The differential effects of fatigue on reflex response timing and amplitude in males and <u>females</u>

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Moore BD, Drouin J, Gansneder BM, and Shultz SJ. The differential effects of fatigue on reflex response timing and amplitude in males and females. *Journal of Electromyography and Kinesiology*. 2002; 12:351-360.

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#### Abstract:

We examined the effects of fatigue on patellar tendon reflex responses in males and females. A spring-loaded reflex hammer elicited a standardized tendon tap with the knee positioned in an isokinetic dynamometer and flexed to  $85^{\circ}$ . We recorded vastus lateralis activity (SEMG) and knee extension force production at the distal tibia (force transducer). Reflex trials were performed before and after (immediate, 2, 4, and 6 min) an isokinetic fatigue protocol to 50% MVC (90°/s). For each event, pre-motor time (PMT), electromechanical delay (EMD), and total motor time (TMT) were obtained, as well as EMG amplitude (EMG<sub>amp</sub>), time to peak EMG (EMG<sub>tpk</sub>), peak force amplitude ( $F_{amp}$ ), time to peak force ( $F_{tpk}$ ), EMG:force ratio (E:F), and rate of force production ( $F_{rate}$ =N/ms). TMT increased significantly in females following fatigue, while males showed no change. The increased TMT was due to an increased EMD with fatigue, while PMT was unaffected. EMG<sub>amp</sub> and  $F_{amp}$  were somewhat diminished in females yet significantly augmented in males following fatigue, likely accounting for the differential changes in EMD noted. Results suggest males and females may respond differently to isokinetic fatigue, with males having a greater capacity to compensate for contraction force failure when responding to mechanical perturbations.

Keywords: Electromechanical delay | Total motor time | Electromyography | Spinal reflex

### Article:

### **1. INTRODUCTION**

With the increased participation of females in team sports over the past decade, a dramatic increase in the rate of knee injuries involving the anterior cruciate ligament (ACL) has been

documented [2], [16], [34] and [45]. A gender discrepancy in ACL injury rates seems to be most prominent in sports requiring intense cutting, jumping, and rapid change-of-direction movements [14]. This gender-bias in ACL injury rate has led to many studies attempting to elicit physiological, hormonal, and anatomical variances that may predispose females to ACL injury [35], [38], [44], [47], [60] and [61]. Gender differences in neuromuscular control and biomechanical function are thought to be primary factors that may account for this gender bias [21].

Functional joint stability, defined as the cumulative stabilization forces required to perform functional activities, consists of both static and dynamic restraints [17] and [21]. While the ACL is the primary static restraint to anterior tibial translation [7], the forces that are applied during physical activity often exceed the capacity of the static restraints [51]. Dynamic muscular activation acts in concert with the static restraints to preserve joint integrity in anticipation of, and in response to, excessive forces imposed on the knee. Neuromuscular control during functional activity is provided through feedforward (pre-activity), reactive (short and long latency reflexes) and voluntary mechanisms. The hamstring muscles in particular provide dynamic protection to the ACL by limiting anterior tibial translation [46] and [51]. Moreover, co-contraction of the quadriceps and hamstring muscle groups effectively stiffens the joint [4], [36] and [46], which is instrumental when movement precision and joint stabilization are critical [31].

The efficacy of dynamic stabilization under sudden loading conditions is dependent on the magnitude, rate and orderly timing of muscle excitation and force production. In response to a loading stimulus, there exists a critical delay before the onset of force generation [5], [8], [20] and [59]. This delay is often referred to as total motor time (TMT) and can be subdivided into premotor time (PMT) and electromechanical delay (EMD). PMT describes the delay between stimulus onset and onset of myoelectric activity as measured with EMG. Although EMD has been defined and measured in many ways, 'true' EMD is described as the time delay from the earliest onset of EMG activity to the initial onset of force generation [64]. Thus, EMD represents that portion of movement where activation of the motor units and shortening of the series elastic component is occurring [8], [18], [59] and [66]. Of the many physiological processes that are thought to account for this mechanical delay [8], the time needed to stretch the series elastic component is thought to be the primary factor [8], [43], [54] and [63].

EMD appears to be strongly dependent on the magnitude of the reflex response [10], [18], [54], [57], [58] and [63]. Time delays in force production have been shown to decrease with increasing contractions intensity (%MVIC) [58] and [63] and reflex stimulus intensity [63], and to be correlated with rate of force development [54] and absolute force production [57]. This interdependence of response magnitude and EMD duration further supports the contention that time required to stretch the SEC is an important factor determining the length of EMD, and suggests both should be considered when exploring factors that alter EMD.

Two factors often proposed to potentially influence neuromuscular control and functional joint stability are gender and fatigue. While considerable research has examined the influence of fatigue on neuromuscular responses, results differ considerably across studies due to variations in methods. In particular, EMD has been found to vary substantially with different muscle

contraction protocols [8] and when comparing reaction (voluntary contraction) vs. reflex (involuntary contraction) [25], [57] and [63] responses. Moreover, literature indicates the influence of fatigue on reflex versus reaction responses may be quite different [25] and [32] and that these differences may further depend on the type of fatigue protocol used [23] and [41]. Studies investigating the influence of fatigue on reflex response latency and magnitude are extremely limited. Moreover, most of the literature to date evaluating the effect of fatigue on neuromuscular reflex behavior has been conducted almost exclusively on males. While few have examined the effects of gender on EMD [5], [59] and [64] and found EMD to be longer in females than males, no studies could be found specific to neuromuscular reflex behavior at the knee as a function of both gender and fatigue.

Given the specificity of the EMD response relative to the aforementioned factors, there is a void in the literature regarding the influence of fatigue and gender on reflexive responses to a sudden perturbation or muscle stretch. Therefore, our objective was to develop a controlled method by which to compare the effect of fatigue on involuntary reflex timing and response magnitude at the knee in males and females. The patellar tendon reflex represents a monosynaptic pathway at the knee that can be used as a reliable research model to evaluate the relationship between gender, fatigue, and EMD. Specifically, our purpose was to measure both the timing and magnitude of EMG and force components of a patellar tendon reflex response before and after an isokinetic fatiguing protocol in males and females.

## 2. METHODS

All testing was performed in a single session in the sports medicine and athletic training research laboratory. A pre-post test design was used to compare the neuromuscular responses of males and females to a patellar tendon tap, before and after a concentric isokinetic fatigue protocol.

### 2.1. Subjects

Fifteen male  $(20.7\pm1.7 \text{ yrs}, 86.94\pm7.45 \text{ kg}, 184.4\pm4.88 \text{ cm}, 58.52\pm2.78 \text{ cm}$  femur length) and 15 female  $(19.47\pm1.3 \text{ yrs}, 64.61\pm5.68 \text{ kg}, 171.87\pm735 \text{ cm}, 57.3\pm3.23 \text{ cm}$  femur length) NCAA Division I endurance athletes volunteered for the study. Participants were selected based on the following criteria: 1) no history of knee surgery on the right limb, 2) no injury in the right lower leg for the past three months and 3) otherwise healthy at the time of the study. Prior to participation in the study, each subject read and signed an informed consent form approved by the University's Institutional Review Board for the Protection of Human Subjects.

### 2.2. Instrumentation

An apparatus was designed to consistently strike the patellar tendon and initiate the patellar tendon reflex (Fig. 1). The device consisted of a spring-loaded reflex hammer, equipped with a contact switch, mounted on the lever arm of the isokinetic dynamometer. The consistency of the stimulus intensity was evaluated by striking the spring-loaded reflex hammer against the force transducer of the isokinetic dynamometer at a standardized release angle of approximately 60 degrees. Ten trials were recorded over two separate days and analyzed using the coefficient of variation (CV) for trials within a day, and the coefficient of variation for the method error

 $(CV_{ME})$  for the difference in trials scores between day 1 and day 2. The device was found to deliver a consistent force of 57.1±1.4 Newtons, with a CV of 1.9% for day 1 trials, 3.6% for day 2 trials, and a  $CV_{ME}$  of 2.9% for the difference in trial scores between days.



Fig. 1. Subject set-up and positioning in the isokinetic dynamometer with patellar tendon apparatus attached.

A Myosystem 2000 eight-channel surface electromyography (SEMG) unit (Noraxon; Scottsdale, Az) was used to identify the onset of muscle activity in the quadriceps following the initiation of the tendon tap. Bipolar Ag-AgCl surface electrodes measuring 10 mm in diameter were placed over the vastus lateralis muscle with a center-to-center distance of 2.5 cm. EMG unit specifications included an amplification of 1 mV/V, a frequency bandwidth of 16–500 Hz, CMRR 114 dB, input resistance from 20 Mohm to 1 Gohm, and a sampling rate of 1000 Hz. To identify the onset of knee extension force production, the subject was positioned in a Kin-Com Isokinetic Dynamometer (Chattecx Corporation, Hixson, TN), with the force transducer (impulse response=1.5 ms) placed at the distal anterior tibia.

Raw data obtained from the reflex hammer contact switch, SEMG and isokinetic force transducer were simultaneously acquired and then analyzed using Data Pac 2000 Version 1.1 Lab Application Systems software (Run Technologies; Laguna Hills, CA).

### 2.3. Procedure

Prior to testing, the skin surface was shaved then abraded with an alcohol pad to ensure satisfactory adhesion and conductance of the surface electrodes. Electrodes were placed in a parallel arrangement over the mid-belly of the vastus lateralis, 1/3 the distance of the femur length from the lateral joint line. Electrode placement was validated by manually muscle testing the extensor mechanism to ensure a strong, clean signal. We then positioned the participant in the Kin-Com isokinetic dynamometer in isometric mode, with the hip at 90° and knee flexed to 85° (Fig. 1). The force transducer was position at the distal tibia, while still allowing complete dorsiflexion of the foot. Stabilizing straps across the torso and upper thigh of the test leg were

used to prevent excessive hip movement. The spring-loaded reflex hammer was then attached to the lever arm of the dynamometer and positioned so that the hammer would strike the mid patellar tendon, identified as the intersection of two lines bisecting the tendon horizontally and vertically.

Once the subject was properly positioned, five pre-fatigue tendon taps trials were performed at random time intervals between 1–10 sec, with the participant's eyes closed and performing the Jendrassik maneuver (elbows out, fingers interlocked and pulling isometrically). Following the completion of pre-fatigue trials, three maximal voluntary concentric contractions (MVCC) of the quadriceps were obtained isokinetically at 90°/s, after allowing each participant three submaximal trials. The highest force value of the three maximal trials was recorded as the MVCC for each subject. Each participant then performed continuous isokinetic contractions until the contraction force fell below 50% of their MVCC for three consecutive repetitions. Immediately following completion of the fatigue protocol, five tendon taps were performed, and repeated again at 2, 4, and 6 min of the recovery period.

#### 2.4. Data analysis

EMG data were processed and minimally filtered with a root mean square (RMS=5 ms time constant) and the first three acceptable trials at each time interval (prefatigue and 0, 2, 4 and 6 min post fatigue) were averaged for statistical analysis (Fig. 2). Acceptable trials were defined as having a quiet baseline and a clear, distinguishable response recorded for both the myoelectric (SEMG) and force (KinCom) signals. The onset of myoelectric activity and force production were determined using a five standard deviation threshold relative to each signal's respective baseline activity. From these events, pre-motor time (PMT; time delay between the stimulus onset and onset of myoelectric activity), electromechanical delay (EMD; time delay between onset of myoelectric activity (PMT) and onset of force production), and total motor time (TMT; time delay from stimulus onset to onset of force production) were obtained.



Fig. 2. Display of an averaged signal indicating stimulus onset (tendon tap) and resultant EMG and force response. (y-scale represents volts)

In an effort to elucidate the potential central or peripheral factors that may contribute to any gender differences in PMT, EMD or TMT with fatigue, we also recorded for each reflex event the peak EMG amplitude ( $EMG_{amp}$ ), time to peak EMG amplitude ( $EMG_{tpk}$ ), peak force amplitude ( $F_{amp}$ ), and time to peak force amplitude ( $F_{tpk}$ ). From these measures, the EMG to force ratio (E:F=peak EMG amplitude/peak force amplitude), and rate of force production ( $F_{rate}=N/ms$ ) were also obtained. EMG<sub>amp</sub> and  $F_{amp}$  were normalized to pre-fatigue values to control for subject differences in size, strength and myoelectric output.

#### 2.5. Statistical analysis

To evaluate any gender difference in rate of fatigue, we used an independent *t*-test comparing the number of repetitions needed to reach 50% maximum isokinetic contraction force failure between males and females. We then used a repeated measureANOVA with one between (sex) and one within (fatigue @ five levels; pre-fatigue and 0, 2, 4 and 6 min post-fatigue) to assess the effects of fatigue and gender on TMT. Differences in TMT were further analyzed using a one between (sex) and one within (fatigue trials @ five levels) repeated measures MANOVA for two dependent measures (PMT and EMD) to determine which time component was responsible for the changes in TMT. Significant findings were further analyzed by univariate ANOVAs and Tukey's post hoc methods. To elucidate potential mechanisms for significant differences in EMD, we used a separate one between (sex) and one within (fatigue trials @ five levels) repeated measure MANOVA for four dependent measures (EMG<sub>amp</sub>, EMG<sub>tpk</sub>, F<sub>amp</sub>, and F<sub>tpk</sub>). Finally, separate one between (sex) and one within (fatigue trials @ five levels) repeated measures ANOVA evaluated EMG: Force amplitude ratio (E:F), and rate of force production (Frate). Dunnet's post hoc was used for pairwise comparisons of post fatigue to pre-fatigue values where significant differences were found. An alpha level of p < 0.05 was used for all statistical analyses.

### **3. RESULTS**

Means and standard deviations for PMT, EMD and TMT are presented in Table 1, with means and standard deviations for secondary variables of  $EMG_{amp}$ ,  $EMG_{tpk}$ ,  $F_{amp}$ ,  $F_{tpk}$ , E:F,  $F_{rate}$  presented in Table 2.

### 3.1. Primary analysis

The average number of reps required to reach 50% of pre-fatigue maximal force output were  $31.7\pm10.4$  for females and  $36.1\pm13.1$  for males (t=1.005, p=0.324). After confirming that the rate of fatigue was similar in males and females, we found TMT to differ within trials (p<0.0001) and within trials by sex (P<0.0001) (Fig. 3). TMT was faster in females pre-fatigue, then increased significantly from pre-fatigue to immediately post fatigued, but not to a level that was significantly slower than males. TMT for females then returned to pre-fatigue values between 2–4 min during recovery, but to a level more equal to that of males (i.e. not as fast as pre-fatigue values). We found no change in TMT for males at any time point, and no difference between males and females at 2, 4 and 6 min of the recovery period. The main effect for sex was not significant (p=0.243,  $\beta=0.290$ ).

Table 1 Means and Standard Deviations (ms) for Premotor Time (PMT), Electromechanical Delay (EMD) and Total Motor Time (TMT) for Males and Females Before and After Fatigue

Variable	Sex	Pre-Fatigue	Post <sub>0 min</sub>	Post <sub>2 min</sub>	Post <sub>4 min</sub>	Post <sub>6 min</sub>
PMT	F	20.8±4.7 24 3+5 7	22.3±5.1 24.9±6.1	20.8±5.3 24.3±6.5	21.3±3.6	22.4±4.3 24 3+3 5
EMD	F	22.1±5.8ª	33.6±11.2=	27.7±6.9	26.0±4.7	26.0±5.1
TMT	F M	28.4±7.9 42.9±7.6* 52.7±9.7	27.1±9.5 55.9±13.2 <sup>b</sup> 52.0±9.6	27.5±7.2 48.5±8.2 <sup>b</sup> 51.7± 8.3	20.7±9.0 47.3±6.0 51.1±8.6	27.1±8.4 48.4±7.6 51.3±9.6

\* Indicates females different from males pre-fatigue

<sup>b</sup> Indicates slower than pre-fatigue trial (P<0.05). Values are means±SD

Table 2 Means and Standard Deviations for EMG and Force Response Characteristics of Males and Female Before and After Fatigue\*

Variable	Sex	Pre-Fatigue	Post <sub>0 min</sub>	Post <sub>2 min</sub>	Post <sub>4 min</sub>	Post <sub>6 min</sub>
EMGamp	F	1.0±0.0	0.58±0.26	0.77±0.36	0.84±0.49	0.92±0.56
	M	1.0±0.0	1.53± 1.47 <sup>b</sup>	1.77±1.87 <sup>b</sup>	2.41±3.25 <sup>b</sup>	1.99±2.02 <sup>b</sup>
EMG <sub>tek</sub>	F	38.0±4.6	39.1±6.2	38.1±5.6	37.3±5.4	37.5±4.7
-	M	40.0±6.3	39.9±5.7	39.2±5.5	40.1±5.1	38.5±5.1
Fame	F	1.00±0.00	0.49±0.26 <sup>b</sup>	0.66±0.25	0.79± 0.38	0.77±0.35
	M	1.00±0.00	1.36±1.35	1.12±0.94	1.60± 1.49 <sup>b</sup>	1.78±1.49 <sup>b</sup>
Ftok	F	137.2±20.7	147.7±29.0	132.7±15.8	135.1±16.6	134.8±21.2
4-	M	123.2±18.9	142.4±36.6	132.8±17.2	122.4±18.7	127.7±20.3
Frate	F	0.22±0.11	0.09±0.04	0.13±0.06	0.16±0.09	0.16±0.08
	M	0.18±0.16	0.15±0.14	0.12±0.08	0.20±0.19	0.22±0.21
E:F	F	2.54±1.69	3.47±2.65	3.06±2.51	2.57±1.61	2.86±1.95
	Μ	1.86±1.21	2.79±3.63	2.92±2.21	2.56±2.04	2 .00±1.18

\* EMG=Myoelectric activity; amp=Amplitude (normalized to pre-fatigue values); tpk=Time to peak amplitude; F=Force; rate=N/ms; E:F=Myoelectric activity to force ratio

<sup>b</sup> Indicates difference from pre-fatigue trial (P<0.05). Values are means±SD



Fig. 3. Changes in total motor time (TMT) from pre- to post-fatigue trials in males and females. (\*) Indicates females different from males prefatigue, (†) Indicates slower than pre-fatigue trial. Values are means±SD.

#### 3.2. Secondary analysis

To determine what time component was responsible for changes in TMT in females, analysis of EMD and PMT revealed significant differences within trial (p=0.007) and trial by sex (p=0.003), but not between sex (p=0.243,  $\beta$ =0.290). Univariate tests indicated a significant change in EMD (p=0.007) but not PMT (p=0.531,  $\beta$ =0.248) by trial, and that changes in EMD across trials were also different by sex (p=0.001). Similar to TMT, EMD was faster in females pre-fatigue, then increased immediately post fatigue to a level that was significantly slower than males. EMD then returned to pre-fatigue values within 2 min during the recovery period, but to a level more equal to that of males (i.e. no longer significantly shorter as in pre-fatigue trials). We found no change in EMD for males at any time point. There was no main effect for sex for either PMT (p=0.090,  $\beta$ =0.395) or EMD (p=0.916,  $\beta$ =0.051).

#### 3.3. Tertiary analyses

To further elucidate changes in EMD, results of the tertiary analyses showed males and females also differed in the magnitude of the reflex and force response following fatigue, as well as the timing and rate of peak force production (See Table 2). The MANOVAinvestigating EMG<sub>amp</sub>, EMG<sub>tpk</sub>,  $F_{amp}$ ,  $F_{tpk}$  identified an overall significant difference across fatigue trials (*p*=0.002) and trial by sex (*p*=0.05). Univariates revealed that peak EMG<sub>amp</sub> was significantly greater in males compared to females (*p*=0.046) and differed across trials (*p*=0.042). Changes across trials also differed by sex (*p*=0.023), with post hoc pair-wise comparisons indicating no difference in reflex amplitude across trials in females, but a significant increase in males immediately post fatigue that remained elevated for all recovery time points. Similar findings were noted for  $F_{amp}$  for both trial (*p*=0.05) and sex by trial (*p*=0.011), and between sex (*p*=0.018). Males again demonstrated an increased force response amplitude following fatigue while females did not. Specifically, force amplitude was significantly greater in males at 4 and 6 min post fatigue compared to prefatigue, but decreased in females immediately post fatigue. While force amplitude remained suppressed in females during the entire recovery period (2–6 min), the difference was no longer statistically different from their pre-fatigue value.

While results of EMG<sub>amp</sub> and F<sub>amp</sub> were similar in direction of change, the relative magnitude of their respective changes, as measured by E:F ratio (Table 2), was found to vary by trial (p=0.034). E:F ratio increased (indicating greater EMG<sub>amp</sub> relative to F<sub>amp</sub>) immediately after fatigue and returning to near pre fatigue levels within 2 min of recovery. However, this change in E:F ratio was not influenced by sex either across (p=0.489, $\beta$ =0.104) or within (p=0.639,  $\beta$ =0.202) trials.

Consistent with our PMT findings, the time to reach peak EMG amplitude (EMG<sub>tpk</sub>) remained unchanged across trials (p=0.451,  $\beta$ =0.286), sex (p=0.377,  $\beta$ =0.139), and within trial by sex (p=0.687,  $\beta$ =0.184). However, the time to peak force production (F<sub>tpk</sub>) differed by trial (p=0.016), increasing immediately post fatigue and returning within pre-fatigue values by 2 min. This fatigue effect on F<sub>tpk</sub> did not differ between males and females (p=0.656,  $\beta$ =0.196). Similarly, F<sub>rate</sub> differed across trials (p<0.001), with force produced at a slower rate immediately post fatigue, and returning to pre fatigue levels by 4 min post fatigue. Consistent with F<sub>tpk</sub>, there were no differences between sex (p=0.525, $\beta$ =0.095) or within trial by sex (p=0.109,  $\beta$ =0.569).

#### 4. DISCUSSION

Our primary finding was that females took significantly longer to produce knee extension force in response to a patellar tendon tap following a bout of fatiguing isokinetic exercise, while males showed no change. Consistent with previous literature [5], [19], [25], [32], [41] and [59], we found no difference in reflex neural activation (PMT) between males and females, or in response to fatigue, suggesting changes in EMD are primarily responsible for the increased force delays in females. Changes in force delays appeared to be short-lived, returning to near pre-fatigue levels within 2 and 4 min post cessation of exercise.

An equally important finding was that the reflex response magnitude (as measured by both peak EMG amplitude and force amplitude) was somewhat diminished in females, yet significantly augmented in males following fatigue. However, it is interesting to note that both sexes showed similar transient changes in widening of the EMG:Force ratio and increases in time to peak force amplitude following fatigue (Table 2). The later findings are consistent with previous literature [19], [22] and [62] and would suggest that males and females demonstrated comparable levels of contraction failure. Thus, under similar fatiguing conditions, males were able to compensate for this contraction failure through augmentation of their reflex force response while females showed a  $\sim$ 50% decrease immediately following fatigue. We believe this disparity in reflex response magnitude between males and females is the primary explanation for the decrease in EMD in females and maintenance of EMD in males following fatigue.

Why reflex magnitude (both EMG and force responses) would be augmented in males and not females following fatigue is unclear, and appears to be inconsistent with the previous literature. While others have found EMG amplitude to increase significantly following fatigue [19], [22] and [56], this is usually accompanied by a loss of force output. However, previous literature has examined reaction (voluntary contraction) response protocols [22], [23], [24], [62] and [65], which may not be representative of reflex responses [25]. Based on our findings and relevant literature, we considered the potential sites and mechanisms for this gender difference.

#### 4.1. Altered muscle spindle sensitivity

When the stimulus intensity is controlled, EMG amplitude can be modified by changes in the excitability of the reflex loop or the synchronization of fiber action potentials[3] and [15]. Hence, reflex excitability may be mediated by alterations in peripheral afferent sensitivity, changes in alpha–gamma motor linkage, and changes in the level of central motor drive and pre-synaptic inhibition at the neuromuscular junction[15] and [19]. While it has been speculated that metabolic changes with fatigue may adversely influence muscle spindle sensitivity [41], others finding an augmentation of EMG amplitude theorized a compensatory mechanism via increased muscle spindle sensitivity in an effort to maintain function and force output [19], [22], [25] and [42]. In fact, there is evidence that suggests fatigue may actually enhance spindle sensitivity [9] and spinal reflex EMG in response to brief perturbations [53]. Since both sexes showed similar increases in E:F and F<sub>tpk</sub>, but only males showed an increase in reflex amplitude, this suggests changes in muscle spindle sensitivity may, in part, be responsible for gender differences in EMD following fatigue.

While spinal reflexes of this nature are an automatic involuntary response, they can be influenced either in an inhibitory or excitatory fashion through central mediation via descending pathways, heightened sensitivity via post-contraction sensory discharge, and changes in afferent feedback from sensory stimuli [15]. Descending pathways continually modulate the strength of the spinal stretch reflex in response to pain, adjusting for previous or anticipated events, motivation and central fatigue [31] and [53]. Postcontraction sensory discharge, an increase in muscle spindle discharge increases dorsal root activity and motor neuron excitability, can occur after a brief bout of intense activity as long as the muscle is not appreciably stretched [15], [27] and [40]. Since our subjects remained in the device, locked at 85 degrees of knee extension, this phenomenon may have played a role. Accumulation of chemical byproducts of anaerobic-type fatiguing exercise may have influence on peripheral muscle afferent feedback and muscle spindle function, resulting in an altered resting muscle length, recruitment of muscle units, or motor neuron excitation and force output [11], [12], [13], [24] and [29].

Whether these factors differed between males and females cannot be determined from our results, and requires further study. Considering that males have been demonstrated to have higher lactate levels in response to fatiguing exercise than females [24], measuring metabolic by-products in addition to mechanical changes in the muscle may aid in this determination. A comparison of M-Wave (by-passing the CNS and muscle spindle), H-reflex (by-passing the muscle spindle) and tendon tap reflex responses may further elucidate the site and mechanism of these differences. Other factors that should be explored include potential gender differences in resting baseline activity (increased preactivity due to increased gamma motor drive) [28] and [33], muscle temperature increase [66], and reflex facilitation using the Jendrassik Maneuver [30], as each are known to influence reflex sensitivity and EMD. The influence of hamstring co-activity, although likely to be minimal, given the joint position, should also be considered. While we found no evidence in the literature to suggest males and females would respond differently on these factors, their effects were not investigated in this study and cannot be excluded as potential variables.

#### 4.2. Fiber type distribution

The distribution of fast (FT) versus slow (ST) twitch muscle fiber types is also thought to influence the rate of force development [41] and [43], with length of EMD being dependent on the type of fibers recruited first [54]. Reflex induced muscle contractions are mediated by slow conducting alpha motor neurons (in that ST fibers are recruited first) while fast voluntary movement is predominantly dependent on FT motor units [63]. Under voluntary conditions, EMD has been found to be shorter in muscles thought to have a greater distribution of fast twitch fibers under both rested [43] and fatiguing conditions [41] and [42]. Nilsson et al. [42] measured the effects of fatigue on EMG during 100 repeated isokinetic contractions (180°/sec) and found peak EMG per unit torque was positively correlated with %FT (r=0.84) while the time lag from EMG to torque was negatively correlated to %FT (r=0.68).

If females in this study had a greater distribution of ST compared to males as found in other studies [1], [50] and [52], it is possible their FT fibers may have fatigued more quickly in a maximal effort fatigue protocol such as ours [26]. Given that reflexes are predominated by ST fibers, greater reliance on fatigue resistant ST (during the isokinetic fatigue protocol) to maintain

effort as fatigue progressed may have had a greater impact on post fatigue reflex responses in females. But while it seems plausible that physiological differences in muscle composition may alter mechanical behavior and, in part, contribute to the overall fatigue effect on EMD, this mechanism is likely not sufficient to explain our findings. Regardless of fiber type recruited first, EMD latencies are typically shorter in reflex (ST fiber predominant) compared to voluntary (FT fiber recruited first) contractions [25] and [63], thus, EMD cannot be dependent on muscle fiber type contractile properties alone [63].

### 4.3. Series elastic component

The series elastic component (SEC) consists of both passive (tendon predominant) and active (muscle cross-bridge) components [63]. It is plausible that greater series elasticity may have two sites of action when considering a patellar tendon reflex. A more compliant patellar tendon may be less sensitive to force per unit stretch than a stiffer tendon, resulting in a lower response magnitude. Additionally, greater elasticity in the contractile machinery would result in greater time required to remove any intrinsic 'slack' in the muscle [8].

Research on *voluntary reaction* (not reflex) times suggests there may be a structural/physiological difference in the series elastic components (SEC) in females and males, with males having a less compliant SEC [5], [8] and [59]. While our pre-fatigue values do not support this contention (further suggesting reflex induced EMD mechanisms may be different from voluntary contractions), it is possible that fatigue may interact with these factors to differentially influence the compliance of the series elastic component. Increased muscle compliance following fatigue has been previously demonstrated by Vigreux et al. [55].

Although merely speculation at this point, gender specific changes in SEC with fatigue may be hormone mediated. Given previous findings of increased EMD [5] and [59] and connective tissue elasticity [6], [39] and [48] in females, the SEC, thus EMD, may be differentially affected in males and females post fatigue. The contention of a hormonal influence is further supported by Zhou et al. [64], who found gender differences in mechanical behavior of the leg extensors appeared after adolescence. Clearly, there is insufficient evidence at this time to support this contention, and further research is needed to evaluate the interaction of gender, fatigue and hormones. Comparing EMD across gender at similar reflex force amplitudes may further elucidate potential differences in tendon/muscle compliance.

#### 4.4. Clinical implications and relevance

Together, PMT and EMD determine the absolute shortest period of time necessary to produce muscle tension (TMT) and potentially provide a prophylactic response to knee joint perturbations. Factors that elongate either time component may delay development of muscular tension, compromising dynamic joint stabilization and increasing the likelihood of injury to the ACL. Regardless of the mechanism(s) that explain the observed differences between males and females in EMD and TMT, these findings alone are clinically relevant in that males appeared to have a greater capacity to compensate for contraction force failure and delays than females under similar levels of fatiguing exercise. The neural and mechanical adaptations noted in the reflex response in males and females after fatigue suggest females have a decreased ability to stiffen

the joint in response to mechanical perturbations when fatigued. However, while we believe this study is one of the first to examine the combined influence of fatigue and gender on reflex response characteristics at the knee, it is not without limitations and clearly more research is needed to fully elucidate gender differences in neuromuscular control and functional knee stability.

It is important to note that our evaluations were conducted in a laboratory setting under resting conditions. While this level of control was necessary adequately to control for confounding variables that could influence EMD measures, the monosynaptic reflex is only one component of the neuromuscular response continuum contributing to dynamic knee joint stability. Further, we assessed only the knee extensor mechanism as measured by vastus lateralis reflexes and similar analyses should be performed for other muscles crossing the knee joint, in particular the hamstring muscles, given their critical role in anterior and rotary tibial stabilization. Finally reflex control can be quite different under active, muscle-loaded conditions [37] and [49] and contributions from other feedforward (e.g. pre-activity) and feedback (e.g. long latency reflexes) mechanisms must also be considered in the determination of adequate functional joint stability. While challenging, functional research models are needed to investigate further differential gender responses to fatigue across the complete neuromuscular response continuum in all relevant knee musculature.

#### **ACKNOWLEDGEMENTS**

We wish to thank Bob Anderson and Jeffrey Quinlavin, Department of Biomedical Engineering Department at the University of Virginia for their assistance with the construction of the patellar tendon apparatus.

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