ENTRAINMENT OF VASTUS MEDIALIS COMPLEX ACTIVITY DIFFERS BETWEEN GENDERS

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ABSTRACT: *Introduction*: That the vastus medialis oblique (VMO) is a functional unit of the vastus medialis (VM) is disputed. Delayed VMO activation predicts patellofemoral pain, which has higher rates in women. *Methods*: Single MUs and surface electromyogram (EMG) were collected from the VMO and VM of 9 men and 9 women. Men were tested once; women were tested during 5 menstrual phases. Coherence was assessed for motor unit (MU) firings within and between the VM and VMO using multilevel logistic models to determine statistical significance. *Results*: Compared with women, men have 741% (MU pairs) and 256% (MU-EMG pairs) greater odds of common drive (0–5 Hz) coherent oscillations. MU pairs from the VMO and the dual VM/VMO complex have 228% and 212% greater odds of coherent oscillations in the beta band (15–35 Hz) compared with VM pairs. *Conclusions*: The VM and VMO are neurologically different muscles; control of the VM complex is sexually dimorphic.

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The existence and functional difference of the vastus medialis oblique (VMO) as a component of the vastus medialis (VM) muscle is controversial among both anatomists[1–3] and physical medicine clinicians.[4–7] There is conclusive evidence, from both *in vivo* and cadaver studies, that the VMO has a greater pennation angle than the VM.[1] A cadaver study using primarily older bodies (79 ± 12 years of age, mean ± SD) indicated that a low proportion of VMO fibers attach to the medial border of the patella[2]; however, an *in vivo* ultrasound study of younger subjects (age range: 20–30 years) reported that the VMO inserted upon an average of 57.8% of the medial patella.[3] In a meta-analysis, 41% of cadavers exhibited 2 distinct nerve trunks, 1 innervating the proximal VM and 1 innervating the distal VM,[1] an area often referred to as the VMO. The VMO has also been reported to be supplied by a greater number of terminal nerve branches than the proximal VM.[8]

Clinicians have long known that VMO onset timing is delayed compared with other vasti muscles in patients suffering from patellofemoral pain syndrome (PFPS)[9] and that effective rehabilitation decreases PFPS pain and "normalizes" VMO onset timing.[4] PFPS occurs in women more than twice as frequently as in men.[10] Therefore, the root cause of increased PFPS rates in women may be due to differences in the modulation of muscles which control patellar tracking. We have previously shown that, at recruitment, motor unit (MU) discharge patterns of the VM and VMO are different between the genders and that changes in the MU discharge rate occur across the menstrual cycle.[11] The large-scale fluctuations in estradiol and progesterone during the menstrual cycle are known to affect neurotransmitter activity in animal models.[12–15] This may affect neuronal modulation of synergistic muscles controlling patellar tracking.

Electromyographic (EMG) signal coherence between 2 muscles indicates that they have a common oscillating neuronal origin.[16,17] For instance, EMG from the forearm is coherent in the beta band with recordings taken directly from the motor cortex of a rhesus monkey.[16] An investigation into coupling of the VM and VMO should determine if a functional relationship exists between these 2 muscle areas at the central nervous system level. As there is a gender discrepancy in PFPS incidence,[10] and recruitment of the 2 muscles is different for the genders and across the menstrual cycle,[11] the neurological relationship of the 2 muscles may also be different. Therefore, the primary goal of this study was to examine the coherent oscillations of single MUs and surface EMG from the VM and VMO in both men and women as well as across the menstrual cycle. The secondary goal was to determine if the theorized differential effects of force generation for the VM and VMO (knee extension vs. patellar tracking, respectively) are apparent in coherent oscillations between the MUs and the knee extensor force trace.

Abbreviations: BBT, basal body temperature; CI, confidence interval; EMG, electromyography; MU, motor unit; MU-EMG, hybrid motor unit and surface electromyography coherence analysis; MU-force, hybrid motor unit and force coherence analysis; MU-MU, point-process analysis of coherence between motor units; MVC, maximal voluntary contraction; OR, odds ratio; PFPS, patellofemoral pain syndrome; VM, vastus medialis; VM/VMO, coherence analysis between motor units from both the vastus medialis and vastus medialis oblique; VMO, vastus medialis oblique

Key words: gender differences; knee; menstrual cycle; motor unit; quadriceps; vastus medialis oblique

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Table 1. Number of participants and MU-MU/MU-EMG pairs for analysis within each grouping.

	Men	Early follicular	Late follicular	Ovulation	Mid- luteal	Late- luteal
Participants	9	9	9	8	8	8
MU-MU pairs	22	44	33	11	42	34
MU-EMG pairs	24	33	29	19	29	25

MATERIALS AND METHODS

Participants and Ethical Approval. Nine men (24.8 ± 5.3 years) and nine eumenorrheic women (24.7 ± 4.5 years) participated in the study. Men participated in 1 study visit, conducted at 10:00 AM. The women participated in 5 study visits. All data collection in women was performed in the morning and standardized within each participant. All participants were free of neurologic, cardiovascular, endocrine or metabolic disorders, previous leg surgery, immobilizations, arthritis, or chronic injury to the dominant leg. Additionally, the women participants were hormonal contraception naïve for at least 6 months before testing and had a history of clinically normal menstrual cycles. All participants gave informed consent in accordance with the Helsinki Declaration, and the study was approved by the Institutional Review Board at the University of Texas at Austin.

Determination of Menstrual Cycle Phase. Data were collected from the women study participants during early follicular, late follicular, ovulatory, mid-luteal, and late-luteal phases of the menstrual cycle. The first point of data collection for each subject was randomized and resulted in a pseudo-counterbalanced design with participants starting data collection in the following distribution: 2 early follicular, 2 late follicular, 1 ovulatory, 2 mid-luteal, and 2 late-luteal. Our method of determining menstrual cycle phase by means of basal body temperature (BBT) in this cohort has been described previously.[11,18]

Briefly, participants obtained their BBT by means of oral thermometer (BD Basal, Franklin Lakes, New Jersey) for 1 month before data collection. The biphasic response in BBT is characteristic of a normal menstrual cycle, with ovulation being defined operationally as the nadir before the luteal phase temperature rise.[19] If a well-defined BBT was not obtained, the participant did not enter data collection. The BBT was assessed and confirmed independently by 2 trained investigators. One participant did not have her EMG data analyzed during the last study visit in the mid-luteal phase because she exhibited a short luteal defect; however, the data from that participant's other trials were included, because the late-luteal trial was collected in the preceding cycle. A second participant was anovulatory, defined by a lack of biphasic response in the BBT in her last study visit during the ovulatory phase; therefore, that participant had only 4 study visits, because her data collection started in the mid-luteal phase. The total number of subject study visits in each phase and motor unit pairs collected is listed in Table 1.

Experimental Protocol. Participants were instructed to not perform strenuous physical activity for 48 h before testing. Additionally, participants were instructed to avoid alcohol and caffeine for 8 h before the visit.

The experimental setup has been described previously.[11] Briefly, participants were seated in an adjustable chair with the dominant hip and knee fixed at 90°. The waist and dominant thigh were immobilized with pads and straps. The participant performed 12 dynamic submaximal knee extensions without resistance before the dominant ankle was secured into a padded restraint attached to a strain gauge (Entran Sensors & Electronics, Fairfield, New Jersey). The participant performed 3 isometric maximal voluntary contractions (MVC) of knee extensors, each separated by 60 s of rest. The average of the 3 MVCs for that trial was used to ascertain the absolute force at which the participant would perform a sustained isometric knee extension during the test protocol.

After completing the MVCs, bipolar intramuscular insulated stainless steel fine-wire electrodes (0.002 mm diameter recording area, California Fine Wire Company, Grover Beach, California) were inserted into the VM and VMO. The VMO insertion point was immediately medial to the patella, and the VM was defined as the area 7 cm superior to the VMO. Two adhesive pregelled Ag/AgCl surface EMG electrodes (5 mm diameter, 10 mm interelectrode distance) were placed 2–3 mm superior to the VM fine-wire insertion point. No surface EMG was collected from the VMO due to the small size of the muscle. A ground electrode was placed over the ipsilateral patella. For the data collection trial, participants performed a force ramp-up to 30% MVC and held that target force until they were instructed to terminate the exercise by the investigator. Target force feedback was provided visually by a screen positioned directly in front of the participant at eye-level. The exercise

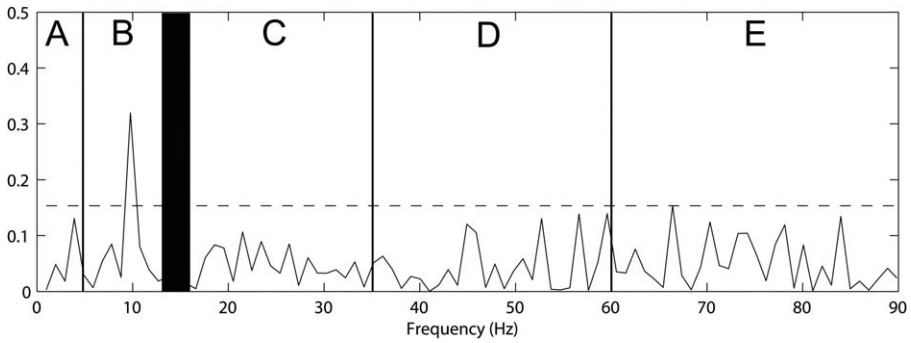

FIGURE 1. Example MU-MU coherence plot. Discrete frequency bands are indicated: Common Drive **(A)**; Tremor Band **(B)**; Beta Band **(C)**; Piper Band **(D)**; Gamma Band **(E)**. The dotted horizontal line is the 95% confidence limited calculated by Neurospec 2.0. Y-axis units are arbitrary (0–1 bounded range).

termination point was defined by either force oscillations greater than ±5% MVC or the inability to maintain force output for 3 s. Data for fine-wire EMG, surface EMG, and force were A/D converted (Micro 1401 Cambridge Electronic Design, Cambridge, England) and collected through Spike2 (version 5.21, Cambridge Electronic Design, Cambridge, England). Force and surface EMG were sampled at 1 kHz, and intramuscular EMG was sampled at 30 kHz.

Motor Unit Data Reduction. All motor unit data reduction was performed in Spike2 (version 7.09a). Fine-wire EMG was band-pass filtered at 100 Hz – 5 kHz with a 4th order Butterworth filter. Individual motor unit action potential trains were identified using the Spike2 template matching algorithm. When a classified motor unit discharged continuously for ≥20 s, the firing times were exported at 1,000 Hz for inclusion in the coherence analysis.

Coherence Analysis. Single motor units from the VM and VMO which discharged concurrently for 20 s were assessed by means of a point-process coherence analysis (MU-MU analysis) with the Neurospec 2.0 core routines[20] for Matlab (version R214a, MathWorks, Natick, Massachusetts). The coherence analysis was performed on all MUs that discharged concurrently for 20 s, both within the VM and VMO sampling areas (i.e., VM analysis and VMO analysis) and between the VM and VMO sampling areas (VM/VMO analysis). The bin of data used for analysis was the first 20 s where both MU pairs discharged concurrently. A hybrid coherence analysis was also performed on MU spike train and surface EMG pairs (MU-EMG analysis) as well as MU spike train and force trace pairs (MU-Force analysis). The surface EMG was full-wave rectified and detrended linearly before analysis. The force trace was detrended linearly before analysis. The coherence analysis was performed on 20 s of MU-MU, MU-EMG, or MU-Force pairs using a series of nonoverlapping discrete Fourier transforms of 1.024 s duration.[20] The resulting weighted periodogram estimate for the analysis had a frequency resolution of 0.98 Hz. For each coherence analysis, the 95% confidence limit calculated by Neurospec 2.0 determined if there were oscillations that were unlikely to be due to random noise or chance within 5 frequency bands: common drive 0–5 Hz,[21–23] physiological force tremor 5–12 Hz,[24,25] beta band 15–35 Hz,[16,25] Piper band 35–60 Hz,[26] and gamma band 60–90 Hz[27] (Fig. 1).

Statistical Analysis. Multilevel logistic regression models were used to ascertain the odds of having significant oscillations in a frequency band. The multilevel logistic regression indicates the likelihood there will be MU-MU pairs that have common oscillations in a frequency band and thus have a common neuronal origin. When a hybrid MU-EMG or MU-Force coherence analysis was performed, similar statistical approaches were used. The multilevel structure controlling for subject-level correlations was performed because previous research has indicated that the discharge patterns of single motor units are correlated within an individual.[28] The necessity of using a multilevel regression was assessed with the intraclass correlation.[28] Initial statistical models included an analysis of covariance-style analysis to control for the time point at which the MU-MU and MU-EMG pair were recorded, as early research on EMG-EMG coherence has indicated that fatigue may affect coherent activity.[29] In our study, the effect of time was never significant statistically and did not alter the interpretation of the results. Therefore, the time covariate was not included in the final models. For each frequency band, the odds of having an MU pair with significant oscillations was determined with gender and MU pair location as predictor variables. Initial modelling attempts also had an interaction effect on these terms, but the interaction caused quasi-complete separation of the variables and led to a termination of the

Table 2. Subject-level Intraclass correlations.

Frequency band	Analysis	ICC
Common drive	MU-MU	<0.01
Common drive	MU-EMG	<0.01
Tremor band	MU-MU	<0.01
Tremor band	MU-EMG	<0.01
Beta band	MU-MU	0.16
Beta band	MU-EMG	<0.01
Piper band	MU-MU	<0.01
Piper band	MU-EMG	<0.01
Gamma band	MU-MU	<0.01
Gamma band	MU-EMG	<0.01

ICC, intraclass correlation.

maximum likelihood iteration process. The multilevel structure controlled for multiple MU pairs observed within each participant with an unstructured covariance structure.

The odds of MU pair significant oscillations across the menstrual cycle were assessed with days from ovulation, MU pair location, and the interaction of these variables as predictors. When assessing the odds ratio results, days from ovulation were observed in 7 day increments.

The multilevel logistic regression for hybrid MU-EMG pairs was similar to the MU-MU analyses. The MU-Force pairs were assessed with both genders pooled, without respect to gender or menstrual cycle. For all logistic regressions, statistical significance was attained when the 95% confidence limits of the odds ratio did not include 1, indicating parameter significance at the $\alpha = 0.05$ level.[30]

RESULTS

A total of 186 MU pairs and 159 MU-surface EMG pairs were used for the gender-based analyses, and 164 MU pairs and 135 MU-surface EMG pairs were used for the menstrual cycle analyses. The distributions of these observations are in Table 1. The intraclass correlation for MU pairs and MU-surface EMG pairs within individuals was notable in the beta band (Table 2).

Multilevel Logistic Regression Between Genders. For the entire vastus medialis complex, men had significantly higher likelihood of having coherent oscillations in the common drive band in both the MU-MU and MU-EMG analyses (Fig. 2). The MU-MU common drive odds ratio (OR) (8.41) indicated that men have 741% greater likelihood of having MU-MU pairs with coherent oscillations. The MU-EMG common drive odds ratio (3.56) indicated that men have 256% greater likelihood of having MU-EMG pairs with coherent oscillations.

For both genders, VM/VMO MU-MU pairs are significantly different from VM MU-MU pairs in the tremor and beta bands (Fig. 3) with odds ratios showing that there is 232% and 228% greater likelihood of having coherent oscillations in these bands, respectively (OR: 3.32 and 3.28). VMO MU-MU pairs also have 212% greater likelihood of having coherent oscillations in the beta band compared with VM MU-MU pairs (OR: 3.12). The MU-EMG analyses demonstrated that VM/VMO MU-EMG pairs in the tremor and beta bands have a 117% and 127% lower likelihood of having coherent oscillations compared with VM MU-EMG pairs (OR: 0.46 and 0.44, respectively).

Multilevel Logistic Regression across the Menstrual Cycle. In both the MU-MU and MU-EMG analyses, there was no significant effect of the menstrual cycle on muscle coherence (Fig. 4). Holding menstrual cycle constant, the MU-MU analyses indicated that VM/VMO pairs have 243% and 320% greater likelihood of having coherent oscillations in the tremor and beta band than VM MU-MU pairs(OR: 3.43 and 4.20, respectively; Fig. 5). Additionally, the VMO MU-MU pairs have 250% greater likelihood of having coherent oscillations in the beta band than VM MU-MU pairs (OR: 3.50). The MU-EMG analyses showed that, holding menstrual cycle constant, VM/VMO pairs have 156% lower likelihood of having coherent oscillations in the beta band compared with VM MU-EMG pairs (OR: 0.39; Fig. 5).

Multilevel Logistic Regression for MU-Force Pairs. When all MU-Force pairs are assessed across both genders without respect to the menstrual cycle, the VMO has significantly higher likelihood of having coherent MU-Force pairs in the beta band than the VM. The odds ratio demonstrated that VMO MUs are 110% more likely to be coherent in the beta band with the force trace than VM MUs (OR: 2.10; Fig. 6).

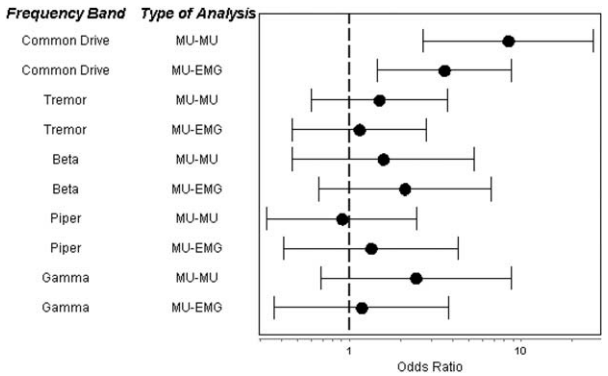

FIGURE 2. Forest plot of odds ratio estimates (±95% CI) by gender after controlling for muscle group. The dashed line at 1 is the Women-based model.

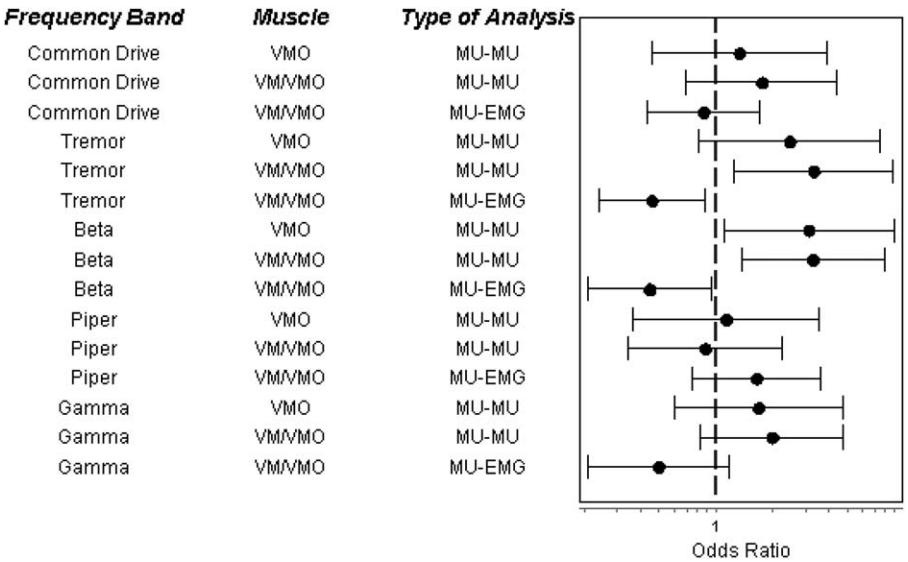

FIGURE 3. Forest plot of odds ratio estimates (±95% CI) for muscle group, after controlling for gender. The dashed line at 1 is the VM based model.

DISCUSSION

The primary goal of this analysis was to determine the effect of gender and/or menstrual cycle on control of the vastus medialis complex. There are systematic differences between neuronal oscillations of the genders but not across the menstrual cycle. Men consistently have higher levels of coherent oscillations in the common drive band and thus have a higher level of common discharge rate modulation[21,22] and common neuronal origin at the spinal level.[23]

The second goal of the study to was determine if the VM and VMO are neurologically different muscles by examining the coherent oscillations of the MUs from both muscles. These findings agree with previous research from our group which showed that the VM and VMO are differentially modulated.[11] This study further demonstrates that the differential modulation is contained primarily within the beta band with a secondary difference in the tremor band, indicating that the primary difference in neuronal origin is at the cortical level.[16,25]

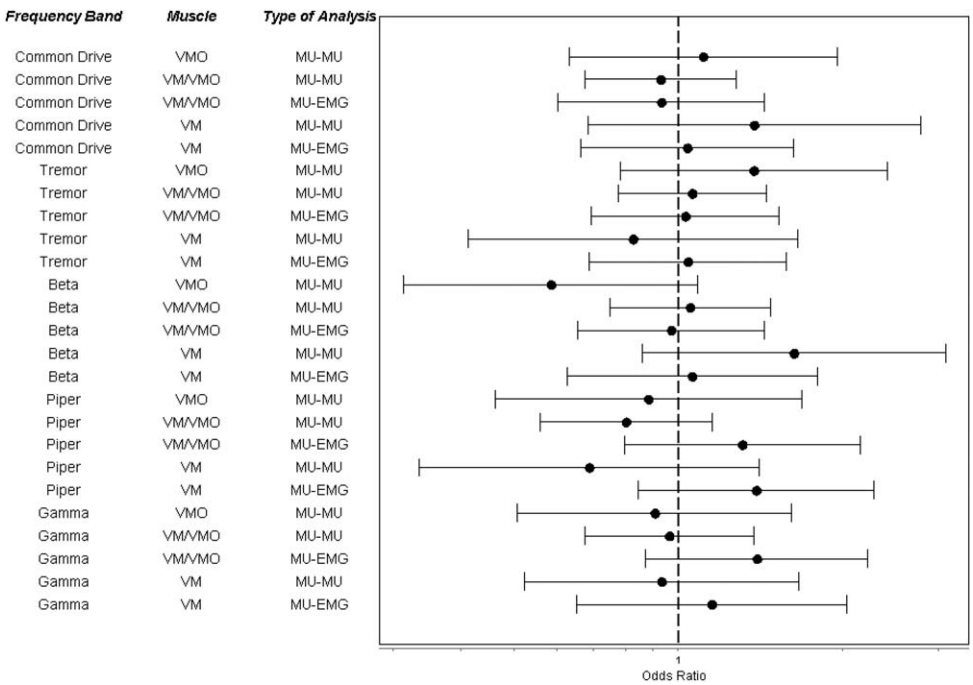

FIGURE 4. Forest plot of odds ratio estimates (±95% CI) across the menstrual cycle. The dashed line at 1 is at ovulation day 0 with the odds ratio estimate at 7 days postovulation.

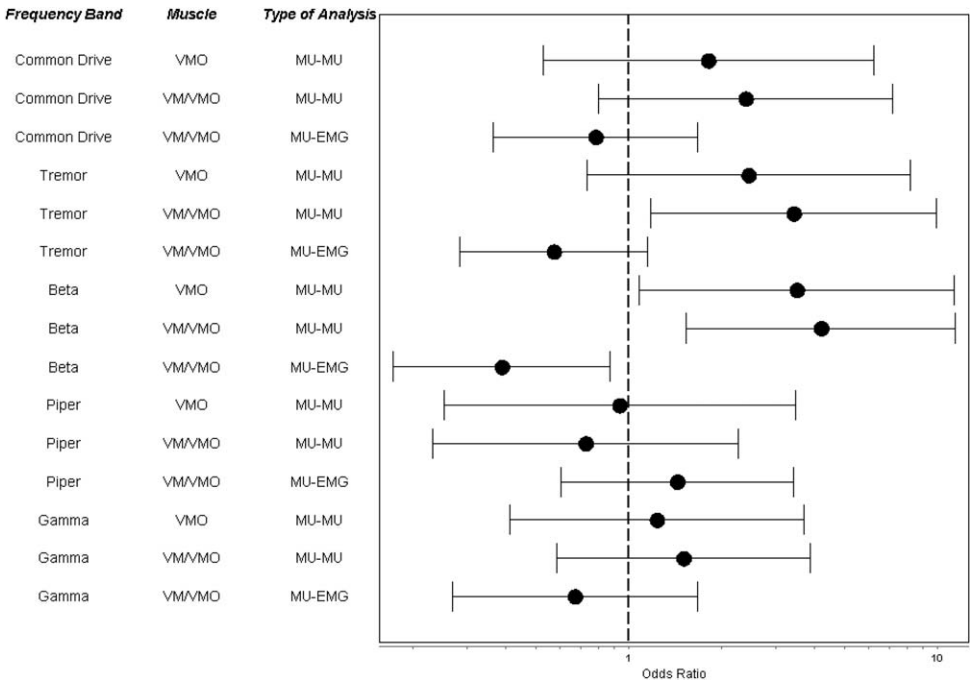

FIGURE 5. Forest plot of odds ratio estimates (±95% CI) for muscle group, holding menstrual cycle constant. The dashed line at 1 is the VM based model.

Gender and Menstrual Cycle. The odds of having coherent oscillations in the common drive band were higher for men than for women. This result is both statistically significant and high magnitude, demonstrating that, for the entire vastus medialis complex, men have 741% greater likelihood of having coherent MU-MU oscillations compared with women. This finding explains our previous research which indicated that women, but not men, have different MU discharge rates for the VM and VMO at recruitment.[11] The common spinal neuronal origins of MUs innervating the VM and VMO in men decrease the possibility of differential activation between the 2 muscles.

The common discharge rate modulations more likely observed in men may be a contributing factor to the lower rate of knee injuries in men.[10,31] If the VMO is activated in continuity with other vasti muscles during knee extension, this should help stabilize the patellofemoral joint. A lack of connectedness or discontinuity in VMO activation in relation to other vasti muscles may lead to more variable internal and external biomechanics and cause injury or pain in women.

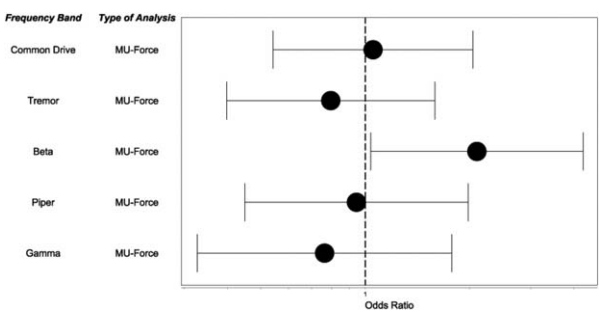

FIGURE 6. Forest plot of odds ratio estimates (±95% CI) for muscle group (pooled from both genders). The dashed line at 1 is the VM based model.

Previous research has shown that the discharge patterns of the VM and VMO are altered across the menstrual cycle.[11] Our study, however, does not demonstrate that any systematic changes occur in the oscillatory patterns of the VM and VMO across the menstrual cycle. We speculate that the disparity in findings may be a result of changes in corticospinal tract excitability across the menstrual cycle without alterations in the neuronal connections within the tract itself. That is, increases in temporal summation at the lower motor neuron, without alterations in spatial summation, could result in increased MU discharge rate during the menstrual cycle without a commensurate change in the coherent properties of motor unit pairs. Future studies of the VM and VMO across the menstrual cycle using transcranial magnetic stimulation will greatly increase our understanding of this corticospinal pathway. Although the analysis we used can account for the greater amount of MU pairs in women, future studies may benefit from a more equal distribution of data between genders.

Are the Vastus Medialis and Vastus Medialis Oblique Different Muscles? This study clearly demonstrates that the VM and VMO are neurologically different muscles. Moreover, the MU-Force data suggest that

the action of the 2 muscles may affect knee extension forces differentially.

VMO and VM/VMO MU-MU pairs have a 212% and 228% greater odds of having common oscillations in the beta band compared with VM pairs, indicating that MUs in the VMO are commonly modulated at the cortex.[16] The higher likelihood of having common oscillations in the beta and tremor bands for MUs sampled from both the VMO and VM locations compared with MUs sampled from the VM location alone suggest that the neurologic distribution of connected MUs in the distal portion of the vastus medialis complex occupy a larger spatial area than anticipated. The MU-EMG analysis, while not as specific as the MU-MU analysis, has the added advantage of sampling from a larger pool of motor activity in the superior portion of the VM. The MU-EMG results indicate that motor activity in the more proximal section of the vastus medialis complex has a greater functional connectivity than the vastus medialis complex as a whole (i.e., motor activity from proximal surface EMG and distal VMO fine-wire insertion point) and that the VM fine-wire insertion point we used may be too distal to truly be considered neurologically distinct from the VMO. Indeed, VM/VMO MU-MU pairs commonly have higher odds of coherent oscillations than VM MU-MU pairs. Overall, the data suggest that the VM fine wire insertion point in this study is receiving innervation from motor neurons which typically predominate in either the proximal or distal sections of the vastus medialis complex, but not both. Obviously, the neurologic architecture of the vastus medialis complex has not been fully elucidated but needs to be considered in concert with the anatomical data to understand how this muscle complex functions *in vivo*.

We also attempted to examine the differential coherence of the VM and VMO with force oscillations. If the VM is the primary muscle of knee extension[32] and the VMO controls patellar tracking,[33,34] the force oscillations observed from the action of knee extension should be more coherent with the VM. Surprisingly, the results demonstrated that the VMO was 110% more likely than the VM to be coherent with force in the beta band. It is possible that because the pennation angle of the VMO creates a different line of pull for the lower leg, the VMO is a primary source of tremor for knee extension. The unexpected results should also be considered critically, because the quadriceps complex is not a simple musculoskeletal structure. We do not know what coherent properties the vastus lateralis, rectus femoris, or vastus intermedius have with knee extension force.

Subject-Level Correlations. This study did not find consistent and robust subject-level correlations when examining coherent oscillatory patterns of MU pairs or MU-EMG pairs, contrary to previous studies that found discharge rate of MUs was correlated within a subject.[28,35] The reason for this discrepancy is unclear. It is possible that, while the descending motor drive and spinal mechanisms by which MUs discharge to create force are variable at the subject-level, the functional structure of the nervous system, as assessed by motor coherence, is not related discernibly in each individual. In many cases MU-MU and MU-EMG pairs can be considered to be statistically independent, though this assumption is sometimes violated (Table 2).

CONCLUSIONS

In summary, men are more likely than women to have MUs that have a common discharge rate modulation mediated by spinal level connectivity. There is no evidence that the menstrual cycle alters motor unit coherence. The motor units supplying the vastus medialis complex appear to be distributed according to their spatial location. Therefore, while gender affects the likelihood of functional connectivity at the spinal level, control of the sub-portions of the vastus medialis complex is distributed at the cortical level. Cortical control of vastus medialis complex sub-sections may allow for differential activation of the VM and VMO; the sexual dimorphism of vastus medialis complex neuroanatomy may predispose women to higher rates of knee pain and injury.

The authors have no competing interests to report.

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