Title: Individuals with patellofemoral pain syndrome have altered inter-leg force coordination

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Highlights

- Patellofemoral pain syndrome (PFPS) is a common overuse leg injury.

- Greater inter-leg motor abundance may encourage greater inter-leg force sharing.

- PFPS impairs inter-leg motor abundance during bilateral hopping.

- Motor deficits occur during periods of shock absorption and peak bodyweight support.

- Impaired inter-leg force sharing may prolong pain in individuals with PFPS.

Abstract

Background: Patellofemoral pain syndrome (PFPS) is one of the most common musculoskeletal disorders. Pain may be further exacerbated by atypical motor coordination strategies. It has been thought that low coordination variability may concentrate loads onto painful knee tissues.

Research question: To investigate if inter-limb force coordination is altered between individuals with and without PFPS.

Methods: 31 individuals (control = 17, PFPS = 14) performed bilateral vertical hopping, on two force plates at three frequencies (2.2, 2.6, 3.0 Hz). Uncontrolled manifold analysis (UCM) was used to provide an index of motor abundance (IMA) in the coordination of inter-limb forces to stabilize the two-limb's total force. UCM was applied to the study of forces in each plane (medial-lateral (ML), anterior-posterior (AP), vertical). Bayesian Functional Data Analysis was used for statistical inference. We calculated the mean (u) with 95% credible interval (CrI) of the difference ($\Delta IMA_{con>PFPS}$) between the two groups. We also calculated the probability P ($\Delta IMA_{con>PFPS} > 0|data$).

Results: Individuals with PFPS had the greatest significant decrement from controls at 6% of stance hopping at 2.6Hz by a mean difference of -0.23 for ML GRF; at 19% of stance hopping at 2.2Hz by a mean difference of -0.14 for AP GRF; and 52% of stance hopping at 2.6Hz by a mean difference of -0.14 for vertical GRF. For vertical GRF, there was a > 0.95 probability that controls had greater IMA

than individuals with PFPS hopping between 12 to 13% of stance at 2.2Hz, and between 48 to 55% at 2.6Hz.

Significance: Individuals with PFPS have reduced inter-leg force coordination for impact force attenuation and body support, compared to asymptomatic controls. The present study provides insights into a plausible mechanism underpinning persistent knee pain which could be used in the development of novel rehabilitative approaches for individuals with PFPS.

Keywords: Motor control, Spring-mass, Biomechanics, Patellofemoral pain syndrome, Uncontrolled Manifold, Coordination.

1. Introduction

Patellofemoral pain syndrome (PFPS) is one of the most common musculoskeletal disorders [1]. Individuals with PFPS commonly experience anterior knee pain during activities which incur high patellofemoral joint (PFJ) loads – such as, running and jump-landing tasks [2, 3]. The overall tissue load during physical activities has been thought to be not only influenced by peak load magnitude, but also by how load varies across repeated movement cycles [4, 5]. High overall tissue loads can occur in the presence of constant (low variability) sub-maximal load magnitudes. The uncontrolled manifold (UCM) is a framework useful for quantifying how variability across repeated movement cycles is structured. Knowledge of how variability is coupled across the human kinetic chain is critical for understanding potentially injurious movement strategies.

The UCM quantifies how much of the inter-cycle variation between individual motor degrees of freedom (DOF) (e.g. force applied by a single leg), stabilizes or disturbs the inter-cycle variation of a movement goal (e.g. total force exerted on the body) [6]. Inter-cycle variation is "good" when the DOFs interact to reduce inter-cycle goal variation – example, when the left leg's force increases, the right leg's force decreases to keep total applied force constant [7]. Inter-cycle variation can be "bad" when their interaction disturbs the movement goal – such as when both legs' forces increase resulting in greater total force exerted. It has been proposed that the central nervous system (CNS) only controls combinations of DOF which disturbs the movement goal [6]. Combinations of DOF which stabilizes the goal remain free to vary [6]. When more of the inter-cycle variation between motor DOFs is "good" than "bad", the motor control system is said to exhibit motor abundance [7].

Uncontrolled manifold analysis first requires identifying relevant task mechanical goals to determine the functional purpose of variability. Bilateral vertical hopping at a constant frequency represents an ideal motor paradigm to investigate since there are at least three behavioural goals to be maintained between cycles (explicit goal - hop frequency; implicit goals – minimise medial-lateral [ML] and anterior-posterior [AP] body displacements). These behavioural goals are in turn reflected by three mechanical goals – constant total vertical, ML, and AP GRF between cycles. In healthy individuals, the body harnesses motor abundance to regulate the vertical GRF, via the coordinated action of

individual joints [8], as well as that of the bilateral lower limbs [9]. It has been thought that motor abundance to stabilize inter-cycle variation of vertical GRF in hopping is a strategy to maintain constant hopping frequency, but also helps minimize joint loading fluctuations, and minimize energy expenditure [7]. Greater motor abundance may be optimal in individuals with PFPS whilst hopping as it allows more flexible use of each leg for force generation, increasing load distribution.

We adopted the UCM framework to investigate inter-limb force coordination during bilateral hopping in individuals with and without PFPS. We hypothesized that individuals with PFPS would exhibit a smaller index of motor abundance in the regulation of the vertical, AP, and ML GRFs compared to healthy individuals. Prior studies have shown a capacity for humans to harness greater motor abundance as task intensity increases [10] . Hence, we hypothesized that motor abundance between individuals with and without PFPS will become more similar at faster than slower hopping intensities.

2. Methods

2.1. Participants

All participants were screened by a clinical physiotherapist for the following criteria. Male and females participants were included into the PFPS group if they were: 1) between 18- 45 years old [4]; 2) have a knee pain intensity of $\geq 3/10$ on the visual analogue scale (VAS) during at least two of the following activities - running, squatting, prolonged sitting, stair climbing, or jumping; 3) ≥ 6 points on the SNAPPS questionnaire (Survey instrument for Natural history, Aetiology and Prevalence of Patellofemoral pain Studies) [11]. Participants were eligible to be included in the control group if they had no lower limb pain within the past 12 months. Participants were excluded from the study if they had 1) knee pain from an acute injury or from other disorders; 2) history of patellar dislocation; 3) previous knee surgeries within the past 12 months; and 4) females currently pregnant. Ethical clearance was obtained from the Ethics Committee of University of Birmingham, United Kingdom (MCR041218-1).

We performed a sample size calculation from a Bayesian perspective using the "BayesMAMS" package in R software, given that Bayesian statistical inference was performed. Given a standard deviation of motor abundance value of 0.4 [12], 13 individuals per group was required to yield a posterior probability >0.95 of detecting a difference in motor abundance between pain groups of 0.5 [13]. Thirty-one participants participated and completed the study (PFPS, n = 14, mean (standard deviation) age 20.86 (1.83) years, height = 1.71 (0.10) m, mass = 64.96 (10.51) kg; control, n = 17, age 23.47 (2.67) years, height = 1.70 (0.08) m, mass = 67.02 (10.87) kg).

2.2. Experimental setting

The following subjective measures were collected for individuals with PFPS: current pain intensity on a visual analogue scale (0 no pain-10 maximum pain), current knee related function using the Knee Injury & Osteoarthritis scale (KOOS), and a KOOS patellofemoral subscale (KOOS-PF). Bilateral vertical hopping was performed on two 60 x 40 cm in-ground force plates sampling at 500 Hz (BTS P6000, BTS Bioengineering, Italy). Participants performed the task in their own comfortable exercise attire and shoes. Participants stood with one foot on each plate, with their arms fixed at 90° abduction. Participants performed continuous vertical hopping in-sync to an auditory metronome, set to three frequencies (preferred 2.2Hz, intermediate 2.6 Hz, fast 3Hz) [14], the order of which was randomized. The preferred human hopping frequency is at 2.2 Hz, and frequencies above this value yield a linear spring-mass behaviour [15]. For each frequency, two successful sets of 15 s hopping was required with one minute of rest provided between sets. A successful set of hopping is defined by a visual inspection of hopping in real-time that each foot was on the same plate, and that participants could keep sync with the metronome beat >50% of the set's duration.

2.3. Data processing

Force data were low-pass filtered at 75Hz (4th order, zero-lag, Butterworth), time-normalised to 100 data points between initial contact and toe-off and scaled to each individual's static standing weight (N). A threshold of 20 N in the vertical GRF was used to identify the hopping events. Only hopping cycles that were within a ± 5% window of the prescribed hopping frequencies were retained for UCM

analysis. Thirty hopping cycles were available for each participant-frequency combination for UCM analysis.

2.4. UCM analysis

UCM analysis (Equations 1 - 5) was performed on each axis of the GRF, and each 1% of the hopping stance phase [7, 8]. In bilateral hopping, forces applied by the right and left legs determine the total force ($Equation$ 1). This simple relationship describes a two DOF system (n = 2) regulating a one DOF movement goal (d = 1), which can be represented by a 1 x 2 Jacobian (J) matrix. We used UCM to partition the cycle-to-cycle inter-leg force variance into 1) Goal-equivalent variance (GEV, "good"): meaning that inter-leg forces co-varied to stabilize total GRF ($Equation$ 2); and 2) Non goal equivalent variance (NGEV, "bad"): when inter-leg forces varied to disturb GRF ($Equation$ 3); 3) total leg force variance per DOF (TOTV), where C is the covariance matrix of leg-forces.

$$F_{net} = F_{left} + F_{right} \ (Equation\ 1)$$

$$GEV = \frac{trace\ (null\ (J)^T \cdot C \cdot null\ (J))}{n - d}\ (Equation\ 2)$$

$$NGEV = \frac{trace\ (orth(J^T)^T \cdot C \cdot orth\ (J^T))}{d}\ (Equation\ 3)$$

$$TOTV = \frac{trace\ (C)}{n}\ (Equation\ 4)$$

An index of motor abundance (IMA) is calculated using Equation 5. An IMA > 0 indicates that the inter-leg force variation is used to stabilize total applied GRF. Clinically, if healthy individuals hop with a more positive IMA than individuals with PFPS, the former uses a more flexible inter-leg strategy than the latter, to stabilize total force variation. An IMA < 0 indicates that inter-leg force variation disturbs total applied GRF.

$$IMA = \frac{GEV - NGEV}{TOTV}\ (Equation\ 5)$$

2.5. Statistical inference

Descriptive statistics (mean with standard deviation [sd]) were calculated for baseline demographic variables of age, height (m), mass (kg), current pain intensity, KOOS and KOOS-PF [16, 17]. The dependent variable was the time-varying IMA, whilst the independent variables were group, frequency, and the group-by-frequency interaction. Bayesian functional regression was performed in R software [18], to quantify $P\ (\beta > u | data)$ – meaning the probability that an effect β exceeds a threshold u given the data we collected. Fixed effect parameters for group, frequency, their interaction, and non-parametric smooth functions (modelled with 15 B-splines) were estimated using a Gibbs sampler with a burn-in of 1,000 and drawing 11,000 inference samples. The residual covariance structure was estimated using Bayesian functional principle components [18]. We calculated the mean with 95% credible interval (CrI) of the difference ($\Delta IMA_{con>PFPS}$) between the two groups. The $P\ (\beta > u | data)$ was calculated using the 10 000 posterior samples. Specifically, we calculated $P\ (\Delta IMA_{con>PFPS} > 0 | data)$. All data, codes, and a step-by-step implementation of UCM analysis using simulated data, are included in the supplementary material.

3. Results

Descriptive statistics of the demographic data can be found Table 1. The group average GRF and the inter-cycle GRF variance plots are found in the supplementary material (Figure S1, S2). The IMA shows a general pattern of > 0 in the second half of stance for the ML GRF (Figure 1a), a pattern of < 0 over the stance phase for the AP GRF (Figure 1b), a pattern of > 0 over the stance phase for the vertical GRF (Figure 1c).

Table 1. Mean (standard deviation) of patient and pain characteristics.

Variables	PFPS (n = 14)	Control (n = 17)
Sex	6M, 8F	9M, 8F
Painful side	6R, 4L, 4Bilateral	-
Leg dominance (side used to kick ball)	14R	17R
Pain VAS (0 no pain-10 max pain)	3.71 (2.02)	-
KOOS-adl (0 indicating extreme symptoms-100 no symptoms)	85.29 (17.83)	100 (0)

KOOS-pain (0 indicating extreme symptoms-100 no symptoms)	74.60 (16.12)	98.69 (2.62)
KOOS-qol (0 indicating extreme symptoms-100 no symptoms)	58.04 (17.24)	97.43 (6.65)
KOOS- sports (0 indicating extreme symptoms-100 no symptoms)	68.93 (26.90)	98.53 (3.43)
KOOS-symptoms (0 indicating extreme symptoms-100 no symptoms)	71.17 (16.42)	96.85 (5.19)
KOOS-pf (0 indicating extreme symptoms-100 no symptoms)	68.99 (18.90)	99.47 (1.71)
Abbreviations: VAS – visual analogue scale; KOOS - Knee Injury & Osteoarthritis Outcome; adl – activities of daily living; qol – quality of life; pf – patellofemoral sub-scale		
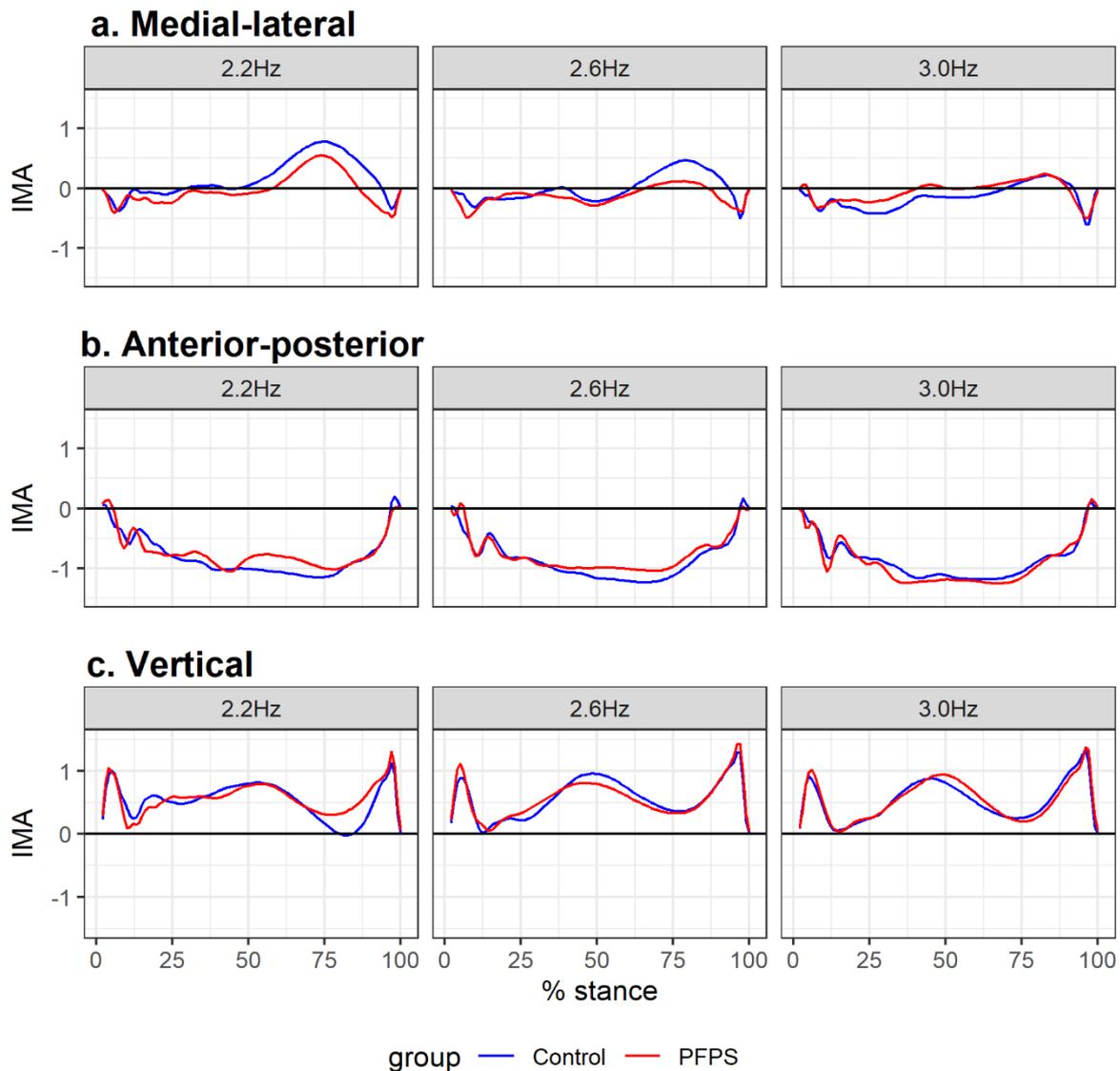
Figure 1

For the ML GRF, there was a > 0.95 probability that controls had greater IMA than individuals with PFPS between 84-95% at 2.2Hz, 4-10% and 75-92% at 2.6Hz (Figure 2a). For the AP GRF, there was a > 0.95 probability that controls had greater IMA than individuals with PFPS between 17-21% at 2.2Hz (Figure 2b). In the stabilization of the vertical GRF, there was a > 0.95 probability that controls had greater IMA than individuals with PFPS between 12 to 13% of stance at 2.2Hz, and between 48 to 55% at 2.6Hz (Figure 2c). Individuals with PFPS had the greatest decrement from controls at 6% of stance at 2.6Hz (-0.23 [95%CrI -0.237 to -0.09]) for ML GRF; 19%

of stance at 2.2Hz (-0.14 [95%CrI -0.28 to 0.02]) for AP GRF; and 52% of stance at 2.6Hz (-0.14 [95%CrI -0.28 to 0.02]) for vertical GRF (Figure 3).

Figure 2

a. Medial-lateral

b. Anterior-posterior

c. Vertical
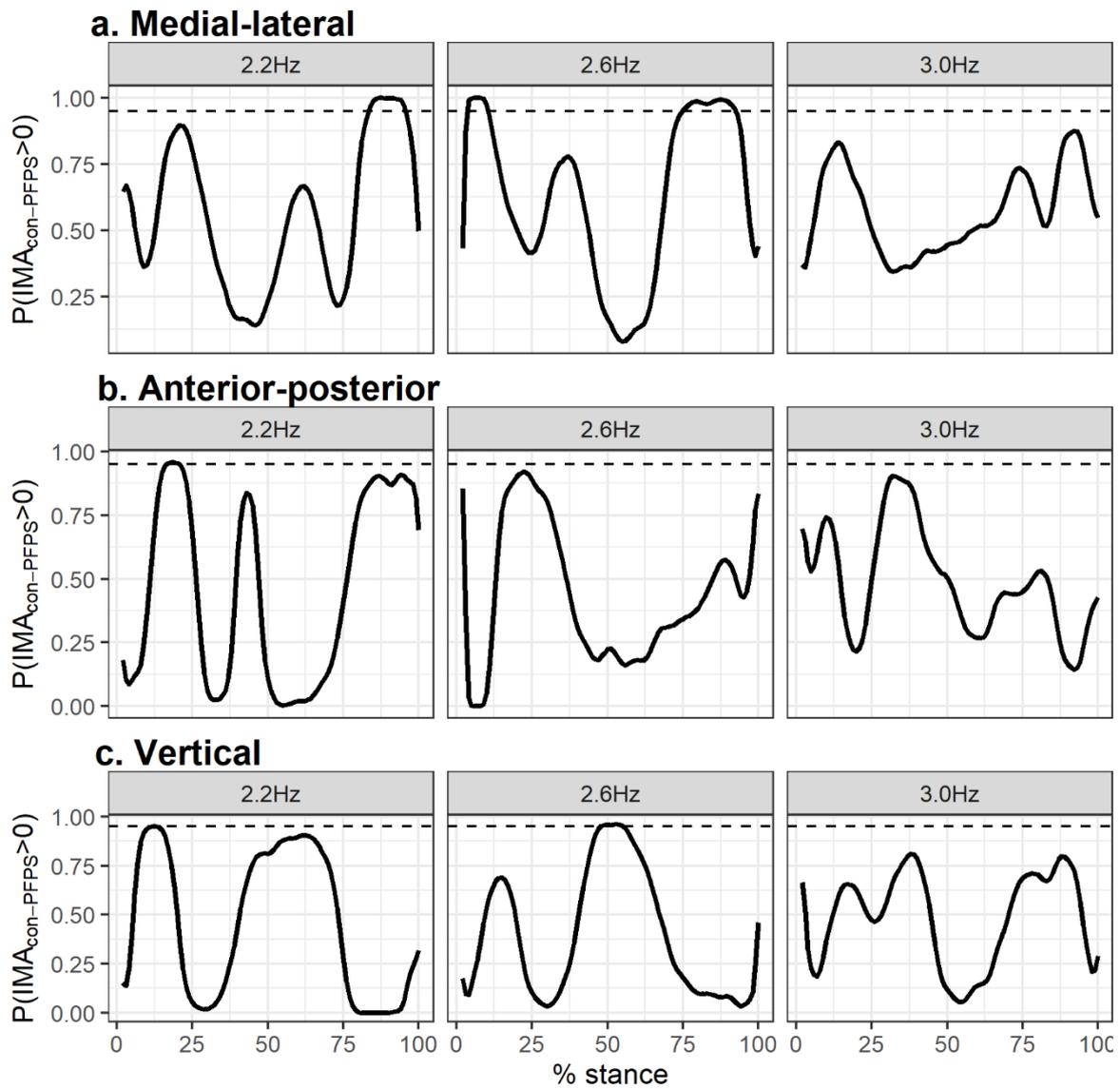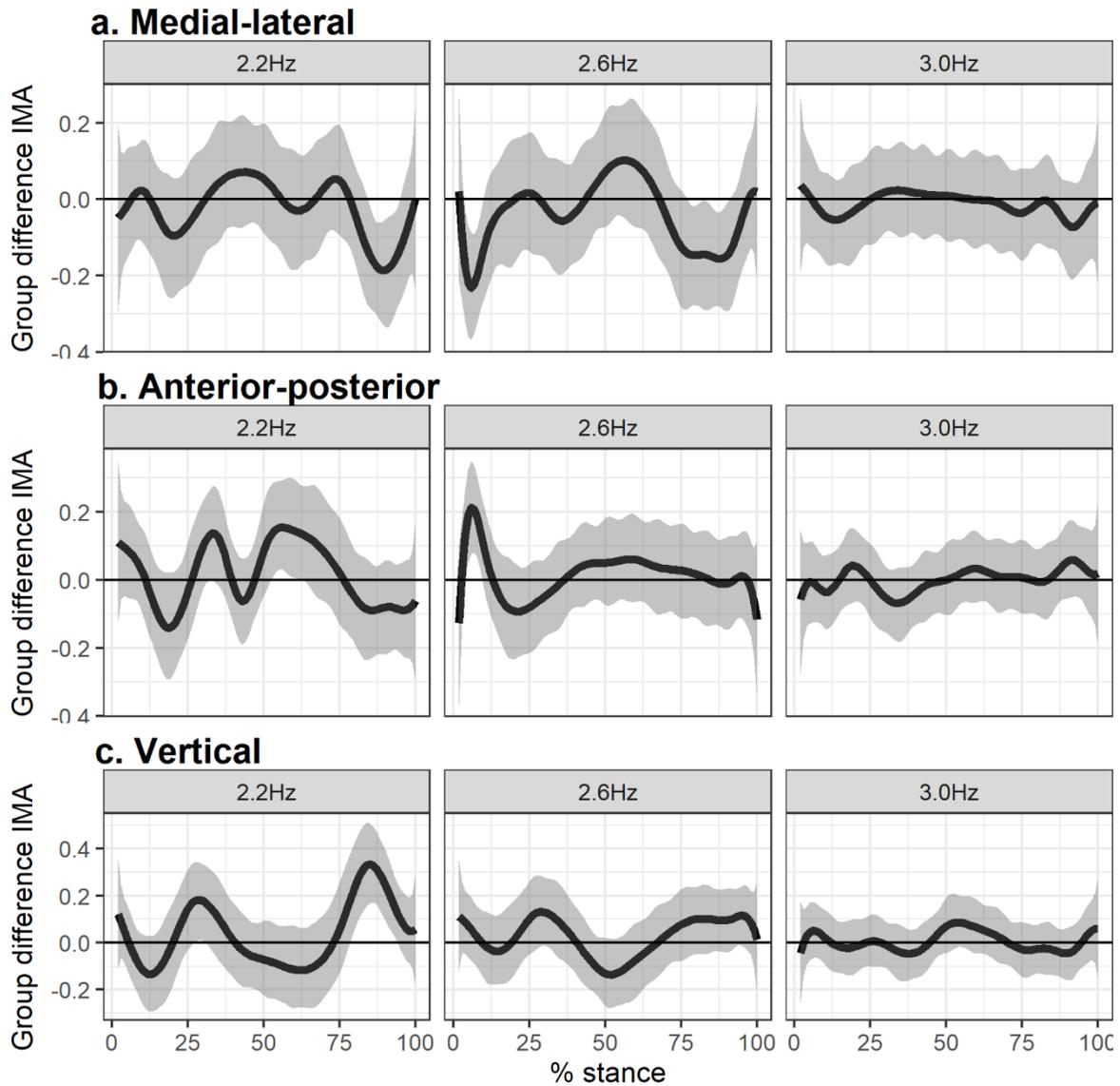
Figure 3

4. Discussion

Individuals with PFPS have been reported to have altered motor control strategies compared to controls [4, 5], which could exacerbate knee loads and pain. In the present study, we observed several findings that stood in partial support of our hypotheses. First, all individuals harnessed inter-leg force co-variation to stabilize vertical GRF, but this co-varying effect disturbed AP GRF. Second, between group differences in motor abundance reduced at faster hopping frequencies.

A common strategy in all participants was to harness inter-leg force co-variation to stabilize the vertical GRF. The overall pattern of the IMA waveform in the vertical direction was consistent with previous studies [7, 8], with peak maxima in IMA happening at landing, mid-stance, and take-

off. A high motor abundance during landing and mid-stance is essential for minimizing vertical force fluctuations, when the rate of force development and peak force are high, respectively in these periods. In attempting to keep constant an explicitly defined goal of constant hopping frequency (and total vertical GRF), the ensuing structure of motor variability may compromise high knee loads across movement cycles. At take-off, inter-leg vertical force co-variation may be important to fine tune force generation that determines aerial time and hence, hopping frequency [7].

Inter-leg force co-variation may not be harnessed to stabilize the AP GRF as the explicit movement goal was not to maintain a precise constant hopping position. This means that the participants can make corrective force adjustments between cycles to minimize disturbance to the average AP position. For example, if greater total posterior GRF was exerted in one cycle, the individual's hopping location will be shifted anteriorly, which can be corrected in the subsequent cycle by generating a greater total anterior GRF. Even though maintaining a similar ML position was not an explicit movement goal, the physical boundaries of the hopping space could have constrained the movement goal. All participants were asked to hop with one foot on each plate, which limits the allowable distance they can deviate medial-laterally. Implicitly, this means that both legs must ensure adequate inter-leg ML abundance, so that the total ML GRF is consistently close to zero. Otherwise, one foot will deviate onto the other foot's force plate. Inter-leg ML IMA is more important in the second half of stance, than in the first half, as the propulsion phase determines the ML COM displacement during the flight phase, and the successive ML landing position.

The periods of hopping where individuals with PFPS have reduced vertical force motor abundance compared to controls, were at landing (12 to 13% stance) and mid-stance (48 to 55%) stance –corresponding to episodes where vertical loading rate is highest [19], and knee joint torque is highest [7], respectively. The magnitude of the vertical GRF loading rate [20] and peak PFJ loads [21] have both been reported to correlate with knee pain intensity. The reduced inter-leg vertical force abundance in these phases may reduce inter-leg load distribution, a potential mechanism for the perpetuation of pain. Alternatively, reduce inter-force abundance with pain could be a consequence of either pain (i.e. "pain adaptation model" [22]) in which muscle activity which produces a painful

movement is inhibited; or fear, in which individuals avoid loading the painful limb [23]. Speculatively, it is possible that a greater unilateral pain experienced during hopping, or fear of loading the painful limb, would encourage a unilateral (less painful side) force control strategy. Future prospective studies are needed to know if altered motor abundance is a cause or consequence of pain or fear, whilst future would benefit from quantifying the actual pain intensity and fear levels experienced with the motor task.

The between-group differences in motor abundance in all three axes reduced as hopping frequency increased. This suggests that individuals with PFPS may have a "reserve capacity" to harness more motor abundance when required [10, 24]. As hopping frequency increases, the body shifts intra-leg control of the vertical GRF from a strategy involving the hip-knee-ankle joints, to an independent ankle strategy [8]. Given that individuals with PFPS have knee extensor strength deficits [25], it may be that the higher hopping frequency shifted the locus of control to the less impaired ankle extensors, which increases each leg's capacity to compensate for force deviations of the opposite leg.

An interesting observation was that individuals with PFPS had more abundance than controls to stabilize the vertical GRF, but less abundance to stabilize the ML GRF during take-off. This suggests that individuals with PFPS used inter-leg coordination to increase stabilization of the vertical GRF to maintain a constant hopping frequency; at the cost of reducing the stabilization of the ML GRF. It is not that humans are incapable of simultaneously stabilizing constant total GRF in all axes with two limbs [7]. Humans can hop at a constant frequency whilst either choosing to hop forward/backwards or remain in-situ. It may be that individuals with PFPS have reduced lower limb proprioceptive capacity than controls [26], which affects the former's ability to perceive slight ML positional deviations and make corrective ML force adjustments. Travers et al. (2013) [27] developed a hopping proprioceptive test to quantify the capacity of individuals to detect subtle variations to vertical ground depth. Such a test has not yet been adopted for individuals with lower limb pathologies but could be adapted to similarly test the proprioceptive ability to detect horizontal positional deviations in hopping. Given that the present study did not further quantify other

biomechanical and neurophysiological measures, the mechanisms underpinning the effects of knee pain on inter-leg force abundance during hopping cannot be presently determined.

Findings from the present study have implications for field monitoring of altered motor control towards the management of lower limb injuries. Clinically, bilateral tibia vertical acceleration measured by wearable accelerometers could be used as surrogate measures of vertical GRF [28]. Visual feedback of motor abundance may then be provided to individuals after task performance, and compared to a healthy cohort. Such feedback may be used as a means for rehabilitation, if an individual has reduced motor abundance than controls. Prior to clinical implementation, prospective studies needs to be conducted in individuals with PFPS to define thresholds such as a minimal detectable change and minimal clinical important change.

Motor abundance for a specific movement goal in individuals with PFPS, may be enhanced by adding motor constraints. For example, motor abundance for stabilizing total AP force may be increased by reducing the physical space available for hopping. A smaller space means that total AP force variance must be low, facilitating greater inter-leg force abundance in that plane [24]. Motor abundance has also shown to be enhanced by using instructional verbal cues that facilitates an external, rather than internal focus of attention [29]. Weakened muscles operating at their force limits cannot compensate for the reduction in forces by other muscles. Given that individuals with PFPS have neuromuscular deficits, resistance training could also be used to enhance motor abundance [30].

5. Conclusion

Individuals with PFPS have a reduced inter-leg force abundance compared to controls to stabilize the vertical GRF in key phases of the hopping cycle, where vertical GRF loading rate and peak magnitude are high. Individuals with PFPS also shifted more inter-leg force control to stabilize the vertical GRF compared to controls, to the detriment of stabilizing the ML GRF at take-off. Collectively, the present results suggest an inability to use inter-leg force control to simultaneously stabilize multiple movement goals in individuals with PFPS. The present study provides insights into

the plausible mechanism underpinning persistent knee pain which could be used in the development of novel rehabilitative approaches for individuals with PFPS.

Figure 1. Group averaged index of motor abundance (IMA) across the stance phase of vertical hopping. IMA in control of (a) medial-lateral, (b) anterior-posterior, and (c) vertical ground reaction forces (GRF). Abbreviation: PFPS = patellofemoral pain syndrome.

Figure 2. Probability of index of motor abundance (IMA) in the control group exceeding that of individuals with PFPS ($P \Delta IMA_{con>PFPS} > 0$). The probabilities of $\Delta IMA_{con>PFPS} > 0$ in the control of (a) medial-lateral, (b) anterior-posterior, and (c) vertical ground reaction forces (GRF). Abbreviation: PFPS = patellofemoral pain syndrome. Dashed (---) lines indicate a 95% probability threshold.

Figure 3. Mean with error clouds as 95% credible intervals (CrI) of the difference (PFPS minus control) in the index of motor abundance (IMA) between individuals with and without PFPS. Mean IMA differences in the control of (a) medial-lateral, (b) anterior-posterior, and (c) vertical ground reaction forces (GRF). Abbreviation: PFPS = patellofemoral pain syndrome.

Figure S1. Group averaged ground reaction force (% bodyweight) in the (a) medial-lateral, (b) anterior-posterior, and (c) vertical direction. Abbreviation: PFPS = patellofemoral pain syndrome.

Figure S2. Group averaged inter-repetition variance of total (right+left) ground reaction force (% bodyweight) in the (a) medial-lateral, (b) anterior-posterior, and (c) vertical ground direction. Abbreviation: PFPS = patellofemoral pain syndrome.

Supplementary figures

a. Medial-lateral

b. Anterior-posterior

c. Vertical
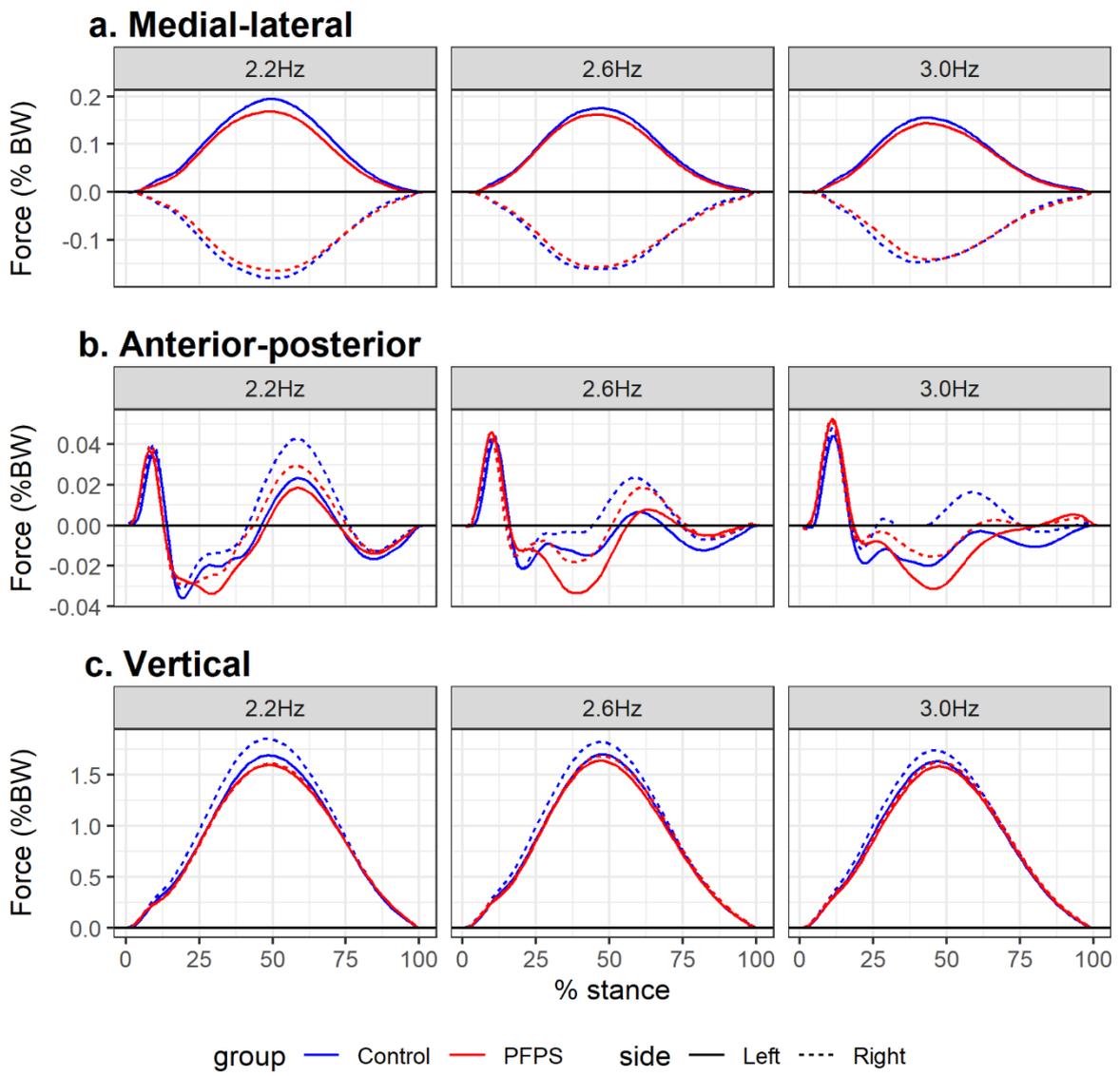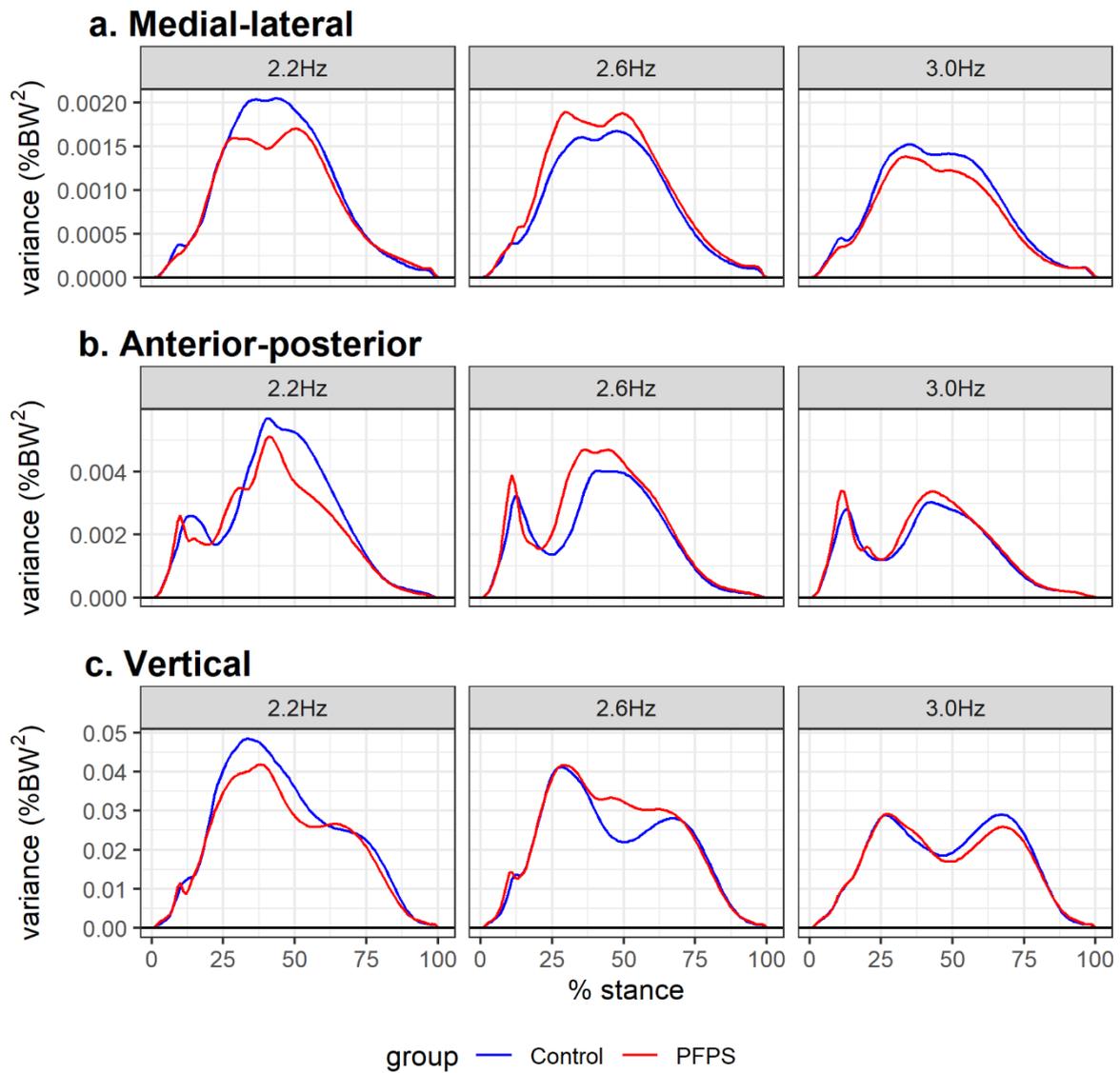
Figure S1

Figure S2

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