15, fig.3).

DISCUSSION:

This study found differences in MU firing rate across individual heads of the quadriceps between females with and without PFP. In females without PFP, VM motor units discharged at higher rates than VL. This difference was not observed in those with PFP and was explained by a higher VL firing rate. We suggest that the greater neural drive to the VL may contribute to altered patellofemoral kinematics, which is proposed to be relevant for PFP.

The evidence of higher neural drive to the VL in females with PFP implies a role of vasti muscle activation in the adaptation to, or in the development of, PFP. Our findings are strengthened by the fact that differences in neural drive cannot be attributed

to the location of the motor unit within the muscle or its recruitment threshold, as neither differed between groups or muscles. Previous studies identified altered timing and amplitude of surface EMG in PFP [10,12,16,18] and with experimental knee pain, [29–31]. Our findings appear to concur with studies that reported earlier activation for VL rather than delayed activation of VM in reflex contractions [32] and when participants with PFP were asked to rise onto their toes [33]. Overall, this study further expanded this research, showing that the distribution of neural drive between VM and VL, measured as motor unit firing rate, differs between females with and without PFP.

Changes in muscle activation with pain and in musculoskeletal disorders are thought to be a purposeful adaptation to avoid pain in the short-term by altering joint kinematics [34]. Previous studies on cadavers identified altered patellar kinematics [7] and pressure distribution within the patellofemoral joint [8] when the relative load of VM and VL was manipulated. In vivo studies showed that anesthetic block of the VM results in altered patellar kinematics [9], and studies using EMG timing and amplitude identified associations between VM/VL activation and patellar tilt [12,16]. Considering the results of these studies, a greater neural drive to the VL may result in larger force produced by the lateral component of the quadriceps. However, caution must be used when inferring forces from muscle activation because muscle force depends on both neural activation and peripheral factors at the muscle level [35]. As individuals with PFP appear to have smaller cross-sectional areas of the quadriceps muscles as a whole (systematic review by Giles and colleagues [36]), the neural drive is likely an important contributor to the relative amount of force produced by VM and VL. However, other factors such as

between-group differences in fiber type composition and structural parameters of the quadriceps should also be considered could also play a role.

Higher discharge rates of VL and similar discharge rate for VM suggest that neural drive to the quadriceps as a whole is higher in PFP. This is in contrast with the clinical belief that the quadriceps muscle is inhibited in PFP, and it could inform the mechanisms that should be targeted in future intervention studies. Functionally, the greater neural drive to VL (or potentially vastus intermedius or rectus femoris – not measured in this study) could be an attempt to compensate for a decreased overall force production capability of the knee extensors, observed as smaller quadriceps cross-sectional area [36]. Due to its architecture, VL mainly produces a force vector towards knee extension [5] and may be more efficient than VM to generate forces due to its greater physiological cross-section area [37]. However, as the VL also applies a laterally-directed force vector on the patella [5–7], a selective increase of neural drive could potentially result in increased lateral forces applied to the patella. In line with this, some studies reported increased lateral patellar spin and translation [38,39] and higher joint reaction forces in the lateral patellofemoral compartment in PFP [40]. The potential association between altered neural drive to the quadriceps and altered force production capabilities at the muscle could be observed in the cross-over effects of interventions targeting the two dysfunctions [42]. Future studies should investigate the association between force production capability of the quadriceps and neural drive to the VL in PFP.

The notion that unbalanced vasti activation may be due to greater neural drive to VL rather than VM inhibition may potentially have clinical implications. Traditionally, putative imbalanced activation of VM and VL in PFP is treated by enhancing the

activation of the medial component using techniques such as taping [43] and therapeutic exercise intended to preferentially target the distal region of the VM [42]. Less frequently, interventions such as taping [44,45] and botulinum injections [46] are aimed at reducing the activation or force produced by the VL. This study suggests that reducing neural drive to the VL as opposed to increasing neural drive to the VM may result in muscle activation patterns similar to individuals without PFP. Techniques that reduced/inhibit VL activation have a potential role in rehabilitation. This might be achieved in clinical practice using a variety of techniques, for instance, with taping techniques [44,45]. Given the assumed link between muscle activity and resultant joint kinematics, our findings support the notion that reducing drive to VL may have positive clinical outcomes. Future longitudinal studies should also evaluate if reducing the neural drive to the VL improves patellofemoral kinematics and kinetics in PFP, resulting in less degeneration of the lateral patellar facet [41]. The findings of this study may also be relevant for prevention. If differences in neural drive were present before the development of PFP, screening and early treatment may reduce the incidence of PFP; this however should be carefully evaluated in prospective studies. Overall, this study suggests that neural drive may be an important variable of interest in PFP, and further research into its clinical and biomechanical implications is warranted.

LIMITATIONS:

Due to the cross-sectional design of our study, whether the greater drive to the VL is an adaptation to, or precursor of, PFP cannot be determined. More research is needed to understand what drives the greater neural drive to the VL and if this motor

control alteration can be observed in tasks other than isometric contractions. The association between altered neural drive and differences in force production capabilities are not examined in the current study and should be assessed to make informed inferences on force production. It should be noted that changes in MU firing rate provide an accurate, but only partial, representation of changes in the neural drive. Changes in motor unit recruitment strategies, such as the number and population of active motor units, have been described with experimental knee pain [48] and are not accounted for by changes in firing rates. In addition, only females with PFP were tested in this study to limit the confounding effect of sex-differences in anatomy, muscle strength and neuromuscular strategies. For this reason, these findings are only generalizable to females with PFP; future studies should investigate whether similar findings are observed in males with PFP.

CONCLUSIONS:

Motor unit firing rate of the vastus lateralis, but not medialis, during low-force, isometric contractions differs between females with and without PFP. Neuromuscular control of individual quadriceps heads could be considered a possible target for future interventions aimed to prevention and management of PFP.

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FIGURES:

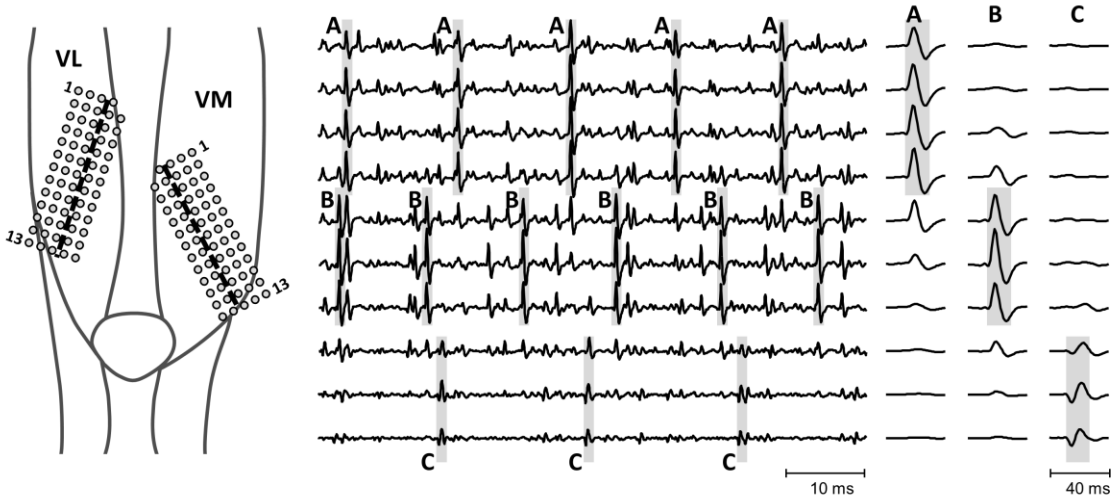

Fig.1: Experimental set-up and example of motor unit identification. Left: Placement of the electrode grids; the dashed line depicts the location of the innervation zones across both muscles. Middle: Double differential EMG signals from 10 channels of the VM of a control participant; three of the motor units automatically identified are highlighted with grey boxes (A, B, C). Right: the triggered-average surface EMG representation of each motor unit.

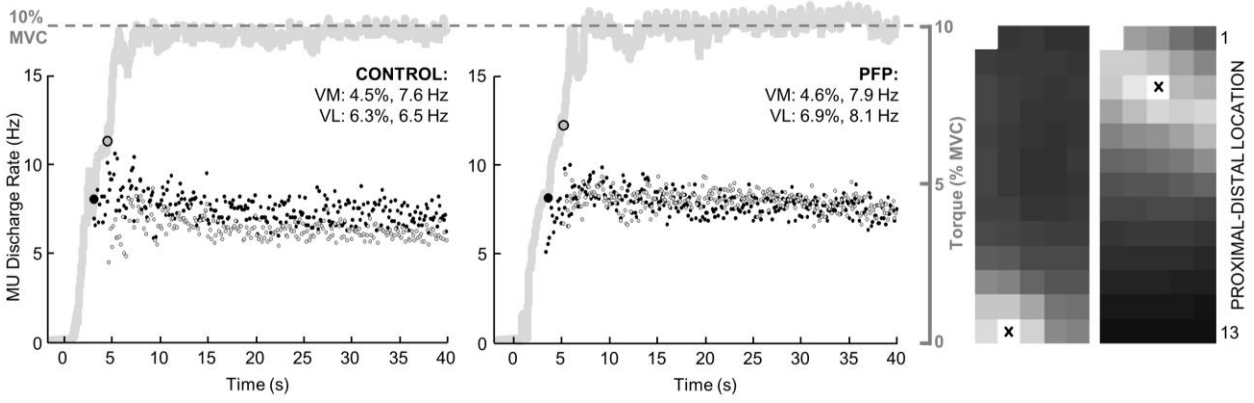

Fig.2: Motor unit discharges and location. Left: firing rate of one motor unit from VM (black) and VL (gray) in one control participant and one with PFP. The torque signal is shown as a thick, light grey line; the recruitment threshold of the VM and VL MU is indicated as a black and a gray circle respectively. Right: examples of motor units located distally and proximally within the VL. Crosses on each surface EMG amplitude distribution identify the peak of the distribution; the Y coordinate of that channel was considered to be the proximal-distal location within the muscle.

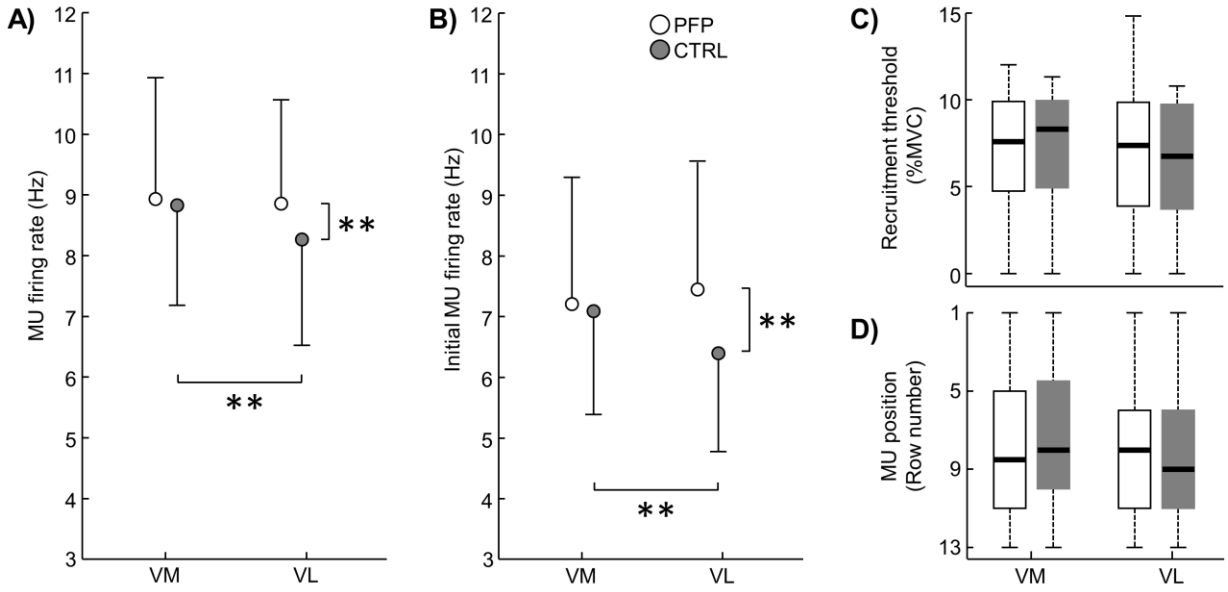

Fig.3: A) MU firing rate while holding 10% MVC. B) Initial MU firing rate. C) MU Recruitment threshold torque. D) MU position. Statistical significance for post-hoc comparisons is indicated. ** $p<0.01$.

TABLES:

Table 1: Participant characteristics and knee extension strength. Pain intensity was subjectively rated indicating a number between 0 (no pain) and 10 (worst imaginable pain). Anterior knee pain scores of 100 indicate maximal function and no pain. KES: knee extension strength; nKES: normalized knee extension strength.

	CTRL	**PFP**	**T-test**
AGE, years	25.6 (4.3)	26.7 (4.1)	*p*=0.38
HEIGHT, cm	167.7 (8.5)	166.4 (7.9)	*p*=0.59
BODY MASS, kg	58.2 (8.5)	62.3 (8.9)	*p*=0.10
BMI, kg/m^2	20.6 (1.7)	22.5 (2.9)	***p*=0.01***
PHYSICAL ACTIVITY [22]**, METmin/week**	3153 (2034)	4018 (2961)	*p*=0.20
PAIN ONSET, months (interquartile range)		12-60	
PAIN INTENSITY, out of 10	0 (0)	4.1 (1.5)	
ANTERIOR KNEE PAIN SCORE [23]**, out of 100**	100 (0)	74.3 (8.1)	

nKES, Nm/kg	2.3±0.4	1.9±0.5	***p*<0.01***
KES, Nm	135.3±32.9	116.5±30.6	***p*<0.05***

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