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Differential Activation of the Vastus Medialis and the Vastus Medialis Oblique in Individuals with and without Patellofemoral Pain Syndrome

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by

Yi-Ling Peng

Dissertation

Presented to the Faculty of the Graduate School of

The University of Texas at Austin

in Partial Fulfillment

of the Requirements

for the Degree of

Doctor of Philosophy

The University of Texas at Austin

May 2019

Abstract

Differential Activation of the Vastus Medialis and the Vastus Medialis Oblique in Individuals with and without Patellofemoral Pain Syndrome

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The University of Texas at Austin, 2019

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An imbalance of medial and lateral quadriceps control can lead to patellofemoral pain syndrome (PFPS). The incidence rate of PFPS is twice as high in females than in males. The aims of this research were to investigate sex differences in quadriceps neuromuscular control and motor unit recruitment properties in healthy individuals comparing to those with PFPS. We also investigated optimal leg position and levels of force production to target the vastus medialis oblique (VMO). In Study One, quadriceps surface EMG onset time and amplitude were examined at different submaximal force levels in asymptomatic males and females with and without PFPS. Females showed a 320 ± 70 ms delay in average quadriceps onset time relative to males. The vastus lateralis (VL) and VMO activated together and prior to the vastus medialis (VM) and rectus femoris. A low force (25%MVC) generated the lower VMO:VL ratio compared to 50% and 75% MVC. In order to determine if the VMO was controlled independently of the VM, Study Two examined motor unit recruitment patterns in the VM and VMO in healthy males and females when performing straight leg tasks in two different hip positions. VMO motor units were recruited 2.92

± 1.28% MVC earlier than VM motor units. Females fired motor units in the vastus medialis complex faster than the males. We found that hip position is a crucial factor influencing motor unit recruitment properties in the vastus medialis complex. In a neutral hip position, motor units in the VM were activated at lower recruitment thresholds and at faster firing rates compared to in lateral hip rotation. Study Three evaluated the effect of PFPS on VM and VMO motor unit recruitment during two different hip positions of straight leg raise in females with and without PFPS. Individuals with PFPS showed an altered control strategy of VMO motor units between the two hip positions compared to healthy individuals. A traditional straight leg raise without hip rotation generated greater VMO motor unit initial firing rates in healthy individuals. However, VMO motor units were recruited at faster rates in lateral hip rotation for individuals with PFPS. The findings from this series of studies indicate that the neuromuscular control strategies of the quadriceps muscle subsections were affected by sex, PFPS, hip position as well as force level. These factors should be taken into consideration when designing rehabilitation protocols.

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Chapter 1: Introduction

Generalized knee pain is the most prevalent source of joint pain in the United States (CDC, 2008). Over the past 20 years, rates of clinical knee pain have increased substantially, afflicting one-fourth of Americans (Foss et al., 2012; Roush & Curtis Bay, 2012). Knee pain diminishes a patient's capacity and desire to ambulate and limits the ability to perform daily activities. The intensity of the initial knee pain is highly predictive of future decreases in the ability to stand up from chair-sitting (Sharma et al., 2003). Patellofemoral pain syndrome (PFPS) is the most common knee joint pathology diagnosis among other causes of anterior knee pain in clinical practice (Foss et al., 2014). It has 2.23 times higher incidence rates in women than in men, which indicates that sex is a crucial predictor in developing PFPS (Boling et al., 2010). Patellofemoral dysfunction is significantly more common in female athletes compared to male athletes in prevalence studies (Foss et al., 2014), and females have 25% more probability to have history of PFPS than males (Boling et al., 2010).

Imbalanced muscle control of the medial and lateral quadriceps causing mal-tracking of the patella is believed to be the primary contributing factor to PFPS (McConnell, 1996; Boling et al., 2006). During walking, the higher the ratio of the vastus lateralis (VL) to the vastus medialis (VM), the more severe was mal-tracking of the patella in individuals with PFPS (Pal et al., 2012). Moreover, delayed and lower recruitment of the vastus medialis oblique (VMO) relative to the VL may lead to the development of PFPS and maintenance of knee pain (McConnell, 1996; Boling et al., 2006). The higher prevalence of PFPS in females may be due to sex differences in VMO:VL activation patterns (Bowyer et al., 2008). Greater medial to lateral quadriceps ratios were found in healthy males compared to healthy females in a maneuver testing quadriceps activation with subjects flexed and leaned on the examined knee (Myer et al., 2005). In contrast, no sex differences in VMO:VL ratio were observed during open and closed kinetic chain exercises (Herrington et al., 2006; Bowyer et al., 2008). Several methodological differences between these studies, such as variable electrode placements and normalization procedures, could be the reasons causing the differences. As inadequate VMO activity in females has been a proposed cause for their higher rate of PFPS, few studies have examined the sex difference in temporal control of the medial and lateral quadriceps.

Anatomical evidence suggests that there is a functional difference between the VM and VMO based upon differences in muscle fiber pennation (Farahmand et al., 1998). The VM is the proximal two thirds of the medial side of quadriceps; the distal one third is another distinct portion, the VMO (Bennett et al., 1993; Prentice, 2003). The VMO runs oblique to the medial side of the patella and assists with medial patellar translation, while the VM runs more longitudinally and contributes to knee extension (Bennett et al., 1993). Anatomical studies have also reported that while the VM and VMO are both innervated by nerve roots originating from L1, L2, and L3, the VMO is controlled by a larger number of terminal nerve branches per area than the VM (Thiranagama, 1990; Jojima et al., 2004). Together, these anatomical findings support the possibility that the VM and VMO can be controlled independently.

More recently, fine-wire EMG studies from our laboratory reported differential discharge patterns between the VM and VMO (Tenan et al., 2013; Tenan et al., 2016). Healthy females showed slower initial motor unit firing rates in the VMO than in VM and this recruitment pattern in the vastus medialis complex changes according to different menstrual phases (Tenan et al., 2013). Gallina et al. used a surface EMG grid to evaluate how changing fiber orientation in the vastus medialis complex affects its peak muscle activation and reported that peak amplitude was higher in the VM than in the VMO during isometric knee extension (Gallina et al., 2016). However, there is still insufficient research regarding targeted VMO training for PFPS in clinical exercise protocols.

Various protocols of seated knee extension (Witvrouw et al., 2000; Crossley et al., 2002; Herrington & Al-Sherhi, 2007; Nakagawa et al., 2008) and supine straight leg raise (Witvrouw et al., 2000; Tyler et al., 2006; Kettunen et al., 2007; Nakagawa et al., 2008) in clinical practice can improve muscle strength, pain severity, and functional activities in individuals with PFPS. Differences in activation patterns among the quadriceps at submaximal force levels has not been found in healthy individuals (Rainoldi et al., 2008; Spairani et al., 2012) or in individuals with PFPS. However, if imbalanced quadriceps activation is a contributing factor to PFPS, the altered muscle recruitment pattern may vary when pain level is aggravated by higher force production.

This dissertation proposes three studies which will examine neuromuscular control of the superficial quadriceps subsections and to evaluate motor unit recruitment properties in the vastus medialis complex in commonly prescribed exercise protocols for PFPS.

Specific Aim 1: Determine the effect of sex on quadriceps onset time and EMG amplitude at different force levels during isometric knee extension in healthy individuals compared to females with PFPS.

Hypotheses: VMO onset time will be delayed and activation amplitude will be smaller relative to VL in healthy females compared to healthy males. Similarly, VMO onset time will be delayed and activation amplitude will be smaller relative to the VL in females with PFPS compared to healthy females. There will be differences in the muscle activation amplitudes in quadriceps and in VMO:VL ratios at different force levels.

Specific Aim 2: Determine the effect of sex on VM and VMO motor unit recruitment properties when performing a straight leg raise with two hip positions in a healthy population.

Hypotheses: VMO motor units will exhibit earlier recruitment thresholds and faster initial firing rates relative to VM motor units. Males will recruit VMO motor units earlier and at a faster rate than females. VMO motor units will be activated earlier at lower recruitment thresholds and at faster rates in lateral hip rotation than in a neutral hip position.

Specific Aim 3: Determine motor unit recruitment properties when performing straight leg raise with two hip positions in females with PFPS compared to healthy females.

Hypotheses: Females with PFPS will demonstrate a delayed recruitment threshold in VMO motor units compared to healthy females. VMO motor units will be activated earlier at a lower recruitment threshold and a faster rate in lateral hip rotation compared to a neutral hip position for both asymptomatic and symptomatic groups.

The overall goal of the research is to examine sex differences in quadriceps neuromuscular control and motor unit recruitment properties in different exercise protocols in healthy individuals and those with PFPS. This dissertation will be the first series of studies to evaluate the differential activation of the VM and VMO in clinical rehabilitation exercises between sexes and between individuals with and without PFPS. It is also the first study to investigate the effects of sex and force on quadriceps onset time and EMG activation patterns in healthy and PFPS populations. This research demonstrates the long-held clinical belief of preferential activation of the VMO to improve patella stabilization. Moreover, it provides a more thorough evaluation on the role of sex in quadriceps neuromuscular control which is believed to be the reason of high occurrence of PFPS in females.

Chapter 2: The Effect of Sex on Neuromuscular Control of Quadriceps Muscles during Various Levels of Knee Extension Force in Individuals with and without Patellofemoral Pain Syndrome

ABSTRACT

Patellofemoral pain syndrome (PFPS) is twice as prevalent in females as in males. The primary reason for higher incidence in females is believed to be imbalanced control of the quadriceps on patellar stabilization. Few studies have evaluated sex differences in quadriceps muscle onset times and activation patterns. Furthermore, it is unknown if the activation patterns of the vasti muscles differ at different force levels in healthy individuals and individuals with PFPS. The purpose of the study is to investigate sex differences in quadriceps onset time and EMG amplitude at three different force levels during isometric knee extension in an asymptomatic population compared to those with PFPS. Thirty-five participants (13 healthy males, 12 healthy females and 10 females with PFPS) performed isometric knee extensions at 25%, 50%, and 75% of maximal voluntary contraction force (MVC). Surface electromyography (EMG) was recorded from the vastus lateralis (VL), vastus medialis oblique (VMO), vastus medialis (VM) and rectus femoris (RF) muscles. Repeated measure ANOVAs with Bonferroni post hoc tests were used to analyze EMG onset time and average holding EMG amplitude (normalized to maximum). The VL activated earlier than the VM and RF, but did not differ from the VMO in the healthy and PFPS groups. Healthy females had delayed quadriceps recruitment compared to healthy males. At 25% MVC, the VL showed a higher activation than the rest of quadriceps while a balanced activation pattern was observed at 50% and 75% MVC. A lower VMO:VL activation ratio was found at 25% MVC. Thus, delayed activation of the quadriceps in females may be a risk factor causing knee pain and relative differences in quadriceps muscle activation are more apparent at low force levels.

INTRODUCTION

Patellofemoral pain syndrome (PFPS) is the most common knee joint pathology diagnosis for anterior knee pain in clinical practice (Foss et al., 2014). Females are 2.23 times more likely to develop PFPS than males (Boling et al., 2010). It has been proposed that excessive activation of the vastus lateralis (VL) relative to vastus medialis oblique (VMO) in healthy females could lead to knee pain or injuries (Myer et al., 2005). However, no sex difference in VMO to VL activation ratio was observed in two subsequent studies (Herrington et al., 2006; Bowyer et al., 2008). Several methodological differences between these studies, such as variable electrode placements and normalization procedures, could be the reasons causing conflicting findings. While both delayed and lower recruitment of the VMO relative to the VL are contributing factors to develop PFPS (McConnell, 1996; Boling et al., 2006), few studies examine sex differences between medial and lateral vasti muscle temporal recruitment patterns.

The VMO serves as a medial patella stabilizer providing an opposing force to the distal portion of the VL (Bennett et al., 1993). Fibers in the vastus medialis (VM) and the proximal VL run more longitudinally and contribute to knee extension (Farahmand et al., 1998), while rectus femoris (RF) is a two-joint knee extensor and hip flexor. Patellofemoral pain syndrome was reported to be caused by imbalanced control between medial and lateral quadriceps with delayed and inadequate VMO activation (Earl et al., 2001; Boling et al., 2006; Cavazzuti et al., 2010; Aminaka et al., 2011; Felicio et al., 2011). However, not all studies observed delays in VMO recruitment or reduced VMO activation in the PFPS group (Karst and Willett, 1995; Powers et al., 1996; Morrish and Woledge, 1997; Gilleard et al., 1998; Laprade et al., 1998; Owings and Grabiner, 2002; Cavazzuti et al., 2010). The considerable disagreement on whether or not there is VMO-VL dysfunction in individuals with PFPS may well be a result of discrepant methodology and varied population characteristics (Powers, 1998; Chester et al., 2008).

There have been few studies which demonstrated quadriceps activations in different submaximal force contractions in healthy population and these did not find any differences in the medial and lateral recruitment ratio (Rainoldi et al., 2008; Spairani et al., 2012) or in other quadriceps components. However, if PFPS is related to imbalanced quadriceps activation, muscle firing patterns might be altered when pain is aggravated by higher force production. No previous publications have reported whether the level of submaximal isometric contraction forces influence the activation pattern in the sub-portions of quadriceps in individuals with PFPS.

The aims of the study were twofold. Aim one was to examine sex differences regarding onset time among the VL, RF, VM and VMO in healthy individuals. We determined whether sex and target force level affected the activation pattern in the four superficial quadriceps muscles in asymptomatic participants during an isometric knee extension. The second aim was to assess differences in muscle onset time and activation amplitude during the holding phases at different force levels among the quadriceps in females with PFPS.

METHODS

Participants and ethical approval

Twenty-five healthy individuals, 13 males (26.1 ± 3.7 yr) and 12 females (27.1 ± 3.9 yr), without any current lower extremity injury or pain, previous leg surgery, immobilization, or arthritis in the dominant leg, participated in the study as the control group for Aim one. An additional ten females (25.9 ± 6.0 yr) who suffered from ongoing retro-patellar or peri-patellar pain were recruited in the PFPS group for Aim two by referrals from local physical therapists and recruitment flyers. The PFPS participants were included if their symptoms lasted at least for one month and could be induced or aggravated by at least two of the following activities: ascending/descending stairs, hopping/jogging, prolonged sitting, kneeling, or squatting (Boling et al., 2010). Participants from both groups filled out questionnaire on health history and exercise habits. The PFPS group also filled out an Anterior Knee Pain Scale (Kujala et al., 1993) to report the pain severity affected by PFPS and the ability to perform functional activities. There was no difference in exercise intensity (F (2, 2.74) = 1.84, p = 0.18) and exercise time (F (2, 15492.51) = 0.27, p = 0.77) among the healthy male, healthy female and PFPS female groups (Table 2.1). All participants signed an informed consent form and all experimental procedures were approved by the University of Texas at Austin Institutional Review Board.

Experimental protocol

All data collection was performed in the Neuromuscular Physiology Laboratory at the University of Texas at Austin. The participants were directed to avoid any intense physical activity for at least 48 hours prior to the experimental procedures. Before data collection, participants were first seated in an adjustable chair for skin preparation and surface EMG application on the tested thigh. The dominant leg was tested for the healthy group and the painful side was tested for the PFPS group. Four pairs of pre-gelled silver/silver chloride surface electrodes were placed on the muscle bellies of the VM, VMO, VL and RF. The trunk, pelvis and both thighs were fixed with straps to ensure the isometric knee extension task was performed in an upright sitting position with the hips and knees flexed at 90°. The ankle on the tested side was secured into a padded restraint that was attached to a strain gauge (Entran Sensor & Electronics, Fairfield, NJ) underneath the adjustable chair.

The participants performed three-second isometric knee extension maximal voluntary contractions (MVCs) with verbal encouragement from the experimenter. A one-minute rest period was given between each contraction to avoid muscle fatigue. MVCs were performed until three equivalent MVC values could be obtained. The averaged value of these three contractions was then used to determine the submaximal contraction force levels. The intraclass correlation coefficient [ICC(3,1)] for the isometric knee extension MVCs was 0.998.

Participants then practiced performing stable ramp contractions up to 25%, 50% and 75% of MVC in a random order to avoid any learning effect. The ramp-up task was performed by tracing a line on a computer screen in front of participants. The display provided feedback of the force output generated at the ankle by the isometric knee extension. The speed of ramp contractions was 7.5% MVC/sec up to the three target forces with ten-second holds at 25% and 50% MVC and five-second holds at 75% MVC. The total time for each trial from the force elevation to the end of holding were approximately 13.5 sec for 25% MVC, 18 sec for 50% MVC, and 16.5 sec for 75% MVC. One successful ramp-up trial with a smooth force generation was collected for each target force. A one-minute rest was given between each ramp contraction to prevent muscle fatigue. The PFPS group was asked to report the location and severity of each occurrence of pain using Visual Analog Scale (VAS) between contraction trials. The descriptive data of pain was reported in Table 2.2. Surface EMG and force data were recorded in Spike2 (version 5.21, Cambridge Electronic Design, Cambridge, England) with sampling rate at 1k Hz.

Surface EMG and force data reduction

Surface EMG data were high-pass filtered at 10 Hz with a fourth-order recursive Butterworth filter in Matlab (version 2017a, Mathworks, Natick, MA). For each ramp up trial to target 25%, 50% and 75% of MVC, the onset time and the average holding activation amplitude was analyzed for each muscle. EMG onset was defined as the time at which the EMG root mean square (RMS) amplitude was five standard deviations higher than its average resting RMS and lasted for a minimum of 25 ms (Brindle et al., 2003). Force onset was calculated as the force RMS reaching five standard deviations higher than the average resting force RMS. The EMG onset time for each muscle was standardized to the force onset because the absolute onset times were different among 25%, 50% and 75% MVC when the speed of force increment was controlled the same. The onset data of the RMS for each muscle and the force channel were graphed for visual validation of the activation order and time by an experienced experimenter. For muscle activity standardization, the average resting RMS was calculated from the most stable 100 ms window during resting sitting posture. Activation amplitude was determined as the average RMS from the most stable 100 ms window during the holding phase standardized to the average resting RMS and normalized to the average RMS from the highest 100 ms window during MVC contractions standardized to the average resting RMS. The equation of the normalized activation amplitude was written as:

$$\text{Activation amplitude} = \frac{RMS_{\text{ramp}} - RMS_{\text{rest}}}{RMS_{\text{mvc}} - RMS_{\text{rest}}}$$

The VMO:VL activation ratio was calculated as the normalized activation amplitude of the VMO divided by the normalized activation amplitude of the VL.

Statistical analysis

Statistical analysis of the surface EMG data was performed in Statistical Package for the Social Science (SPSS) software (version 25.0) (IBM Corp, 2017). Repeated measure ANOVAs with univariate approach and Bonferroni adjustment for multiple comparisons were used to evaluate differences in onset time, activation amplitude and VMO:VL ratio. The assumption of sphericity was tested and Huynh-Feldt epsilons correction was used to adjust the degrees of freedom for the averaged tests of significance. The α level of significance was set at $p < 0.05$. A two-way repeated measure ANOVA was used to examine the between-subjects effect of sex (healthy males and healthy females) and the within-subjects effect of muscle (VM, VMO, VL, and RF) on onset time in the healthy individuals. Another two-way repeated measure ANOVA was applied to analyze the influence of the between-subjects effect of group (healthy females and PFPS females) and within-subjects effect of muscle on onset time in the female participants. Because there was no main effect of sex or group on activation amplitude, the data were pooled together from all participants for a two-way repeated measure ANOVA analysis to assess the effect of the two within-subject factors, muscle and force (25%, 50%, and 75% MVC), on activation amplitude. Similarly, the data of VMO:VL ratio were pooled from all participants because no significant main effect of sex or group was observed. A one-way repeated measure ANOVA was used to evaluate the effect of force on VMO:VL ratio. Two one-way ANOVAs with Fisher LSD post hoc tests were used to analyze the differences in exercise intensity and exercise time among the three groups. Data are presented as mean ± standard error.

RESULTS

Onset time

In the healthy participants, there was a main effect of muscle (F (2.21, 2.63) = 11.53, $p <$ 0.001) and sex (F (1, 7.77) = 20.77, $p < 0.001$) on onset time. Bonferroni pairwise comparisons revealed that onset time in the VL was 380 ± 60 ms earlier than the RF ($p < 0.001$) and 250 ± 40 ms earlier than the VM ($p < 0.001$). However, it was not significantly different from the VMO (p = 0.06) (Figure 2.1). Onset time in the male participants was 320 ± 70 ms earlier than in female participants with pooled data from all muscles ($p < 0.001$) (Figure 2.2). For healthy and PFPS female participants, there was a main effect of muscle (F (3, 1.55) = 5.24, $p = 0.002$) on onset time, while the main effect of group did not reach statistical significance (F (1, 1.69) = 2.77, $p = 0.1$). Bonferroni post hoc tests showed that onset time in the VL was 240 ± 90 ms earlier than the RF

(p = 0.039) and 350 ± 100 ms earlier than the VM (p = 0.007), yet not significantly different from the VMO (p = 1.00) (Figure 2.3).

Activation amplitude

There was an interaction effect between force and muscle (F (3.91, 0.05) = 4.33, p = 0.003) on activation amplitude with pooled data from all participants. At the lowest force level at 25% MVC, the activation amplitude in the VL was 7.0 ± 1.9 % EMGmax higher than in the VMO (p = 0.004), 5.6 ± 1.8 % EMGmax higher than in the VM (p = 0.025) and 8.8 ± 2.2 % EMGmax higher than in the RF (p = 0.001) (Figure 2.4). There was no difference in the activation amplitude among the four muscles in the 50% MVC and 75% MVC force levels.

VMO:VL ratio

There was a main effect of force on VMO:VL activation ratio (F (1.57, 1.00) = 16.75, $p <$ 0.001) with pooled data from all participants. The VMO:VL ratio increased with higher force level. The VMO:VL ratio in 25%MVC was 0.20 ± 0.04 lower than in 50%MVC ($p < 0.001$) and was 0.29 ± 0.06 lower than in 75%MVC ($p < 0.001$) (Figure 2.5). The VMO:VL ratio in 50%MVC was 0.10 ± 0.05 lower than in 75%MVC but this was not a significant difference (p = 0.14).

DISCUSSION

The main purpose of this study was to evaluate the sex differences in the recruitment sequence of quadriceps muscles, in addition to the activation amplitudes, that might explain the higher risk for females suffering PFPS. We also evaluated whether force had an effect on the quadriceps activation pattern and if PFPS altered the muscle control strategies. In the asymptomatic group, males exhibited an earlier onset of the quadriceps than females. Among the quadriceps, the VL was activated earlier than the VM and RF, but no difference in onset between the VL and VMO was found for both healthy and PFPS groups. The VL showed a higher activation amplitude than the other quadriceps muscles during the holding phase at the lowest target force. At the higher force levels, no difference in the activation level was found among the quadriceps. Similarly, the VMO:VL ratio was lower in the 25% MVC force level compared to the two higher force levels.

Effect of muscle on onset time in healthy individuals

In the healthy control group, both males and females showed an early onset of the VL compared to the VM and RF, but this earlier onset of the VL did not differ from the onset of the VMO. Counterbalanced forces pulling on the superior-medial and superior-lateral border of the patella were generated by contraction of the VMO and VL, respectively (Lin et al., 2004). An appropriate activation sequence and comparable activation amplitude of the two muscles assure the patella stability during knee movements (Neptune et al., 2000). Our findings support the clinical theory that the VMO and VL are activated simultaneously to stabilize the patella while initiating isometric knee extension. Previous studies examined the medial and lateral vasti muscles in asymptomatic knees and reported a similar temporal activation relationship between the VMO and VL (Cowan et al., 2001 & 2002; Brindle et al., 2003; Dieter et al., 2014). Simultaneous recruitment of the VMO and VL occurred when performing voluntary ankle and knee movements that challenge knee stability (Cowan et al., 2001 & 2002). Other studies also showed no difference between the onset of the VMO and VL while performing ascending/ descending stairs (Brindle et al., 2003) and during cycling trials (Dieter et al., 2014).

Sex differences in onset time

The healthy female participants had a delayed onset of the quadriceps compared to the healthy male participants, yet this onset of the quadriceps in healthy females did not differ from the females with PFPS. Slower quadriceps activation may compromise patellar stability during knee extension initiation and may relate to the occurrence of PFPS in females. Sung and Lee (2009) reported that sex differences in muscle onset and activation level vary according to different phases of a movement. Females with anterior knee pain exhibited a delayed onset of the VM and a lower percentage of VM activation compared to males while descending stairs. However, during stair ascension, females displayed an earlier VM onset and equivalent activation level compared to males (Sung and Lee, 2009). They suggested that activation delays observed in the medial quadriceps of females with current knee pain during descending stairs could be a risk factor of knee injuries (Sung and Lee, 2009). However, there are few studies that have examined sex differences in the medial and lateral quadriceps onset time in both healthy and PFPS population.

No effect of PFPS on onset time

It is believed that delayed VMO activation is one of the contributing factors to PFPS (McConnell, 1996; Boling et al., 2006). However, we did not observe an effect of PFPS on the onset time of the quadriceps between symptomatic and asymptomatic females. The onset pattern among the four muscles studied is similar to the pattern observed in the asymptomatic group showing an earlier onset of the VL than the VM and RF but not earlier than the VMO. It is possible that the healthy female sample in the study were more sedentary, and therefore showed a greater difference compared to the healthy male participants than to the PFPS females. Briani et al. (2016) proposed that people with PFPS demonstrated varied onset of VMO relative to VL dependent upon their physical activity level. The females with PFPS who participated in intense physical activity showed a delayed onset of the VMO when ascending stairs, while the PFPS females who engaged in moderate physical activity showed no delay of the VMO onset (Briani et al. 2016). Therefore, absence of delayed VMO onset in the females with PFPS may be explained by their approximately moderate physical activity level.

Interaction effect of muscle and force level on muscle activation amplitude

A more balanced muscle activation among the quadriceps sub-portions was observed during the holding phase in higher force levels compared to the lowest force level regardless of sex and groups. When maintaining isometric knee extension at the lower force level of 25% MVC, the VL displayed a higher activation amplitude relative to the RF, VM and VMO. The VL displays the largest cross-sectional area in the quadriceps (Narici et al., 1989) and it is essential to the power production in knee extension movement (Farahmand et al., 1998). The earlier onset of the VL relative to the RF and VM observed in both healthy and PFPS groups indicates a preferential activation of the muscle in the isometric knee extension task. With increasing force level, the muscle activation amplitude increased as expected, and the activity was more evenly distributed over the quadriceps muscles. More specifically, at 25% MVC, the VL was activated at 27% EMGmax while the RF, VM and VMO were activated at 18%, 21% and 20% EMGmax respectively. All four muscles were activated higher than their 50% and 75% MVC when performing the 50% and 75% of the MVC force target.

Rainoldi et al. (2008) and Spairani et al. (2012) claimed that different submaximal contraction levels had no effect on the quadriceps activation pattern in 10%, 60% and 80% MVC isometric knee extension contractions. The two studies used the same analysis for the absolute muscle activity and reported a higher absolute activity of the VMO compared to the VM in isometric knee extension over different force levels (Rainoldi et al., 2008; Spairani et al., 2012). Despite the statistical significance, the magnitude of these differences was not reported. Dissimilar data reduction methods in the two studies might account for the different results regarding muscle activation patterns in different force levels (Martines-Valdes et al., 2018). However, during walking, a low-force functional activity, the VL exhibited a higher activation amplitude relative to the VMO and RF throughout different phases of level walking in individuals with PFPS (Salarie Sker et al., 2017). This agrees with our results suggesting a preferential VL recruitment in a low-force activity with 15.4% to 23.6% EMGmax of quadriceps activation.

Effect of force level on VMO:VL ratio

The 50% MVC and 75% MVC force levels demonstrated a higher VMO:VL ratio than the 25% MVC. At 25% MVC target force, the activation amplitude of the VL was higher than 20% EMGmax, while the activation amplitude of VMO was lower than 20% EMGmax. With increasing target force, the activation amplitude of the VMO increased. These results suggest a 50% MVC force level best facilitates an equivalent medial-lateral quadriceps activation. A 75% MVC force level proved to be strenuous for subjects to maintain the force at 75% for more than 10 seconds and therefore cannot be recommended to achieve the aforementioned equivalency.

Limitations of the study

The use of the surface EMG presents the possible issue of cross-talk from the vasti muscles and therefore the possibility of an increased EMG amplitude in signals from adjacent muscles cannot be discounted. We did not measure the antagonists of the quadriceps to evaluate possible compensated pattern for a more comprehensive explanation on the effect of sex and group. This study focused on the effect of sex in healthy population and the effect of PFPS only in females with symptoms due to their higher prevalence of anterior knee pain. Therefore, the findings between the healthy and PFPS females may not be generalized to male population.

CONCLUSION

This study showed that the VL activated prior to the VM and RF and was accompanied by the VMO recruitment to stabilize the patella for both healthy and PFPS population. Asymptomatic females had delayed onsets of the quadriceps compared to asymptomatic males and these activation delays did not differ from the PFPS females. This suggests a possible higher risk of knee pain or injury for healthy females relative to males. An imbalanced quadriceps muscle activation with a lower VMO:VL ratio were observed at 25% MVC. Isometric knee extensions at a 50% MVC is therefore recommended to generate a more evenly distributed quadriceps activation and a higher VMO:VL ratio.

Table 2.1. Descriptive data of average exercise habits for the groups of participants

	Average exercise intensity*	Average exercise time (mins/week)
Healthy males	2.7 ± 1.4	279.8 ± 305.8
Healthy females	1.9 ± 1.1	208.7 ± 140.0
PFPS females	2.8 ± 1.2	266.1 ± 251.6

** Scores of the exercise intensity: 1-light, 2-light to moderate, 3-moderate, 4-moderate to high, 5: high. Values are means ± SD.*

Table 2.2. Descriptive data of pain in PFPS group (n=10)

Side of leg being tested	6 right legs and 4 left legs
Symptom duration	1 month – 1 year (n=4) 1 year – 3 years (n=4) 6 years (n=2)
Anterior Knee Pain Scale	74.9 ± 13.5 (Full function score: 100)
VAS before and after experiment	0.1 ± 0.3 (Range: 0 – 1)
VAS during isometric knee extension task	3.0 ± 2.7 (Range: 0 – 8)

* *Values are means ± SD.*

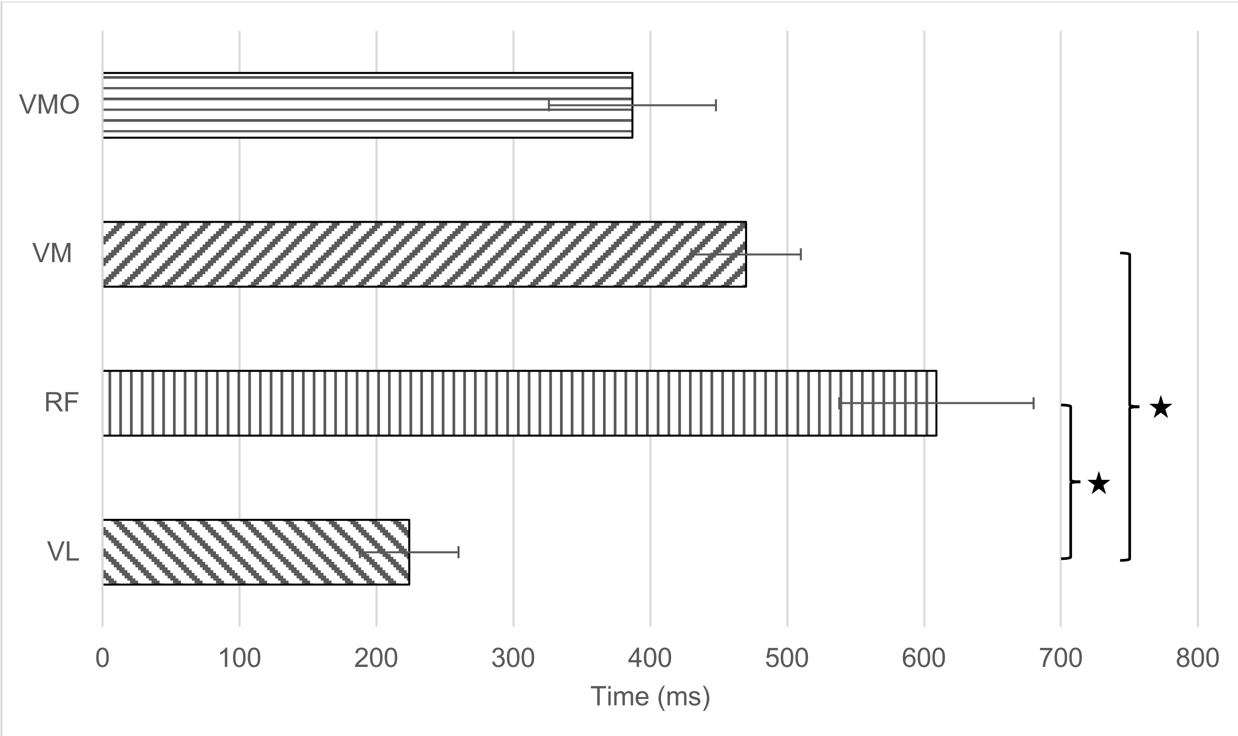

Figure 2.1. EMG onset time of VL, RF, VM and VMO with pooled data of healthy males and healthy females. All bars are aligned to the onset of force at zero seconds. * Indicates a significant difference in EMG onset between two muscles.

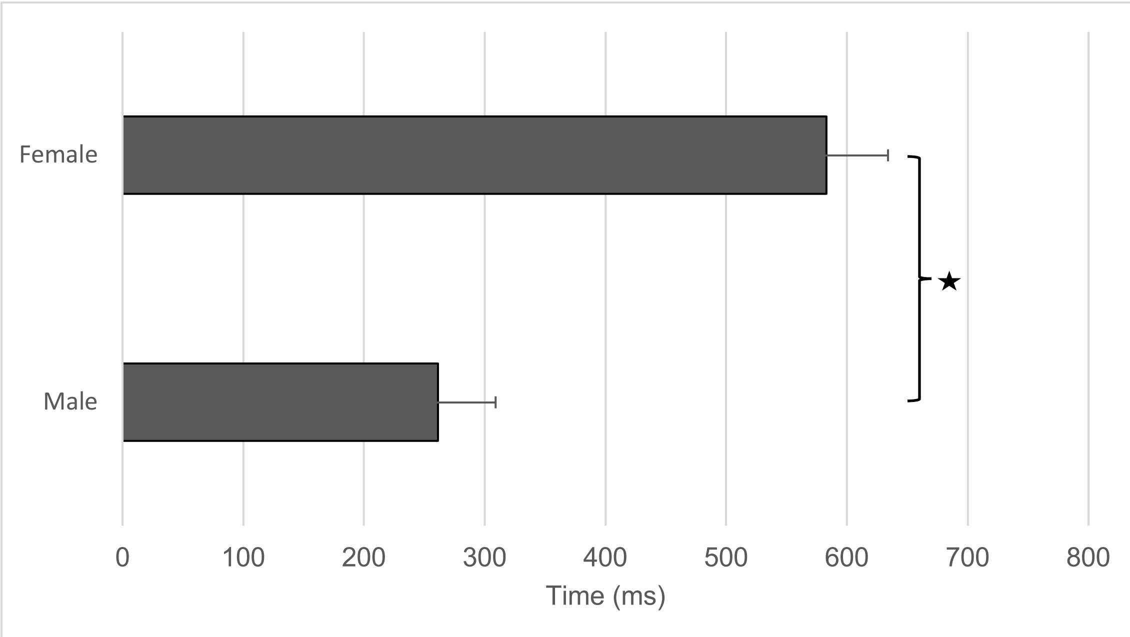

Figure 2.2. EMG onset time in healthy females and males with pooled data of the four muscles. All bars are aligned to the onset of force at zero seconds. * Indicates a significant difference in EMG onset between females and males.

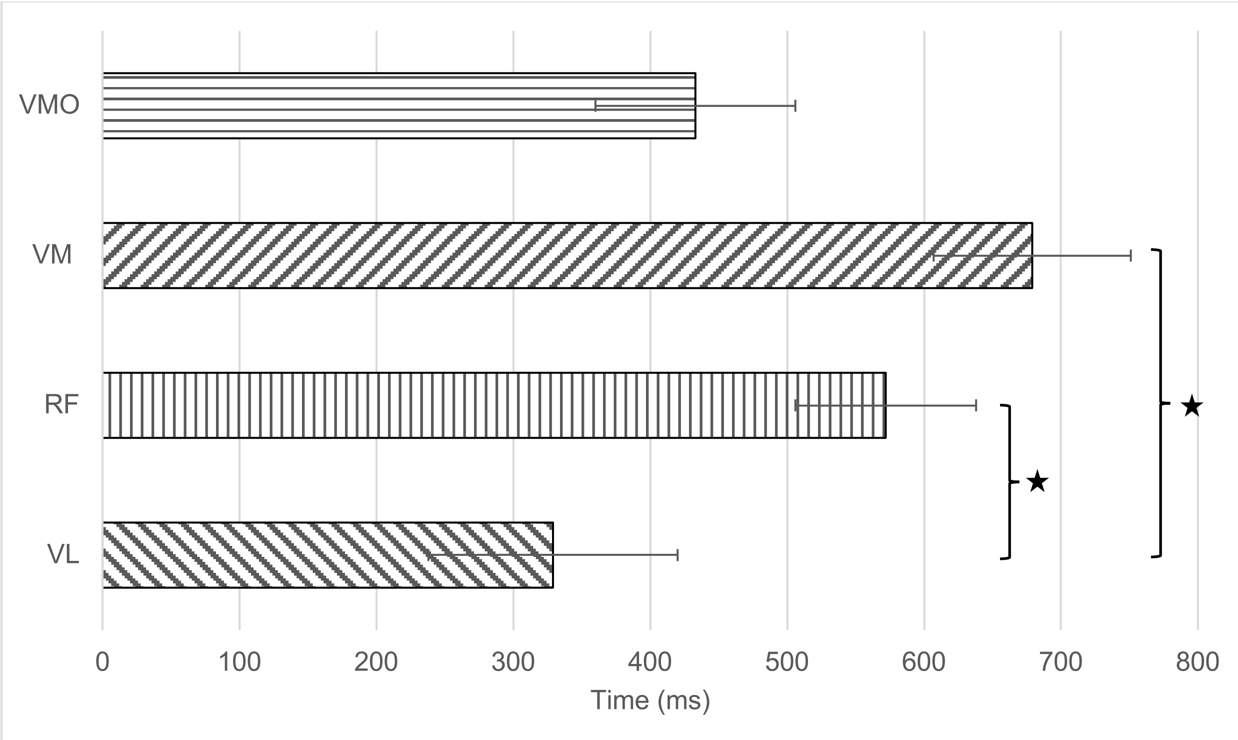

Figure 2.3. EMG onset time of VL, RF, VM and VMO with pooled data of healthy and PFPS females. All bars are aligned to the onset of force at zero seconds. * Indicates a significant difference in EMG muscle onset between two muscles.

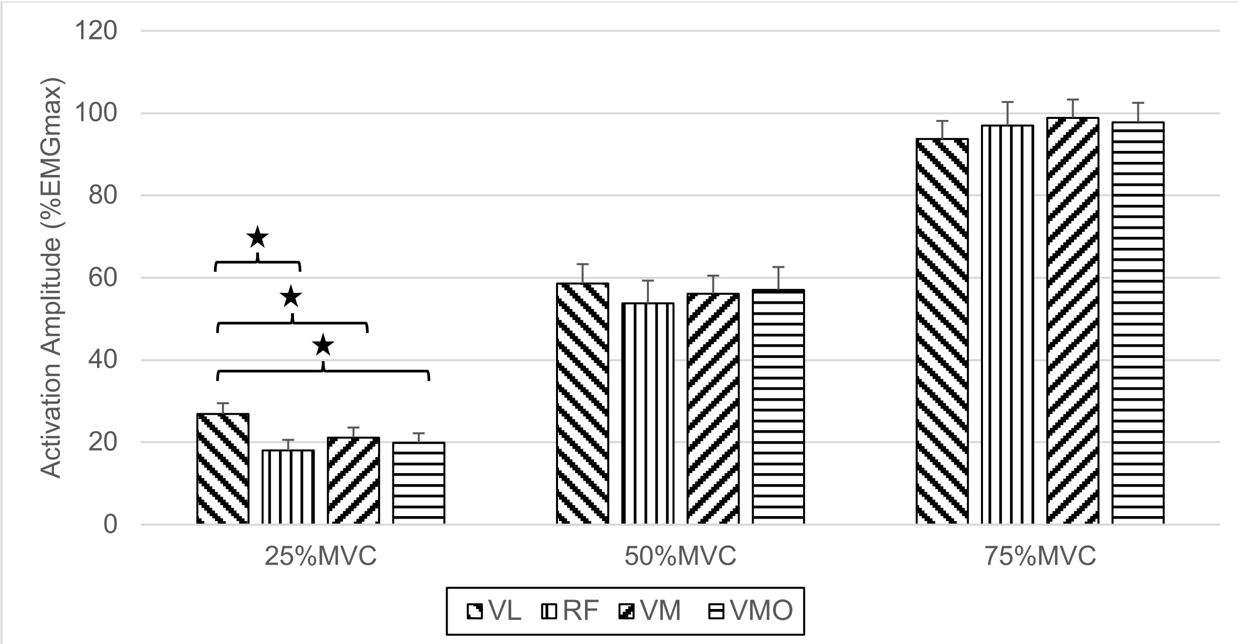

Figure 2.4. Normalized RMS EMG activation amplitude for VL, RF, VM and VMO during isometric knee extension holding phase in the three force levels with pooled data from all participants. * Indicates a significant difference in EMG amplitude between two muscles.

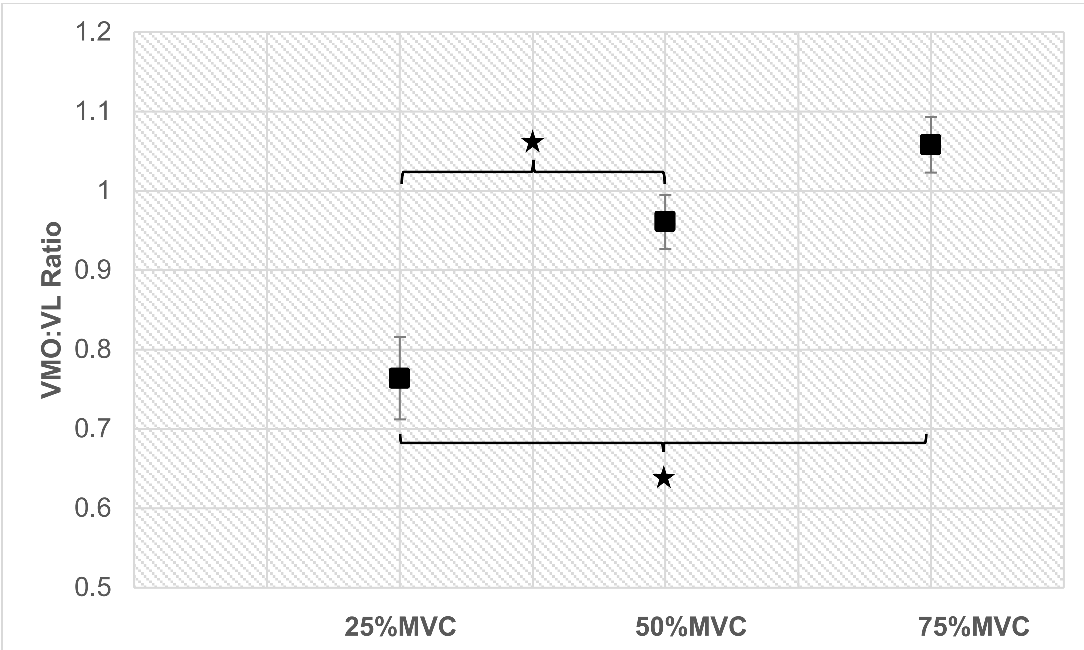

Figure 2.5. VMO to VL normalized activation amplitude ratio during isometric knee extension holding phase at three force levels with pooled data of all healthy and PFPS participants. * Indicates a significant difference in VMO:VL ratio between two force level.

[1]Chapter 3: Hip Position and Sex Differences in Motor Unit Firing Patterns of the Vastus Medialis and Vastus Medialis Oblique in Healthy Individuals

ABSTRACT

Weakness of the vastus medialis oblique (VMO) has been proposed to explain the high prevalence of knee pain in females. Clinicians commonly use exercises in an attempt to preferentially activate the VMO. Recently, our group found evidence to support clinical theory that the VMO is neurologically distinct from the vastus medialis (VM). However, the ability to voluntarily activate these muscle sub-sections is still disputed. The aim of this study was to determine if VM and VMO activation varies between sexes and if control of the two muscles is different between rehabilitation exercises. Thirteen males and 13 females performed isometric straight leg raises in two hip positions, neutral hip rotation and 30 degrees lateral hip rotation. Bipolar intramuscular fine-wire electrodes were inserted into the VM and VMO to obtain motor unit recruitment thresholds and initial firing rates at recruitment. Linear mixed models and Tukey post hoc tests were used to assess significant differences in 654 motor units. Females demonstrated faster motor unit firing rate at recruitment, 1.18 ± 0.56 Hz higher than males. Motor units fired 0.47 ± 0.19 Hz faster during neutral hip rotation compared to lateral hip rotation. The VMO motor units were recruited 2.92 ± 1.28% earlier than the VM. All motor units were recruited 3.74 ± 1.27% earlier during neutral hip rotation than lateral hip rotation. Thus, the VM and the VMO can be activated differentially and their motor unit recruitment properties are affected by sex and hip position.

[1] This study has been published in Journal of Applied Physiology.
Full citation: Peng YL, Tenan MS, Griffin L. Hip position and sex differences in motor unit firing patterns of the vastus medialis and vastus medialis oblique in healthy individuals. J Appl Physiol (1985) 1;124(6):1438-1446, 2018.

Peng YL contributed to experiment conception and design, data collection, analysis, data interpretation and the drafting and critically revising of the manuscript.
Tenan MS contributed to experimental conception and design, data interpretation and critically revising of the manuscript.
Griffin L contributed to experimental conception and design and critically revising of the manuscript.

INTRODUCTION

There is a long-held belief among physical medicine clinicians that the vastus medialis oblique (VMO) and vastus medialis (VM) are anatomically and neurologically distinct (Crossley et al., 2002; Syme et al., 2009). While early surface electromyography (EMG) research disputed this clinical ideology (Stensdotter et al., 2007; Rainoldi et al., 2008), our research group recently demonstrated differential discharge patterns between the VM and VMO (Tenan et al., 2013; Tenan et al., 2016). Furthermore, Gallina et al. (2016), demonstrated regional muscle activation induced by electrical stimulation in the vastus medialis complex. They found that the proximal portion of the VM could be activated separately from the distal portion in an isometric knee extension task and that the distribution of the localized activation was influenced by knee flexion angle (Gallina et al., 2016). Anatomical studies on human cadavers report that the VMO is innervated by a larger number of terminal nerve branches originating from L1-L3 per area than the VM (Thiranagama, 1990; Jojima et al., 2004). These findings support the notion that the VM and VMO can be controlled independently.

Anatomical evidence also suggests that there is a functional difference between the VM and VMO based upon dissimilar muscle fiber pennation angles (Farahmand et al., 1998). The VMO runs oblique to the medial side of the patella and assists with medial patellar translation, while the VM runs more longitudinally and contributes to knee extension (Bennett et al., 1993). An advanced and adequate medial force generated by the VMO not only decreases patellofemoral joint load but also reduces the lateral dominant forces from the vastus lateralis (VL) (Neptune et al., 2000). An imbalance of muscle forces between the medial and lateral sides of the patella, caused by VMO weakness or activation delay, is considered to be a primary contributing factor to patellofemoral pain syndrome (PFPS) (McConnell, 1986).

Females are more likely to experience PFPS and knee injury than males (Boling et al., 2010; Foss et al., 2014; Tenan et al., 2016). A plausible explanation may be due to sex differences in the activation patterns of the VMO in relation to the VL (Bowyer et al., 2008). If the VMO is too weak to counteract the excessive force of the VL, pain can result from mal-tracking of the patella (Pal et al., 2012). A lower medial to lateral quadriceps activation ratio is evident in healthy females compared to healthy males (Myer et al., 2005). However, not all EMG studies support the notion that higher incidence of PFPS in female populations is a result of differential VMO/VL intensity (Herrington et al., 2006; Bowyer et al., 2008). The discrepancy in the results may be related to the inconsistent surface EMG electrode placements (Herrington et al., 2006). This is especially true for the electrode location of the VMO, which is sometimes not specified and confused with the VM (Myer et al., 2005).

Clinical assessments and rehabilitation protocols commonly assume VMO weakness. Some studies have found that the relative activation amplitude and onset timing of the VMO to the VL can be affected by different exercises (Felicio et al., 2011), eccentric versus concentric contractions (Herrington et al., 2006), tibia rotation (Laprade et al., 1998; Serraoa et al., 2005), and hip adduction (Laprade et al., 1998; Earl et al., 2001). Conversely, others have not observed differences in the relative activation of the VMO and VL across exercise type (Herrington et al., 2006), hip rotation (Herrington et al., 2006), or hip adduction (Peng et al., 2013). It is possible that much of the research on quadriceps activity to date were confounded by cross talk with the use of surface EMG since the standard surface electrodes lack the ability to reliably detect VMO activity apart from other adjacent muscles due to signal cross talk (Byrne et al., 2005). The use of fine-wire EMG recording can overcome the problem of cross talk between recordings of muscles in close proximity.

The straight leg raise (SLR) is an exercise commonly prescribed by clinicians to strengthen the quadriceps in general and, in particular, the VMO (Sykes and Wong, 2003). The SLR is beneficial for people with general knee pain or post knee surgery because it induces minimal compression force on the patellofemoral joint (Singerman et al., 1995; Mesfar and Shirazi-Adl, 2005). Some researchers have suggested that simultaneous activation of the hip adductor and quadriceps muscles preferentially recruits the VMO (Hanten and Schulthies, 1990; Irish et al., 2010). Since the VMO muscle fibers arise mainly from the adductor magnus tendon (Bose et al., 1980), concurrent contraction of the hip adductor may provide a stable origin for the VMO and facilitate its neuromuscular activation (Hanten and Schulthies, 1990). Using surface EMG, Sykes and Wong (2003) found that the SLR with external hip rotation was the most effective position for strengthening the VMO. However, they noted that the higher EMG amplitudes of the VMO during hip external rotation could have been due to cross talk from the hip adductors (Sykes and Wong, 2003). Conversely, Karst and Jewett (1993) found that SLR with external hip rotation actually elicited a lower mean VMO/VL EMG ratio compared to standard SLR without hip rotation (Karst and Jewett, 1993). During various exercises, such as isometric quadriceps setting exercise, end range knee extension and squatting, VMO recruitment was not facilitated by concurrent hip external rotation or hip adduction, even with increased adductor magnus activation (Cerny, 1995; Wong et al., 2013). Thus, the ambiguous surface EMG literature suggests a need for more specific intramuscular fine-wire EMG investigations to evaluate vastus medialis complex activity during the SLR.

The purpose of this study is to evaluate muscle activation patterns during the SLR in two hip rotation positions and to determine if one position facilitates preferential motor unit recruitment of the VMO compared to the VM. With methodological control of the female menstrual phase, the study also examines if sex can account for differences in performance of the two muscles.

METHODS

Participants and ethical approval

Thirteen young males (26.1 ± 3.7 yr) and 13 young eumenorrheic females (26.5 ± 4.3 yr) participated in one study visit. The inclusion criteria for both males and females were: absence of ongoing hip, knee, or ankle pain, previous leg surgery, immobilization, arthritis to the dominant leg, and neurologic, cardiovascular, or metabolic disorders. In addition, the female participants had regular menstrual cycles for the three months prior to the experiment. The females participated during their late follicular phase (For example, day 8 to day 14 in a 28-day menstrual cycle), because single motor unit firing rates and recruitment thresholds in females are comparable with those of males during this phase (Tenan et al. 2013). All participants signed an informed consent form and all experimental procedures were approved by the University of Texas at Austin Institutional Review Board.

Experimental protocol

All data collection procedures were conducted in the Neuromuscular Physiology Laboratory at the University of Texas at Austin. All participants were instructed to avoid strenuous exercise 48 hours before the study visit and refrain from consuming caffeine and alcohol for eight hours prior to testing. Participants were seated in an adjustable chair for fine-wire EMG electrode placement in the dominant leg. Two pairs of bipolar intramuscular insulated stainless steel fine-wire electrodes (0.002 mm, California Fine Wire Company, Grover Beach, CA) with 3 mm of insulation removed from the tip were inserted into the VMO and VM with thin (25 gauge, 16 mm length), disposable hypodermic needles. Signals obtained from the wires were pre-amplified and bandpass filtered at 8 Hz–3.12 kHz with a gain of 330 (B&L Engineering, Tustin, CA). All electrodes and needles were fully autoclaved and sterilized before use. The two fine-wire electrodes for the VMO were placed at 4 cm and 5 cm proximal to the superomedial border of the patella and oriented 55° medially from the femoral axis. The two electrodes for the VM were placed at 11 cm and 12 cm proximal to the superomedial border of the patella and oriented 15° medially from the femoral axis (Travnik et al., 1995; Rainoldi et al., 2004). An adhesive pregelled Ag/AgCl surface electrode of 5 mm diameter was placed on the ipsilateral patella as a ground.

After electrode placement, the volunteer was positioned lying supine on a medical examination table with the legs straight. The upper trunk, waist, and non-dominant thigh were immobilized with straps and the dominant ankle was affixed to a padded restraint attached to a strain gauge (Entran Sensor & Electronics, Fairfield, NJ) underneath the table. An isometric SLR was performed in two different hip positions: neutral (no rotation) and 30° of lateral hip rotation. The foot was securely positioned between two boards to maintain the required hip rotation and neutral foot position during the contraction. The instruction for the movement was to "lift your leg straight up with your knee fully extended." The participants were guided to perform three, three-second isometric maximal voluntary contractions (MVCs) with a one-minute rest between contractions to prevent muscle fatigue. MVCs were performed until three equivalent MVC values were obtained. The intraclass correlation coefficient (ICC (3,1)) for the MVCs was 0.99. The average of the three MVCs were used to determine submaximal contraction target levels.

Following the MVC's, the participants practiced a slowly-controlled ramp contraction following a line on a computer screen in front of them with a rate of rise of 7.5% MVC/sec up to

75% MVC and then and then a hold at 75% MVC for 5 seconds. One successful trial ramp with smooth force generation for each hip position was recorded. Thus, a total of two ramp contractions were recorded and analyzed for each participant. Intramuscular EMG and force data were recorded in Spike2 (version 5.21, Cambridge Electronic Design, Cambridge, England) with sampling rate at 30k Hz and 1 Hz, respectively.

Motor unit and force data analysis

The intramuscular EMG data was bandpass filtered at 100 Hz – 8,000 Hz using a fourth-order recursive Butterworth filter in Matlab (version 2010b, Mathworks, Natick, MA). Single motor units were analyzed visually and identified based upon individual shape, amplitude, and discharge frequency in Spike2. The recruitment threshold and initial firing rate at recruitment for each individual motor unit was analyzed. Recruitment threshold for each motor unit was defined as the force when the first of the four consecutive spikes occurred at regular intervals (Van Cutsem et al., 1998; Tenan et al., 2013). Initial firing rate at recruitment was calculated as the average of the first three interspike intervals converted into hertz (Figure 3.1). The force data was notch filtered at 60 Hz using a fourth-order recursive Butterworth filter in Matlab (version 2010b, Mathworks, Natick, MA) and the DC offset was removed.

Statistical analysis

All statistical analysis was performed in R, using RStudio (version 3.2.2) (RStudio Team, 2013), using the lmerTest (Kuznetsova et al., 2016), lme4 (Bates et al., 2015), and nlme (Pinheiro et al., 2016) packages. The α level of significance was set *a priori* at $p < 0.05$. Linear mixed models with an unstructured variance covariance structure and Tukey post hoc tests were used to evaluate the effect of muscle (VM and VMO), sex (male and female), and hip position (no hip rotation and 30 hip lateral rotation) on initial firing rate and recruitment threshold during the SLR. Mixed effects models were used because multiple motor units from an individual are statistically correlated (Tenan et al., 2014) and mixed models account for this correlation. In the linear mixed models, the first level was single motor unit. Single motor units were nested according to each subject to form the second level, which was defined as the subject level. Muscle and hip position were the predictor variables for the motor unit level, while sex was the predictor variable for the subject level. There were three implied cross-level interactions, one 3-way interaction among muscle, hip position, and sex, and two 2-way interactions between muscle and sex, and hip position and sex. The absolute force at which a single motor unit was recruited was used as a covariate for initial firing rate due to the correlation between recruitment threshold and initial firing rate (Milner-Brown et al., 1973). Because the firing patterns of single motor units are correlated within an individual participant, we assessed the intraclass correlation of initial firing rates at the subject level in the mixed model. We checked the assumption of normality of residuals and ensured that the linearity and equal variance within each level were not violated. The linear mixed model equation for initial firing rate was written as:

Level 1

$\text{Initial Firing Rate}_{ij} = \beta_{0j} + \beta_{1j}\text{Muscle}_{ij} + \beta_{2j}\text{Hip position}_{ij} + \beta_{3j}\text{Muscle*Hip position} + \beta_{4j}\text{Force} + e_{tij}$

Level 2

$\beta_{0j} = \gamma_{00} + \gamma_{01}\text{Sex} + u_{0j}$

$\beta_{1j} = \gamma_{10} + \gamma_{11}\text{Sex}$

$\beta_{2j} = \gamma_{20} + \gamma_{21}\text{Sex}$

$\beta_{3j} = \gamma_{30} + \gamma_{31}\text{Sex}$

$\beta_{4j} = \gamma_{40}$

The majority of the single motor units, 531 out of 654 motor units, were recruited within the lower force level of 25% MVC. The natural logarithm transformation was used on the raw recruitment threshold data to meet the assumptions of normality of residuals and constant variance within each level. Further statistical analysis for recruitment threshold was performed on the transformed data and the mixed model equation were written as below. To help the interpretation of the findings, the recruitment threshold data presented in the figures were exponentiated back to the original units as the percentage of the MVC. We did not use the averaged absolute force as a covariate because of the clear mathematical relation.

Level 1

$\text{Recruitment Threshold}_{ij} = \beta_{0j} + \beta_{1j}\text{Muscle}_{ij} + \beta_{2j}\text{Hip position}_{ij} + \beta_{3j}\text{Muscle*Hip position} + e_{tij}$

Level 2

$\beta_{0j} = \gamma_{00} + \gamma_{01}\text{Sex} + u_{0j}$

$\beta_{1j} = \gamma_{10} + \gamma_{11}\text{Sex}$

$\beta_{2j} = \gamma_{20} + \gamma_{21}\text{Sex}$

$\beta_{3j} = \gamma_{30} + \gamma_{31}\text{Sex}$

The differences in the absolute MVC force were tested by a two-way repeated measure ANOVA (with one between factor of sex and one within factor of hip position) and Bonferroni post hoc tests.

RESULTS

Motor Unit Recordings

A total of 654 motor units were recorded from the 26 participants. The distributions of the number and percentage of single motor units between the levels of each predictor variable are shown in Table 3.1.

Initial Motor Unit Firing Rate at Recruitment

The subject-level intraclass correlation was 0.23, showing that initial motor unit firing rates were mildly correlated within individuals. There was a main effect for sex (F (1, 26) = 4.77, p = 0.04) and a main effect for hip position (F (1, 630) = 6.45, p = 0.01) on initial firing rate. Averaged across the two hip positions after controlling for force, Tukey's post hoc analysis revealed that initial motor unit firing rates of the pooled data for the VM and VMO were higher in females (9.64 ± 0.40 Hz) than in males (8.46 ± 0.39 Hz) (t (28) = 2.10, p = 0.045; Figure 3.2, left).

Initial motor unit firing rates were lower during lateral hip rotation than during no hip rotation (t (637) = 2.52, p = 0.01), with averaged results over the levels of sex and muscle, after controlling for force. Motor units in the VM and VMO fired at slower rates during lateral hip rotation (8.81 ± 0.30 Hz) than during no hip rotation (9.29 ± 0.30 Hz) (Figure 3.2, right). A trend for an interaction effect between muscle and hip position was observed for possible effect on initial firing rate (F (1, 629) = 3.17, p = .08) (Figure 3.3).

Recruitment Thresholds

The linear mixed model revealed a main effect for muscle (F (1, 641) = 4.94, p = 0.03) and a main effect of hip position (F (1, 633) = 8.91, p < 0.01) on the log-transformed recruitment thresholds. Averaged across sex and hip position, Tukey's post hoc analysis revealed that recruitment threshold was lower in the VMO than in the VM (t (648) = -2.21, p = 0.03; VMO: 11.89 ± 1.18 %MVC; VM: 14.81 ± 1.24 %MVC) (Figure 3.4, left). Higher recruitment thresholds were observed during lateral hip rotation than during no hip rotation (t (639) = -2.97, p < 0.01), with results averaged over the levels of sex and muscle. Motor units in both muscles were activated at lower forces during no hip rotation (11.48 ± 1.21 %MVC) than during lateral hip rotation (15.22 ± 1.21 %MVC) (Figure 3.4, right). There was a borderline interaction effect between sex and hip position (F (1, 633) = 3.70, p = 0.0547) (Figure 3.5).

Absolute MVC Force

There was a significant interaction effect between sex and hip position on the absolute MVC force (F = 6.948; p = 0.01). Males exhibited a significantly higher absolute MVC force in SLR with neutral hip rotation than SLR with lateral hip rotation ($p < 0.05$). They also showed a significantly higher mean absolute MVC force than female participants in both neutral ($p < 0.05$; Male: 147.48 ± 35.42 N; Female: 96.79 ± 26.23 N) and lateral ($p < 0.05$; Male: 127.08 ± 23.89 N; Female: 91.90 ± 27.44 N) hip rotation positions (Figure 3.6). However, females did not demonstrate different absolute MVC forces between hip positions ($p > 0.05$).

DISCUSSION

The primary goal of the study was to examine if control of the VMO and VM are neurologically distinct during the performance of different exercises. We examined how lateral hip rotation during a SLR affects selective activation of the VMO and VM between sexes. The results of this study confirm clinical theory that healthy individuals recruit motor units within the VMO at an earlier force level compared to motor units within the VM, indicating that the VMO serves as an initial stabilizer of the patella. Females fire motor units in the vastus medialis complex at a faster rate than males after controlling the force. Neutral hip rotation allows motor units to be recruited earlier and to fire at higher rates than lateral hip rotation.

To our knowledge, this is the first study to evaluate differential performance of the VM and VMO in clinical exercise protocols. Numerous studies have endeavored to find the best exercise protocols to properly activate the VMO and generate medially-vectored forces on the patella in relation to the VL (Karst and Jewett, 1993; Cerny, 1995; Laprade et al., 1998; Earl et al., 2001; Sykes and Wong, 2003; Serraoa et al., 2005; Felicio et al., 2011). While these studies appear to be based on the assumption of the different functions of the VM and VMO, none provided evidence regarding whether particular exercise parameters differentially activated the VMO from the rest of the vastus medialis complex. An effective VMO strengthening protocol is essential for resolving clinical complications and will save time and money spent on therapy visits.

The VM and VMO have some level of sequential activation; the VMO motor units are recruited earlier than the VM motor units at lower force level suggesting that these two muscles are functionally distinct. The muscle fibers of the VM align vertically, generally running within 10° to 35° to the longitudinal axis of the femoral shaft, while the fibers of the VMO align more obliquely from 40° to nearly horizontally at the most distal portion (Thiranagama, 1990). The force vectors caused by shortening of the muscle fibers with such divergent orientation contribute to dissimilar patella movements. Evoked VMO contractions pull the patella medially, and the stimulation of the VM guides the patella in a more proximal direction (Lin et al. 2004). The changing fiber orientation in the vastus medialis complex affects its peak muscle activation area measured by a surface EMG grid in different knee flexion angles (Gallina et al., 2016). The peak amplitude of surface EMG exhibited was higher in the VM than in the VMO during isometric knee extension (Gallina et al., 2016). The summation of current scientific evidence indicates that different sub-sections of the vastus medialis complex are both mechanically, functionally and neurologically distinct.

Spinal reflex activity of the vastus medialis complex also differs depending on the location of the stimulus applied (Gallina et al. 2017). Regional stretch reflexes are more distal in response to a distal stimulus, suggesting that drive from the spinal cord also differentially recruits motor neurons in the VM and VMO (Gallina et al. 2017). Cabral et al. (2017) has previously shown that motor unit discharge patterns derived from the VM and the VMO are similar within their respective region, but functionally less correlated when the two regions are pooled (Cabral et al., 2017). In the present study, VMO motor units were recruited earlier than VM motor units at low force levels. The differential recruitment pattern between the VM and VMO may be related to biological differences in the distribution of input resistance of the motor units, or it may be due to a modulation in the nervous system to control movement (Gallina et al., 2016; Tenan et al., 2016). These results also provide evidence of their distinct chronological functions: the VMO pulls the patella medially in advance of the VM to counteract the lateral force of the VL for patellar alignment.

A trend toward earlier VMO motor unit recruitment was also observed in a seated knee extension task (Tenan et al. 2013). This may not have reached statistical significance because the magnitude and direction of patella translation produced by the contraction of the VMO and VM differs with knee flexion angle (Lin et al., 2004). In the full knee extension position, the patella shifts medially when the VMO is activated, and the patella glides mainly to the proximal direction when the VM is triggered. With increasing knee flexion angle, there is a decrease in the amount of patella medial translation generated by the VMO compared to the full knee extension position. Whereas, during knee flexion there is a large medial shift of the patella produced by the VM compared to the fully extended leg position (Lin et al., 2004). Thus, the SLR may be a preferable position to differentiate the early recruitment of the VMO compared to the 90° knee flexion.

In the present study, motor unit recruitment thresholds were lower in the neutral hip position. The finding that motor units are recruited earlier in the neutral position also supports previous work examining the interference patterns of fine-wire EMG in the VMO during hip rotation (Cerny, 1995). Cerny (1995) reported greater VMO activation with a neutral hip position than during lateral hip rotation in terminal knee extension and isometric holding. They also monitored the distal part of adductor magnus activity concurrently with the VMO and reported that it was neither contributing to hip lateral rotation nor facilitating the VMO activation (Cerny, 1995). Others have suggested that lateral hip rotation facilitates VMO activity (Hanten and Schulthies, 1990; Irish et al., 2010) because the origin of the VMO attaches to the adductor magnus (Bose et al., 1980). However, recent anatomic studies have found that the longitudinal aspect of the medial adductor magnus, the ischiocondylar portion adjacent to the VMO and inserting on the adductor tubercle of the medial epicondyle of the femur (Broski et al., 2016), is innervated by the tibial division of the sciatic nerve (L4, 5, S1, 2, 3) (Barrett and Arthurs, 2010). This is different from the innervation of the VMO, which is innervated by the medial branch from the posterior division of the femoral nerve (L1, 2, 3) (Thiranagama, 1990). The ischiocondylar portion of the adductor magnus mainly serves to extend the hip (Broski et al., 2016), and may not contribute to lateral rotation of the hip.

While moving the knee joint in the sagittal plane, the nervous system may respond to the displacement force applied on the patella by adjusting motor unit activity in the surrounding musculature. When performing a SLR, lateral hip rotation can reduce the knee extension torque required to maintain full knee extension. This requires less VMO activation than a neutral hip position (Karst and Jewett, 1993). However, more activities of daily life occur with the hip in a neutral position in sagittal plane movements, such as walking, running, and biking. Performing the SLR with neutral hip rotation may generate a more effectively-controlled VMO muscle contraction that relates to everyday activity.

Our data show that VM and VMO motor units in female participants exhibit significantly higher initial firing rates at recruitment than in males, despite standardizing data collection to the late follicular phase, when females are most similar to males (Tenan et al., 2013). This suggests that sex is indeed a contributing factor for the differences in rate-coding of the vastus medialis complex. The statistically significant 1.18 Hz difference in motor unit firing rates observed between the sexes can contribute substantially to changes in muscle force (Oya et al., 2009) and is considered to be physiologically meaningful (Tucker et al., 2009; Tenan et al., 2013). Females exhibit greater proportion of slow twitch fibers and less fast twitch fibers in the VL than males (Simoneau and Bouchard 1989; Miller et al., 1993). It is possible that differences in motor unit discharge patterns in the VM and VMO reflect differences in motor unit type distributions between the sexes.

The borderline interaction between sex and hip position for recruitment threshold suggests that the female motor units predominantly drove the difference in recruitment thresholds between the two hip positions. Females activate motor units in vastus medialis complex earlier in neutral hip position than in lateral hip rotation, while males recruit their motor units at a relatively similar force level for both positions. Thus, dissimilar control of the vastus medialis complex in two hip positions during targeted quadriceps strengthening exercise may potentially be more beneficial for females. These sex differences may also be related to the finding that females managed to reach similar absolute force levels of MVC force for both hip positions, yet males had a much lower MVC force in the lateral hip rotation compared to neutral hip rotation.

The VMO accounted for the majority of the difference in initial firing rate at recruitment between the two hip positions. A faster initial firing rate occurred in neutral rotation compared to lateral rotation. Thus, SLR with neutral hip rotation is more beneficial for targeting the initial activation of the VMO. Other studies reported that populations of single motor units within a muscle, including the first dorsal interosseous, deltoid, and biceps, can be recruited preferentially for particular movements according to the force direction (Desmedt and Godaux 1981; Herrmann and Flanders, 1998). The preferential recruitment of the VMO when performing a SLR with no hip rotation indicates that regional motor neuron inputs may modulate differential activation of the sub-regions of the vastus medialis complex.

Future studies are necessary to evaluate other clinical exercise protocols that have been advocated to preferentially activate the VMO for individuals with knee pathology. This will promote more tailored and effective VMO strengthening strategies for both sexes. In summary, we have demonstrated that the VMO motor units are recruited earlier at lower force levels compared to the VM motor units. Females fire their VM and VMO motor units at faster rates at recruitment than males. The SLR with neutral hip rotation is a more effective hip position for strengthening the VMO in healthy individuals.

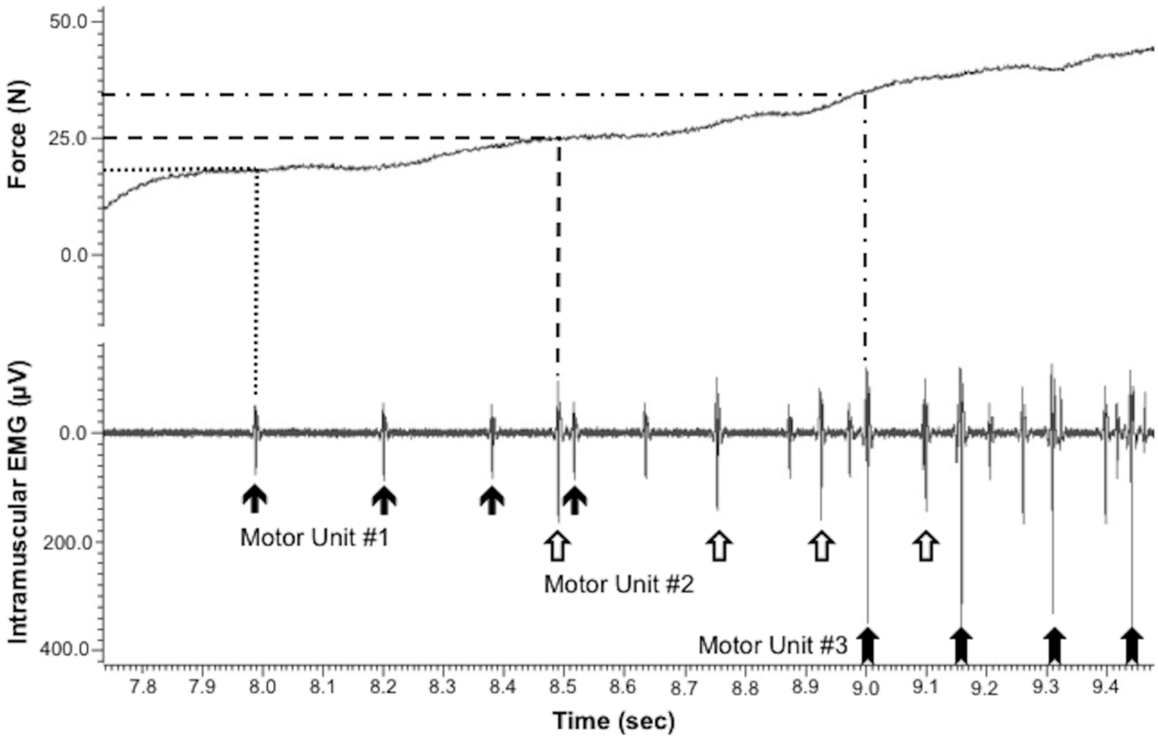

Figure 3.1. Single motor unit data reduction. The first four spikes of each single motor unit were identified as recruitment threshold. Initial firing rates and recruitment thresholds were calculated and recorded for each single motor unit.

Table 3.1. Distributions of the number and percentage of single motor units between levels of each predictor variable

Predictor Variables		Number of motor units
Sex	Male	359 (54.9%)
	Female	295 (45.1%)
Muscle	Vastus Medialis	302 (46.2%)
	Vastus Medialis Oblique	352 (53.8%)
Hip Position	Lateral Rotation	324 (49.5%)
	Neutral Rotation	330 (50.5%)

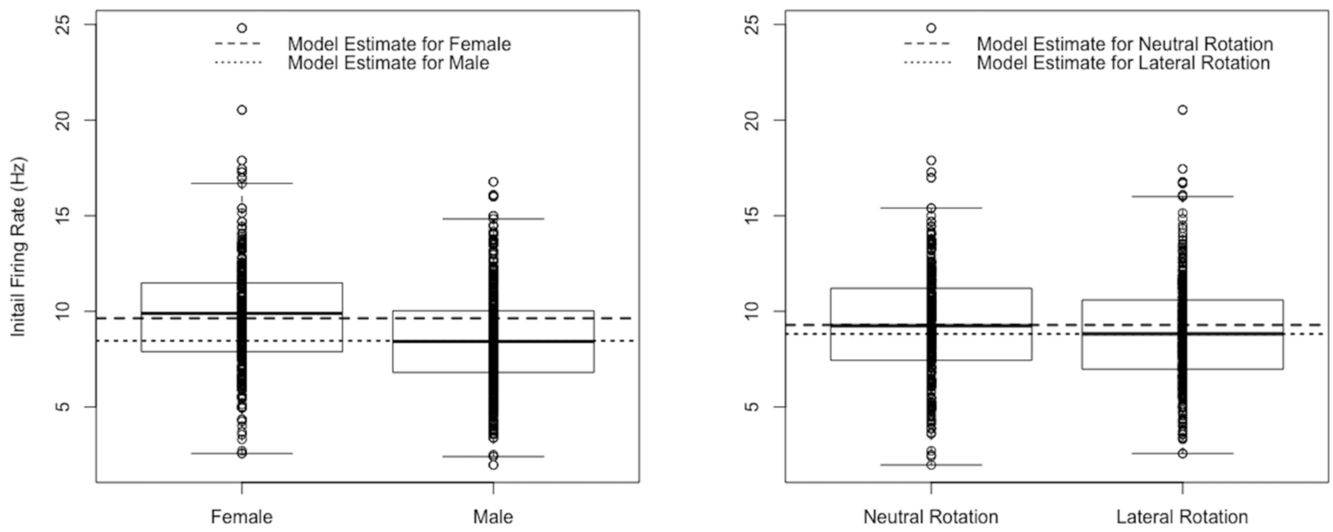

Figure 3.2. Data distributions of initial firing rates at recruitment and model estimates from linear mixed models in females and males with pooled averages over levels of muscle and hip position (left) and in neutral and lateral hip rotation with pooled averages over levels of sex and muscle (right). The circles indicate the raw data points. The dashed lines represent the model estimates for the respective variables. Each box contains the middle 50 percent of values with top and bottom borders representing the 75th and 25th percentile. The solid lines in the box represents the raw data median.

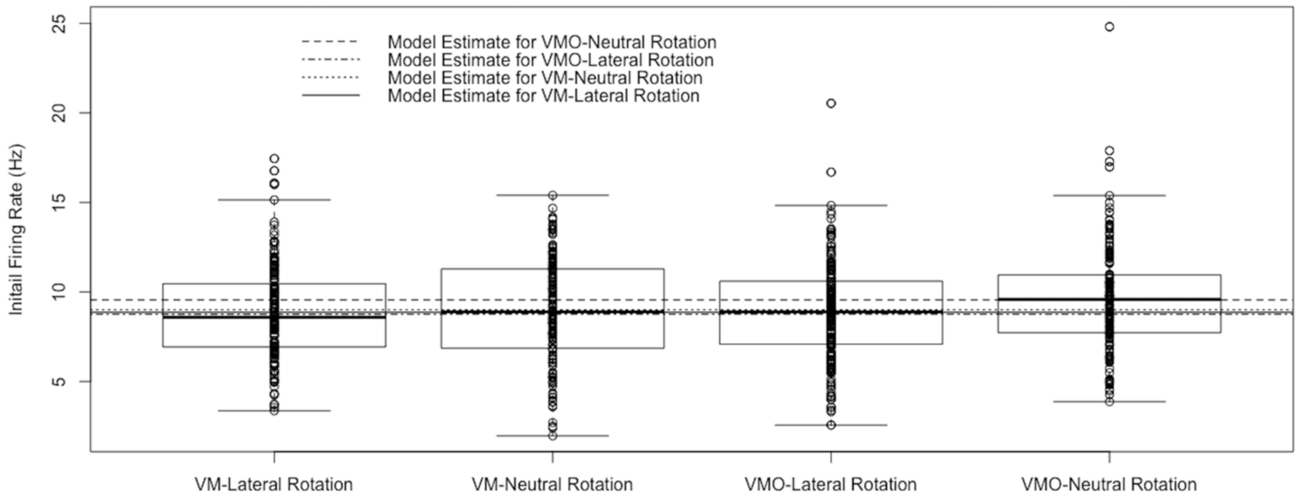

Figure 3.3. Data distributions of initial firing rates at recruitment and model estimates from linear mixed models of the VMO and VM in neutral and lateral hip rotation with pooled averages over male and female. The circles indicate the raw data points. The dashed/solid lines across the four boxes represent the model estimates for the respective variables. Each box contains the middle 50 percent of values with top and bottom borders representing the 75^{th} and 25^{th} percentile. The solid lines in the box represents the raw data median.

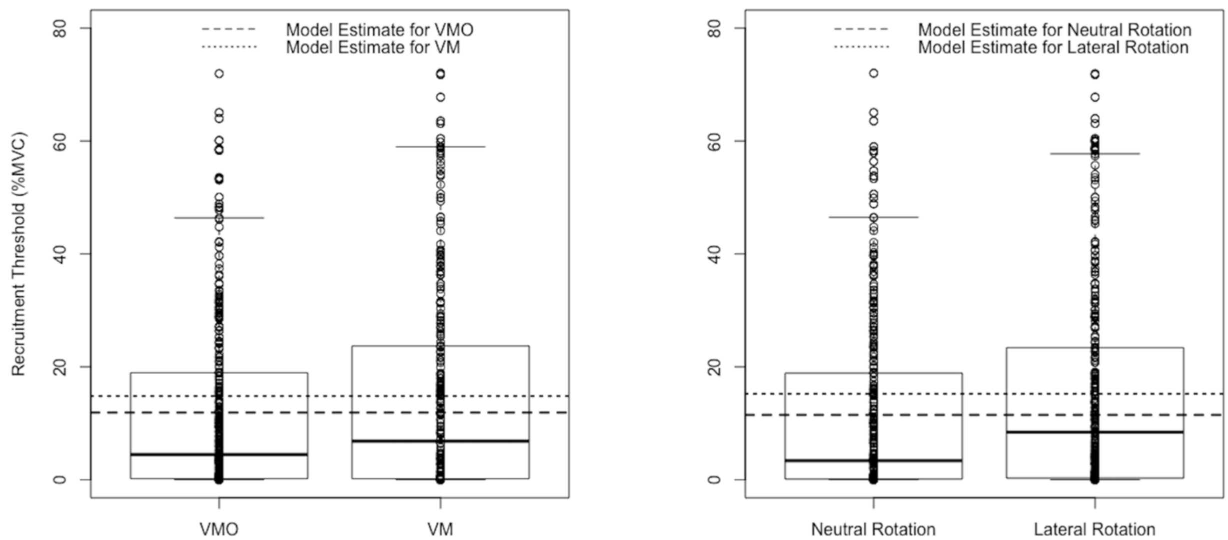

Figure 3.4. Data distributions of motor unit recruitment threshold forces and model estimates in the VMO and VM from linear mixed models with pooled averages over levels of sex and hip position (left) and in the two hip positions with pooled averages across sex and muscle (right). The circles indicate the raw data points. The dashed lines represent the model estimates for the respective variables. Each box contains the middle 50 percent of values with top and bottom borders representing the 75th and 25th percentile. The solid lines in the box represents the raw data median.

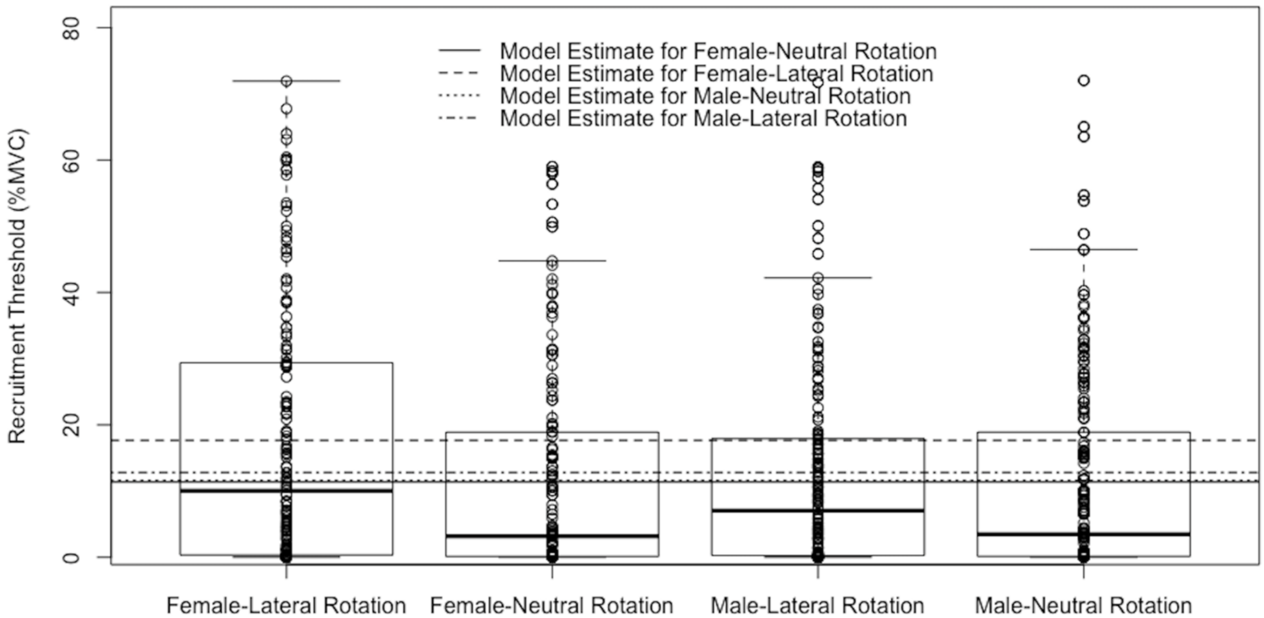

Figure 3.5. Data distributions of recruitment thresholds and model estimates from linear mixed models in female and male in neutral and lateral hip rotation with pooled averages over two muscles. The circles indicate the raw data points. The dashed/solid lines across the four boxes represent the model estimates for the respective variables. Each box contains the middle 50 percent of values with top and bottom borders representing the 75th and 25th percentile. The solid lines in the box represents the raw data median.

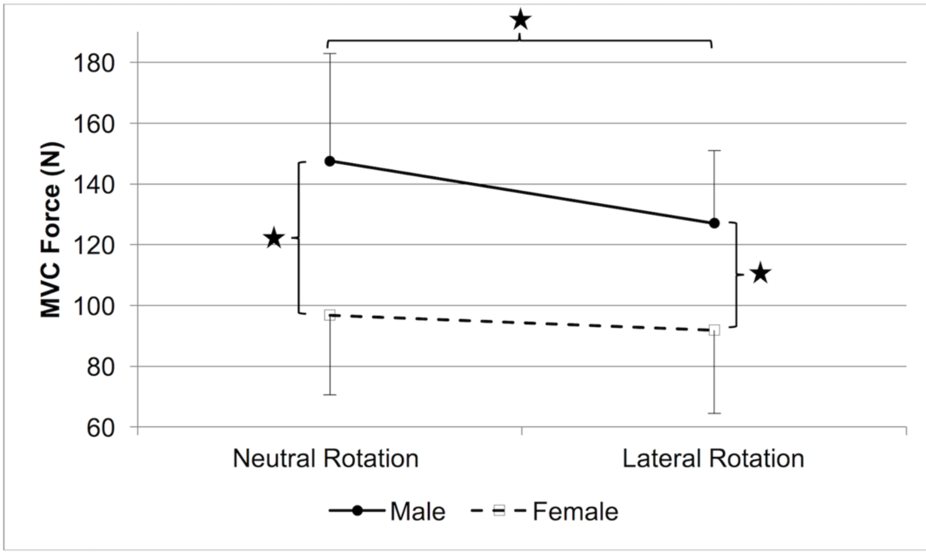

Figure 3.6. Means and standard deviations of MVC force between sex and hip position.

Chapter 4: Vastus Medialis and Vastus Medialis Oblique are Controlled Differently according to Hip Position in People with Patellofemoral Pain Syndrome

ABSTRACT

Patellofemoral pain syndrome (PFPS) is a commonly diagnosed knee pathology that is twice as prevalent in females. Clinicians prescribe exercises attempting to preferentially activate the vastus medialis oblique (VMO) to enhance medially vectored forces on the patella. Recently, our group confirmed clinical theory that the VMO is neurologically distinct from the vastus medialis (VM). However, the ability to voluntarily activate these muscle sub-sections in the PFPS population is unknown. The primary aim of this study is to determine how PFPS affects neuromuscular control of VM/VMO and to examine if hip rotation during a straight leg raise (SLR) modifies motor patterns. Thirteen healthy females and ten females with PFPS performed isometric SLRs in neutral hip position and lateral hip rotation. Bipolar intramuscular fine-wire electrodes were inserted into the VM and VMO. Linear mixed models were used to assess differences in initial firing rates at recruitment and recruitment threshold forces in 579 motor units. VMO motor units in the PFPS group fired 0.97 ± 0.45 Hz faster in lateral hip rotation than in the neutral hip position. Whereas the healthy participants exhibited an opposite pattern with 0.97 ± 0.42 Hz faster VMO firing rates in neutral hip position than in lateral hip rotation. The PFPS group showed delayed recruitment thresholds in VMO motor units and a delayed activation of vastus medialis complex in neutral hip position. Thus, a SLR with lateral hip rotation is a more efficient hip position to differentially activate the VMO in individuals with PFPS.

INTRODUCTION

Generalized knee pain is the most prevalent source of joint pain in the United States (CDC, 2008). Among the causes of anterior knee pain, patellofemoral pain syndrome (PFPS) is the most common diagnosis (Foss et al., 2014) with 2.23 times higher incidence in females than in males (Boling et al., 2010). Delayed and inadequate vastus medialis oblique (VMO) recruitment can lead to mal-tracking of the patella, which is believed to be a main contributing factor to PFPS (McConnell, 1996; Boling et al., 2006). Exercise programs often assume VMO weakness and focus on VMO strengthening to counteract excessive vastus lateralis (VL) force on the patella.

Differential activation within the vastus medialis complex has been substantiated in recent years by using fine-wire EMG and surface EMG grid techniques (Tenan et al., 2013 & 2016; Gallina et al., 2016 & 2017; Peng et al., 2018). The ability to selectively control the distal fibers of the vastus medialis complex supports the existence and differential function of the VMO. The VMO serves as a medial stabilizer for the patella due to its distal location and its large pennation angles relative to the vastus medialis (VM) (Farahmand et al., 1998). Innervations of the VM and VMO both originate from L1, L2, and L3, yet the VMO is controlled by a larger number of terminal nerve branches per area than the VM (Thiranagama, 1990; Jojima et al., 2004). Thus, the VM and VMO are functionally and neurologically distinct from each other. Moreover, our research group recently demonstrated that the VMO can be preferentially recruited from the VM in a healthy population (Peng et al., 2018).

Numerous clinical studies have used surface EMG to examine activation amplitude and onset timing of the VMO in healthy populations and in individuals with PFPS. However, there is conflicting evidence regarding the ability to preferentially recruit the VMO through various exercise protocols, making exercise prescription difficult (Hanten & Schulthies, 1990; Laprade et al., 1998; Tobin & Robinson, 2000; Boling et al., 2006). Some clinical studies have reported that the activation amplitude and onset timing of the VMO are affected by exercise type (Herrington et al., 2006; Felicio et al., 2011), limb position (Karst and Jewett, 1993; Laprade et al., 1998; Sykes and Wong, 2003; Serraoa et al., 2005) and PFPS (Cowan et al., 2001; Cowan et al., 2002; Cavazzuti et al., 2010; Aminaka et al., 2011). Others have not observed differences in the VMO recruitment among these factors (Laprade et al., 1998; Owings and Grabiner, 2002; Herrington et al., 2006). Long-held disagreement on the existence of the VMO (Boling et al., 2006; Smith et al., 2009) may explain inconsistencies in electrode placement and different findings in the aforementioned studies when using standard surface EMG to record VMO activity. Due to the narrow arrangement of the quadriceps musculature, the surface electrode placed on the VMO is susceptible to EMG cross-talk from adjacent muscles, including the VM and adductors (Byrne et al., 2005; Tucker et al., 2009; Wong et al., 2013). The use of fine-wire EMG recording eliminates signal cross-talk noise and is the gold standard for evaluating changes in single motor unit behavior, especially within a singular muscle such as the vastus medialis complex.

By using fine-wire intramuscular EMG recording, our group published a definitive work on differential activation of the VM and VMO motor units in a healthy population, demonstrating that the VMO can be preferentially recruited when the hip is positioned in neutral hip rotation during a straight leg raise (SLR) (Peng et al., 2018). The SLR is a popular self-training exercise for people with PFPS to specifically strengthen the VMO (Sykes and Wong, 2003) with minimal compression force on the patellofemoral joint (Singerman et al., 1995; Mesfar and Shirazi-Adl, 2005). The purpose of the present study is to further the research by investigating VM/VMO control in individuals with PFPS when performing SLR between two hip rotation positions. This data is then contrasted with our previously-reported data in a healthy female population to determine if those with PFPS exhibit different VM and VMO motor unit recruitment patterns during a SLR with and without hip rotation.

METHODS

Participants and ethical approval

Thirteen healthy females (26.5 ± 4.3 yr) without any ongoing hip, knee, or ankle pain, previous leg surgery, immobilization, or arthritis to the dominant leg, were recruited as the control group. Some of the control group data has been published previously (Peng et al., 2018), but is necessary to include it in this study for adequate comparison with PFPS patients. Ten females (25.9 ± 6.0 yr) experiencing current retro-patellar or peri-patellar pain were enrolled in the PFPS group by referrals from local physical therapists and recruitment flyers. Participants must have had symptoms for at least one month that could be induced or aggravated by at least two of the following activities: ascending/descending stairs, hopping/jogging, prolonged sitting, kneeling, or squatting (Boling et al., 2010). Participants from both groups were excluded if they had a history of traumatic leg injuries (either leg), neurological, cardiovascular, or metabolic dysfunction, impaired sensorimotor capability, or medication affecting the central nervous system and cardiovascular system, as well as medication that could affect the nervous system. All participants had regular menstrual cycles for at least two months prior to the experiment, except for two who were amenorrheic for more than a year before the experiment. The eumenorrheic females participated in the study during their late follicular phase (for example, day 8 to day 14 in a 28-day menstrual cycle), because females have comparable single motor unit firing rates and recruitment thresholds to males during this phase (Tenan et al. 2013). We did not control for the menstrual cycle phase for the two amenorrheic females. Cook's distance statistics were run to determine if the amenorrheic women had an overly influential effect on the analysis and no adverse influence was found; therefore, all women were assessed together. All participants signed an informed consent form and all experimental procedures were approved by the University of Texas at Austin Institutional Review Board.

Experimental protocol

All study visits were administered in the Neuromuscular Physiology Laboratory at the University of Texas at Austin. Participants were instructed to avoid strenuous exercise 48 hours prior to data collection and to refrain from caffeine and alcohol consumption eight hours prior to their visit. All participants filled out a health-history questionnaire. Additionally, the PFPS group filled out an Anterior Knee Pain Scale to report pain severity affected by PFPS and their ability to perform functional activities (Kujala et al., 1993).

Participants were seated in an adjustable chair for skin preparation and fine-wire EMG electrode placement in their dominant leg. Two pairs of bipolar intramuscular insulated stainless-steel fine-wire electrodes (0.002 mm, California Fine Wire Company, Grover Beach, CA) with 3 mm of insulation removed from the tip were inserted into the VMO and the VM with thin (25 gauge, 16 mm length), disposable hypodermic needles. Signals obtained from the wires were pre-amplified and hardware bandpass filtered at 8 Hz - 3.12 kHz with a gain of 330 (B&L Engineering, Tustin, CA). All electrodes and needles were fully autoclaved and sterilized before use. The two fine-wire electrodes for the VMO were placed at 4 cm and 5 cm proximal to the superior medial border of the patella and oriented 55° medially from the femoral axis. The two electrodes for the VM were placed at 11 cm and 12 cm proximal to the superior medial border of the patella and oriented 15° medially from the femoral axis (Travnik et al., 1995; Rainoldi et al., 2004; Peng et al., 2018). An adhesive pre-gelled Ag/AgCl surface electrode of 5 mm diameter was placed on the ipsilateral patella as a ground.

After the EMG setup, the participant was positioned lying supine on a medical examination table with the knees fully extended. The chest, waist, and non-dominant thigh were immobilized with straps and the dominant ankle was affixed with a padded restraint attached to a strain gauge (Entran Sensor & Electronics, Fairfield, NJ) underneath the table. Participants were instructed to perform an isometric SLR in two different hip positions, neutral (no rotation) and 30° of lateral hip rotation. The plantar surface of the foot was slightly pushed against a flat board to hold the ankle in neutral position and the foot was fixed between two boards to maintain the required hip rotation angles. Verbal instruction was provided as "Try to lift your leg straight up with your knee fully extended." Three three-second isometric maximal voluntary contractions (MVCs) were performed with a one-minute rest period between contractions to prevent muscle fatigue. The intraclass correlation coefficient (ICC (3,1)) for the MVCs was 0.99.

Following the MVCs, a 75% MVC target force was determined from the average of the three MVCs and the participants practiced a controlled ramp contraction. The ramp contraction consisted of following a line on a computer screen in front of them with a rate of rise of 7.5% MVC/sec up to 75% MVC and then a hold at 75% MVC for 5 seconds. One successful trial with smooth force generation was collected for each hip position. The location and severity of each pain occurrence before, during and after a ramp-up contraction was recorded after each trial using a Visual Analog Scale (VAS) for the PFPS group (Table 4.1). Intramuscular EMG and force data were recorded in Spike2 (version 5.21, Cambridge Electronic Design, Cambridge, England) with sampling rate at 30k Hz and 1 Hz, respectively.

Single motor unit and force data reduction

Intramuscular EMG and force data were analyzed in Matlab (version 2010b, Mathworks, Natick, MA) and Spike2 (version 7.09) software. Signals from the fine-wire electrodes were zerolag bandpass filtered at 100 Hz – 8 kHz with a 4th-order Butterworth filter. Individual motor unit action potentials were identified visually based upon shape, amplitude and discharge timing. Recruitment threshold and initial firing rate at recruitment of each single motor unit were identified from the VM and VMO during the SLR ramp-up trials in the two different hip positions. Recruitment threshold for each single motor unit was defined as the force at which the first of four consecutive spikes discharged at regular intervals normalized to the MVC force (Van Cutsem et al., 1998; Tenan et al., 2013; Peng et al., 2018). Initial firing rate at recruitment is reported as the reciprocal of the first three interspike intervals averaged in hertz. The force data was notch filtered at 60 Hz using a 4th-order recursive Butterworth filter and the baseline subtraction DC offset was removed using Matlab (version 2010b, Mathworks, Natick, MA).

Statistical analysis

All statistical analysis was performed in RStudio (version 1.1.456) (RStudio Team, 2016) with R Core version 3.5.1 using ggplot2 (Wickham, 2009), influence.ME (Nieuwenhuis et al., 2012), lmerTest (Kuznetsova et al., 2016), lme4 (Bates et al., 2015) and lsmeans (Lenth, 2015) packages. A linear multilevel model with an unstructured variance covariance structure and unadjusted post hoc tests was used to evaluate the effects of group (healthy and PFPS), muscle (VM and VMO) and hip position (neutral rotation and lateral rotation) on initial firing rate and recruitment threshold during the SLR. The multilevel model approach accounts for the correlation among collective motor units from an individual (Tenan et al., 2014). The first level of the model was single motor unit level with muscle and hip position as the predictor variables. Above clusters of single motor units level was the second individual subject level with group as its predictor variable. This mixed model analysis examined cross-level interactions including one three-way interaction among muscle, hip position, and group, and two two-way interactions between muscle and group, and hip position and group.

The multilevel model equation for initial firing rate at recruitment was written as below (i). The model assumption of normal residuals and constant variance within each level were met. Consistent with our previous work (Tenan et al., 2013; Peng et al., 2018), we use the absolute force at which each single motor unit was recruited as a covariate in the model due to the correlation between recruitment threshold and initial firing rate (Milner-Brown et al., 1973). We also examined the intraclass correlation of initial firing rates at the subject level because the motor unit firing patterns are correlated within an individual (Tenan et al., 2014).

Level 1

Initial Firing $Rate_{ij} = \beta_{0j} + \beta_{1j}Muscle_{ij} + \beta_{2j}Hip\ position_{ij} + \beta_{3j}Muscle*Hip\ position + \beta_{4j}Force + e_{tij}$

Level 2

$\beta_{0j} = \gamma_{00} + \gamma_{01}Group + u_{0j}$

$\beta_{1j} = \gamma_{10} + \gamma_{11}Group$

$\beta_{2j} = \gamma_{20} + \gamma_{21}Group$

$\beta_{3j} = \gamma_{30} + \gamma_{31}Group$

$\beta_{4j} = \gamma_{40}$ ……………………………………………………………………………….....(i)

The linear mixed model equation for recruitment threshold was written as below (ii). The raw recruitment threshold data was natural logarithm transformed before entering the model to meet the assumptions of normality of residuals and constant variance within each level. However, to help the interpretation of the findings, the recruitment threshold data presented in the result section and in the figures were exponentiated back to the original units as percentage of MVC. We use violin plots to show the data distribution of the raw recruitment thresholds because the majority of the single motor units were recruited within the lower force level of 25% MVC. The averaged absolute force did not serve as a covariate in the model because of its mathematical relation to the recruitment threshold.

Level 1

$$\text{Recruitment Threshold}_{ij} = \beta_{0j} + \beta_{1j}\text{Muscle}_{ij} + \beta_{2j}\text{Hip position}_{ij} + \beta_{3j}\text{Muscle*Hip position} + e_{tij}$$

Level 2

$$\beta_{0j} = \gamma_{00} + \gamma_{01}\text{Group} + u_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11}\text{Group}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}\text{Group}$$

$$\beta_{3j} = \gamma_{30} + \gamma_{31}\text{Group} \quad \text{(ii)}$$

A two-way repeated measure ANOVA and Bonferroni post-hoc tests were used to evaluate the differences in the absolute MVC forces between the two hip positions and two groups.

RESULTS

Motor unit recordings

A total of 579 motor units were recorded from the 23 participants. Distributions of the number and percentage of single motor units between the levels of each predictor variable are shown in Table 4.2.

Initial motor unit firing rate at recruitment

There was a three-way interaction effect among group, muscle, and hip position for initial firing rate at recruitment (F (1, 557) = 4.07, p = 0.04). Post hoc analysis revealed differences in initial firing rates at recruitment for VMO motor units between the two hip positions for healthy individuals and for people with PFPS after controlling for force (Figure 4.1). In the healthy group, the initial firing rates of the VMO motor units were faster in the neutral hip position (10.28 ± 0.46 Hz) than in lateral hip rotation (9.31 ± 0.44 Hz; t (565) = 2.29, p = 0.02). For individuals with PFPS, VMO initial motor unit firing rates were slower in the neutral hip position (9.00 ± 0.49 Hz) than in lateral hip rotation (9.97 ± 0.50 Hz; t (564) = -2.17, p = 0.03). However, initial motor unit firing rates in the VM exhibited similar patterns between the neutral and lateral hip rotation for both healthy (t (565) = 1.40, p = 0.162) and PFPS (t (565) = 1.124, p = 0.262) groups. A difference in firing rates between the VM and VMO was observed only in people with PFPS when performing SLR in the neutral hip position (t (566) = -3.09, p = 0.002); VMO motor units fired at slower rates (9.00 ± 0.49 Hz) than the VM (10.37 ± 0.50 Hz) after controlling for force. While not significant at the prescribed alpha level, it is possible that a difference exists in VMO firing rates between the groups in neutral hip position (t (55) = 1.89, p = 0.06), suggesting that the healthy participants fired their VMO motor units at faster rates (10.28 ± 0.46 Hz) compared to individuals with PFPS (9.00 ± 0.49 Hz) in neutral hip position.

Recruitment thresholds

The linear mixed model revealed a main effect for hip position (F (1, 560) = 5.01, p = 0.03) on the log-transformed recruitment thresholds. Post hoc analysis indicated an earlier motor unit recruitment in the vastus medialis complex in the neutral hip position (13.13 ± 1.19 %MVC) than in lateral hip rotation (16.25 ± 1.19 %MVC; t (566) = -2.22, p = 0.03) (Figure 4.2). However, we cannot ignore the possible interaction effect since the effect of the hip position may depend on the other two variables contained within interaction effects that affect the main effect estimates. A potential difference in log-transformed recruitment threshold was discovered between group and hip position (t (560) = 3.79, p = 0.052). This possible interaction effect indicates that the majority of the difference between the two hip positions was derived from earlier recruitment of the motor units in the vastus medialis complex in healthy individuals during neutral hip rotation (10.36 ± 1.64 %MVC) compared to lateral hip rotation (16.12 ± 1.63 %MVC; t (566) = -2.961, p = 0.003) (Figure 4.3). Recruitment threshold forces in the neutral hip position were also lower in healthy participants (10.36 ± 1.64 %MVC) than in individuals with PFPS (15.96 ± 1.73% MVC) with pooled averages over the two muscles (t (47) = -2.079, p = 0.04) (Figure 4.3). While not statistically significant, another interaction showed possible effects in log-transformed recruitment threshold between muscle and group (F (1, 567) = 2.88, p = .09). Healthy participants were able to recruit the VMO motor units earlier at lower force levels (11.81 ± 1.58 %MVC) compared to individuals with PFPS (17.14 ± 1.73 %MVC; t (44) = -1.990, p = 0.053) (Figure 4.4).

Absolute MVC force

There was no significant difference in the absolute MVC force in SLR between groups or hip positions ($p > 0.05$). Healthy individuals exhibited an average absolute MVC force of 96.79 ± 7.28 N in the neutral hip position and 91.90 ± 7.61 N in lateral hip rotation. People with PFPS displayed an average absolute MVC force of 120.19 ± 16.26 N in the neutral hip position and 109.15 ± 12.67 N in lateral rotation. The slightly higher absolute MVC forces in the PFPS group can be explained by a more active exercise habit compared to the control group with a higher averaged exercise intensity (PFPS group: moderate; healthy group: light to moderate) and longer average exercise time per week (PFPS group: 266 ± 252 minutes/week; healthy group: 213 ± 135 minutes/week).

DISCUSSION

The main purpose of the study was to evaluate the effect of PFPS on motor unit firing patterns in the VM and VMO between two different hip positions when performing a SLR. The results demonstrate that the PFPS group has an altered VMO control pattern in initial motor unit firing rate at recruitment between neutral and lateral hip rotation compared to the healthy group. Healthy individuals fired VMO motor units at a faster rate at recruitment in the neutral hip position than in lateral hip rotation, while the PFPS group exhibited an opposite relation between the two hip positions. The PFPS group also showed a compensated faster firing rate at recruitment in the VM in response to the slower firing rate in the VMO in the neutral hip position. While not reaching statistical significance, a possible lower initial firing rate at recruitment in the PFPS group relative to healthy individuals was observed in the VMO during SLR with neutral hip position. Hip position is a main contributing factor for recruitment threshold, showing that a neutral hip position allows the motor units in the vastus medialis complex to be recruited earlier at a lower force level compared to lateral rotation. A potential interaction effect between hip position and group implies that the healthy individuals accounted for the majority of the differences between the two hip positions, while similar recruitment thresholds were observed between neutral and lateral hip rotation were observed in the PFPS group.

Hip position is a crucial contributing factor to the different VMO firing patterns between healthy individuals and those with PFPS. In the healthy individuals, neutral hip rotation is a more efficient posture to recruit VMO motor units at a faster rate and this hip position also allows the motor units in the vastus medialis complex to be activated at lower force levels compared to lateral hip rotation. Such directional tuning of the firing pattern in the vastus medialis complex has been reported in our previous study (Peng et al., 2018), suggesting that the motor units in the VMO receive different descending signals that are dependent on the postural changes of limbs (Flanders and Soechting, 1990).

Our results coincide with a previous study illustrating that a neutral hip position allows greater VMO activity compared to lateral hip rotation in different exercises in a healthy population, using fine-wire EMG interference patterns (Cerny, 1995). Examples of the exercises include maintaining terminal knee extension with isometric holding and quadriceps setting (Cerny, 1995). Similar to these exercises, the isometric SLR required participants to keep their knees fully extended. The nervous system may adjust the motor unit behavior according to the force applied on the patella. Laterally rotating the hip from a neutral posture can diminish the demand of the extension torque on the knee and therefore less recruitment of the VMO is needed (Karst and Jewett, 1993).

Studies on upper extremity muscles show that the recruitment of single motor units in a muscle can be modulated depending on joint action (ter Haar Romeny et al., 1982 and 1984; van Zuylen et al., 1988), movement direction (Flanders and Soechting, 1990; Theeuwen et al., 1994; Herrmann and Flanders, 1998), and joint angle (van Zuylen et al., 1988; Flanders and Soechting, 1990). Flanders and Soechting (1990) proposed that limb position is a substantial determinant of muscle activation patterns. Shoulder rotation altered the capacity of peak EMG amplitudes in upper arm and forearm muscles and changed the direction of force exerted on the wrist joint (Flanders and Soechting, 1990). Moreover, when force generated by a muscle fiber approached its ideal contraction direction, the recruitment threshold of the motor units would gradually lower and the firing rate would progressively increase (Herrmann and Flanders, 1998).

However, motor unit recruitment may be modified by pain. In the present study, the PFPS group exhibited an opposite VMO activation pattern to the healthy participants, with a higher initial motor unit firing rate at recruitment in lateral hip rotation compared to a neutral hip position. Hip movements in daily activities more commonly occur in the sagittal-dominant plane, such as sit-to-stand, walking, running and biking. However, with the interference of pain at the patellofemoral joint, the SLR with neutral hip position fails to efficiently utilize the VMO, which may compromise patella stability while maintaining an extended knee. Instead, a more uncommon hip position, hip lateral rotation, allows for the recruitment of the VMO motor units for people with PFPS.

Pain can cause a re-distribution of recruited motor units from sub-regions of a muscle. In order to maintain force output, a newly recruited motor unit population in the VMO and VL was identified after an injection of experimentally induced pain (Tucker et al., 2009; Tucker and Hodges, 2009 & 2010). A change in the population of motor units may correlate with a change in the preferred movement direction (Herrmann and Flanders, 1998; Tucker et al., 2009; Tucker and Hodges, 2010). Thus, it is possible that the VMO motor units recruited during pain were a different population with different muscle fiber pennation angles than occurs in a healthy population and that the SLR with lateral hip rotation was a more favorable position to activate the VMO motor units in the PFPS group. Moreover, Berger et al. (2011) reported that additionally-recruited motor units during pain are larger in size to compensate for reduced firing rates in the originally activated motor units (Berger et al., 2011). In the PFPS group, we observed higher motor unit recruitment thresholds in the vastus medialis complex in neutral hip position compared to the healthy individuals. Thus, it is possible that a different population of larger motor units were engaged in painful contractions.

Slower motor unit firing rates at recruitment in the VMO may occur in the PFPS group compared to the healthy participants during SLR with neutral hip rotation. Previous research demonstrated that reduced motor unit firing rates are accompanied with acute experimental induced pain (Sohn et al., 2000; Farina et al., 2004; Tucker et al., 2009; Tucker and Hodges, 2009

& 2010). Tucker and colleagues (2009, 2009, 2010) proposed a redistribution strategy in recruiting motor units in the VMO and VL after induced pain in the infra-patella pad, which indicates decreased firing rates in pre-existing motor units and newly recruited motor units in the same muscle (Tucker et al., 2009; Tucker and Hodges, 2009 & 2010). This modulation of motor unit recruitment may be explained by uneven distribution of input to the motoneuron pool which not only takes account of task completion but also considers pain minimization (Tucker and Hodges, 2009 & 2010).

The amount of difference in the VMO firing rate was 1.28 Hz between the healthy and PFPS groups. This difference is comparable to previous studies with 1-1.7 Hz differences before and after acute experimentally-induced pain (Farina et al., 2004; Tucker et al., 2009; Tucker and Hodges, 2009 & 2010) and 0.7 Hz difference between healthy and chronic pain in knee osteoarthritis (Berger et al., 2011). The range of firing rate in the vastus medialis complex is relatively narrow from 8 Hz at 10% MVC to 26 Hz at MVC (Roos et al., 1999). Therefore, even though the firing rate reduction in the VMO did not reach statistical significance ($t\ (55) = 1.89$, $p = 0.06$), the effect of PFPS should be carefully considered because a small change in firing rates may indicate substantial change in motor control strategy (Berger et al., 2011).

Unlike the previously-mentioned experimentally-induced pain, the duration of symptoms in our PFPS group were at least one month long. Berger et al. (2011) demonstrated a lower motor unit firing rate in the distal vastus medialis complex as a result of chronic knee pain was associated with knee osteoarthritis. They suggested a permanent motor unit remodeling process might be in progress, which relates to an increased recruitment of larger size motor units with lower discharge rates to maintain the submaximal target force (Berger et al., 2011). Smaller size motor units are usually engaged earlier at lower recruitment thresholds (Hennenman, 1957) and display greater firing rates (De Luca and Erin, 1994) to permit fine control of force output (Hennenman, 1957). A trend of delayed recruitment of the VMO motor units in the PFPS group was reported in our study, which can be explained by additional recruitment of larger motor units with higher recruitment threshold in the VMO. Delayed activation of the motor units may compromise the ability of the VMO to stabilize and fine-tune the patella movement and further result in PFPS and maintenance of pain.

We did not observe decrement in initial firing rates in response to pain for the VM motor units. This supports the previous findings demonstrating differential control between the VM and VMO (Tenan et al., 2013 & 2016; Gallina et al., 2016 & 2017; Peng et al., 2018), and it also indicates that these two muscles react dissimilarly to PFPS. As a synergist of the VMO, motor units in the VM increase their firing frequency when the initial firing rate drops in the VMO during a SLR in the neutral hip position. Synergistic muscles increase their activity to compensate for reduced recruitment during pain (Farina et al., 2004). However, Hodges (2008) reported that the firing rates in synergetic muscles decreased along with the painful muscle in an experimentally-induced pain injected to the lateral gastrocnemius (Hodges et al., 2008). They suggested another possible strategy to maintain force by recruiting additional higher threshold motor units in the same muscle (Hodges et al., 2008). Although it is not feasible in the current study to identify existing motor units and newly recruited motor units, a delayed recruitment threshold in the VMO motor units corresponds to the theory of additional recruitment of higher threshold motor units for individuals with PFPS.

Individuals with PFPS adopt a different control strategy for how hip position changes the differential activation of the VMO from the vastus medialis complex when performing a SLR task. In painful contractions recorded in the PFPS group, we observed a faster VM motor unit firing rate at recruitment, which may compensate for the reduced initial firing rate in the VMO motor units in neutral hip rotation. The SLR with lateral hip rotation may consequently be more beneficial in selectively recruiting VMO motor units in people with PFPS, while a neutral hip position is more favorable for the healthy participants. Moreover, the PFPS group loses the advantage of advanced recruitment of the motor units in the vastus medialis complex in neutral hip rotation compared to the healthy group. Because the recruitment patterns within the vastus medialis complex are altered in the population suffering subacute to chronic knee pain, future studies should evaluate how VMO motor unit recruitment occurs in other clinical exercise protocols devised to target on VMO strengthening.

Table 4.1. Descriptive data of pain in PFPS group (n=10)

Side of leg being tested	6 right legs and 4 left legs
Symptom duration	1 month – 1 year (n=4) 1 year – 3 years (n=4) 6 years (n=2)
Anterior Knee Pain Scale	74.9 ± 13.5 (Full function score: 100)
VAS before and after experiment	0.1 ± 0.3 (Range: 0 – 1)
VAS during straight leg raise	3.2 ± 1.9 (Range: 0 – 6)

* *Values are means ± SD.*

Table 4.2. Distributions of the number and percentage of single motor units between levels of each predictor variable

Predictor Variables		Number of Motor Units
Group	Healthy	295 (50.9%)
	PFPS	284 (49.1%)
Muscle	VM	273 (47.2%)
	VMO	306 (52.8%)
Hip Position	Lateral Rotation	288 (49.7%)
	Neutral Rotation	291 (50.3%)

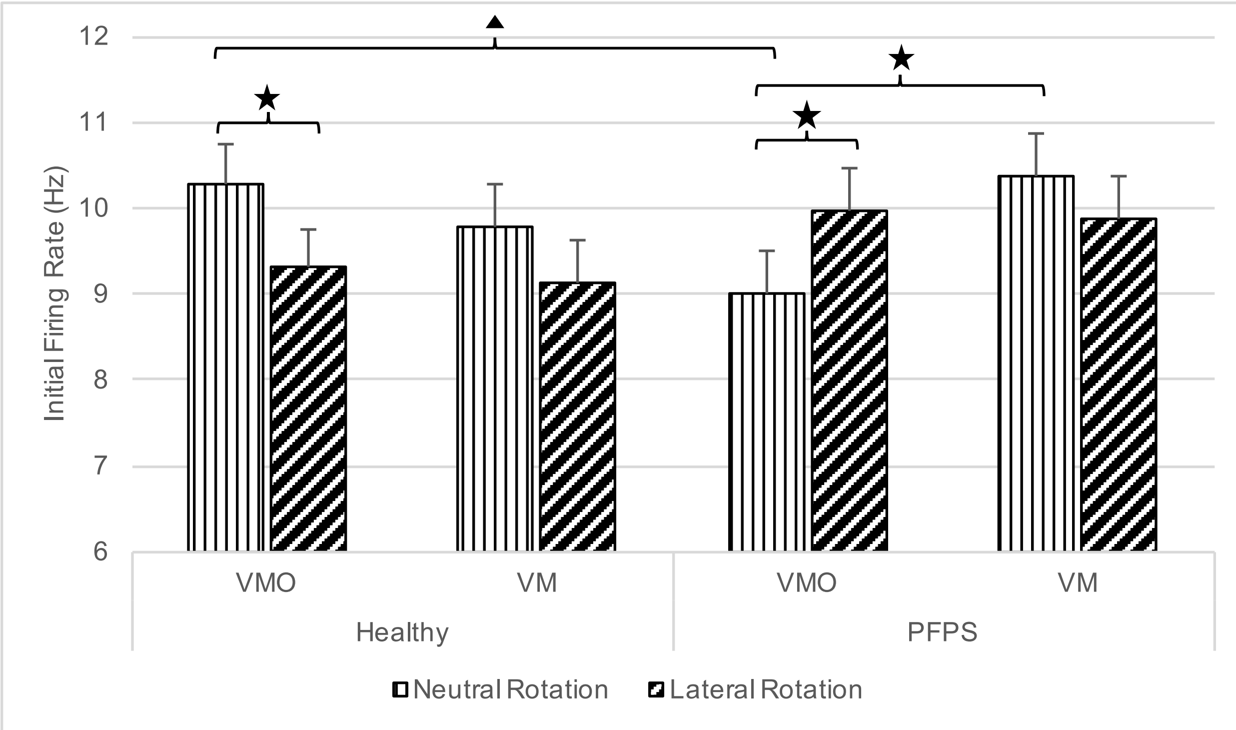

Figure 4.1. Model estimates and standard errors of initial firing rates at recruitment from the 3-way interaction effect of group (healthy and PFPS), muscle (VM and VMO), and hip position (lateral and neutral hip rotation) in the linear mixed model. ★: p value < 0.05; ▲: p value < 0.10.

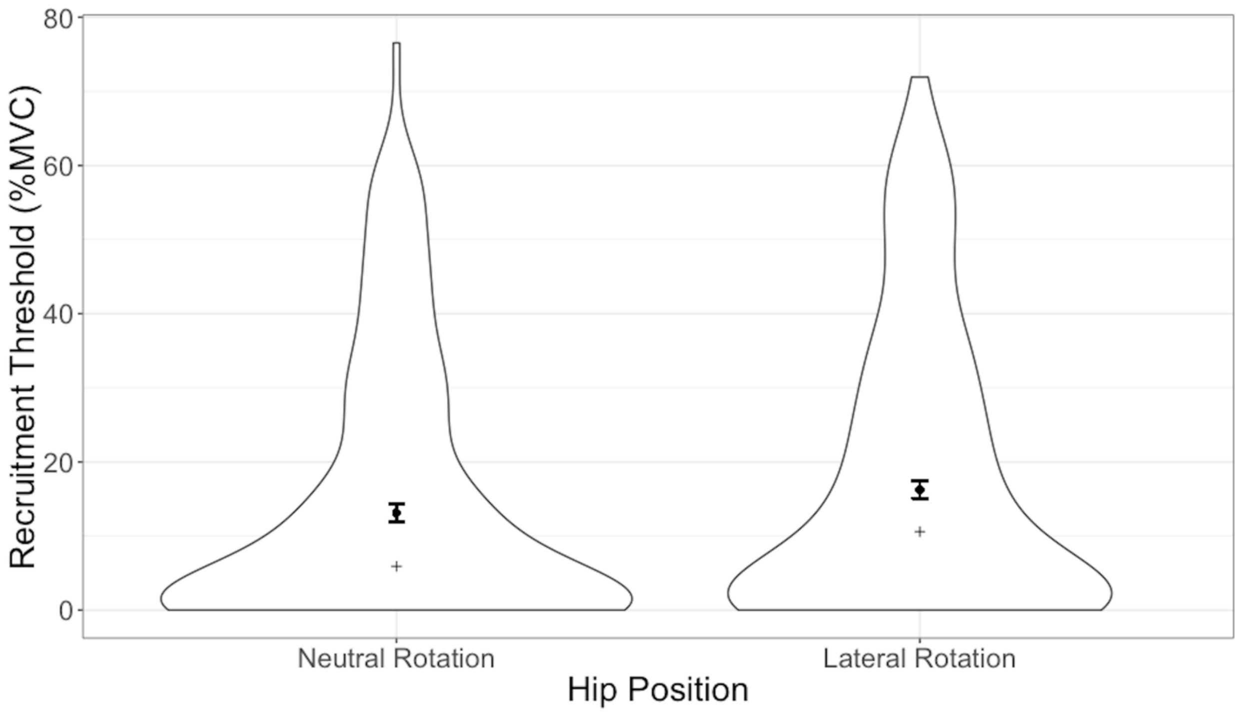

Figure 4.2. Model estimates (solid circles) and standard errors (error bars) of recruitment threshold forces from linear mixed model for the neutral and lateral hip rotation with pooled averages over levels of group and muscle. The violin plot outlines illustrate kernel probability density with the enclosed area representing the data distribution. The plus sign indicates the raw data median.

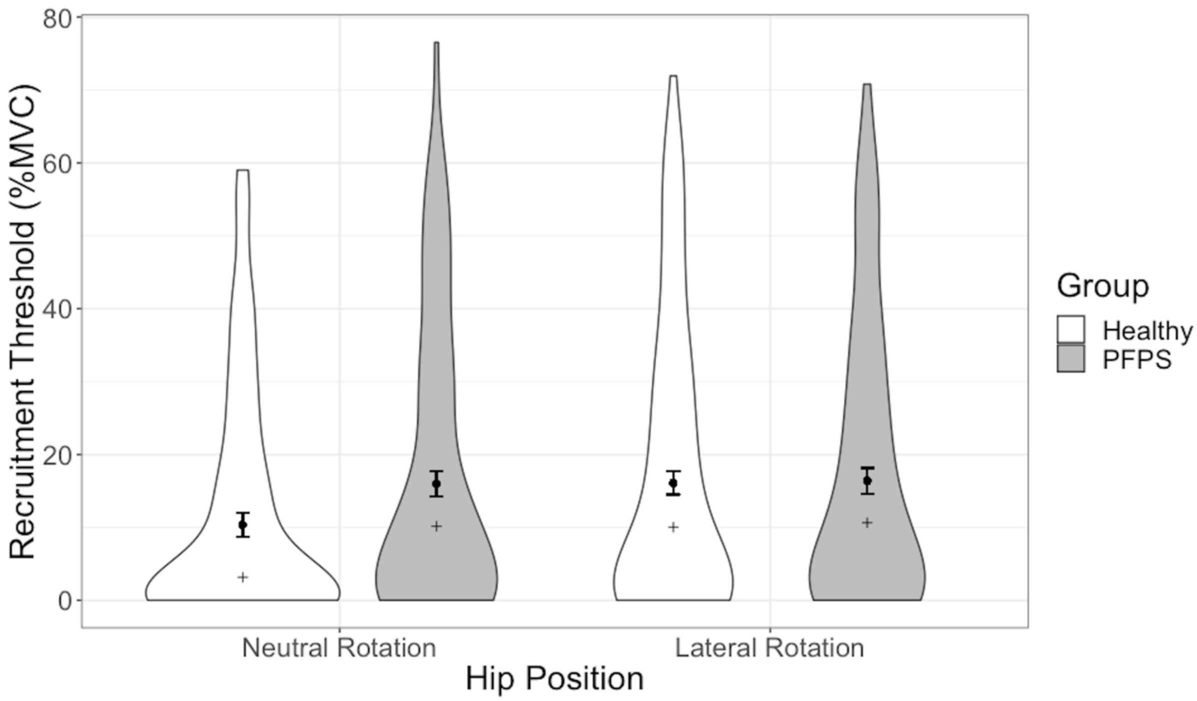

Figure 4.3. Model estimates (solid circles) and standard errors (error bars) of recruitment threshold forces from linear mixed model for healthy individuals and people with PFPS in neutral and lateral hip rotation with pooled averages over the two muscles. The violin plot outlines illustrate kernel probability density with the enclosed area representing the data distribution. The plus sign indicates the raw data median.

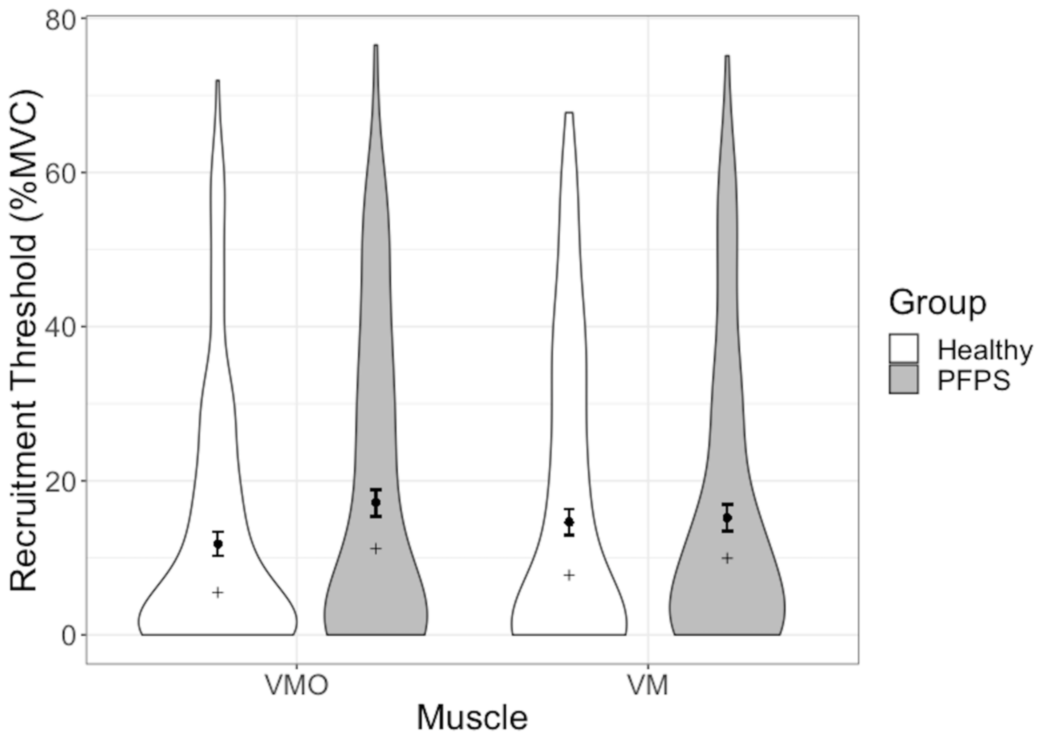

Figure 4.4. Model estimates (solid circles) and standard errors (error bars) of recruitment threshold forces from linear mixed model for healthy individuals and people with PFPS in the VM and VMO with pooled averages over the two hip positions. The violin plot outlines illustrate kernel probability density with the enclosed area representing the data distribution. The plus sign indicates the raw data median.

Chapter 5: Summary and Conclusion

The research aims of this project were to investigate sex differences in neuromuscular control of the quadriceps muscle subsections in a healthy population in addition to how PFPS affects control strategies. Menstrual cycle phases were controlled when comparing male and female motor unit recruitment properties to rule out possible hormone effect. These differences may help explain discrepancies in the rate of knee injuries between sexes. Furthermore, this dissertation incorporated commonly-prescribed rehabilitation protocols to successfully build an appropriate exercise program for different populations.

Sex has a profound effect on quadriceps onset time during isometric knee extensions in addition to initial motor unit firing rates when performing a straight leg raise. Study One demonstrated that females had a delay in quadriceps onset time compared to males during knee extensions. This agrees with the findings of Study Two, which found that females have higher motor unit recruitment thresholds in the vastus medialis complex than males, specifically during a straight leg raise with the hip in a laterally rotated position. This lack of timely neuromuscular control compared to males may explain the high risk of knee pain and injuries in females.

The findings of Studies One and Two regarding the effect of muscle onset time and motor unit recruitment thresholds in asymptomatic participants coincide with accepted clinical theory. The VMO and VL create the medial and lateral force vectors to stabilize patella movement. The fine-wire data evaluating the vastus medialis complex showed lower motor unit recruitment thresholds in the VMO relative to the VM. The surface EMG data monitoring the superficial quadriceps demonstrated that the VL activated earlier than the VM and RF, but did not activate prior to the VMO. Cross-talk from the surface EMG must be considered to account for lack of onset timing differences between the VM and VMO in Study One.

Hip position during a straight-leg raise is a crucial factor when evaluating the recruitment properties of the vastus medialis complex in healthy participants. Surprisingly, the VM and VMO are controlled differently according to hip position in individuals with PFPS. The findings of Studies Two and Three showed that the vastus medialis complex demonstrated earlier motor unit recruitment thresholds and higher initial firing rates in a neutral hip position compared to a laterally rotated hip position regardless of sex and PFPS effects. While the VMO motor units in healthy females showed higher initial firing rates in a neutral hip position (relative to a laterally rotated hip), the VMO motor units in the females with PFPS demonstrated a higher firing rate in laterally rotated hip rather than a neutral hip. Since individuals with PFPS adopt a different VMO neuromuscular control strategy, a laterally rotated straight leg raise may elicit more VMO firing relative to healthy individuals.

Targeted VMO strengthening has been a well-accepted PFPS clinical treatment for decades. In recent years there continues to be a growing focus on VM and VMO differential activation. In addition, there is also increasing attention on a deeper understanding of how sex may influence the neuromuscular control of these muscles. The studies within this dissertation help deepen our knowledge regarding how sex differences play a key role in vasti neuromuscular recruitment while controlling for the hormonal responses throughout the menstrual cycle.

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