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Abstract

Activity-related knee joint dysfunction is more prevalent in females than males. One explanation for the discrepancy is differences in movement patterns between the sexes. However, the underlying mechanisms responsible for these differences remain unidentified. This study tested spinal motor control mechanisms influencing motor neuron pool output and subsequent muscle activation in 17 males and 17 females. The following variables were assessed at the soleus: the gain of the unconditioned H-reflex, gain of both intrinsic

pre-synaptic inhibition (IPI) and extrinsic pre-synaptic inhibition (EPI), the level of recurrent inhibition (RI), the level of supraspinal drive determined by the ratio of the $V_{max}:M_{max}$ (V-wave), electromechanical delay (EMD) and the rate of force development (RFD). The Wilks Lambda multivariate test of overall differences among groups was significant ($p = 0.031$). Univariate between-subjects tests revealed males had greater RI ($p = 0.042$). However, the sexes did not differ on any of the other variables tested. In conclusion, the sexes differ on modulation of spinal motor control. Specifically, RI, a post-synaptic regulator of force output, was greater in males.

Introduction

The prevalence of activity-related knee joint dysfunction, for example non-contact anterior cruciate ligament (ACL) injuries and patellofemoral pain syndrome (PFPS), is greater in females compared to males (Agel et al. 2005; Boling et al. 2010). One explanation is the existence of biomechanical and neuromuscular differences between the sexes during certain functional tasks (Griffin et al. 2006). Despite this knowledge, the underlying mechanism for these movement pattern differences remains unclear. In order to better understand these differences, it is of interest to examine the spinal motor control mechanisms influencing motor neuron pool output and subsequent muscle activation.

One of the most commonly utilized measures of spinal level motor control is the H-reflex. The H-reflex specifically measures the effectiveness of the synaptic transmission of the Ia afferent and the alpha motor neuron in the motor neuron pool within the spinal cord (Capaday 1997). The importance of this input–output pathway cannot be overstated due to the fact that all activities of the muscles of the extremities are a direct result of activation of the alpha motor neurons (Wolpaw 2001).

Although previous reports have compared H-reflexes between males and females, the results are contradictory (Hoffman 2010; Christie et al. 2004). The equivocal results may in part be explained by the fact that these studies examined different characteristics of the Ia-alpha motor neuron synapse. An important consideration is that in both studies H-reflexes were tested alone. When H-reflexes are tested alone, they do not account for the influences from other known modulators of the Ia-alpha motor neuron synapse, specifically pre- and post-synaptic inhibition and supraspinal drive (Knikou 2008; Del Balso and Cafarelli 2007). The effects of these inputs can be assessed by H-reflex conditioning protocols that target pre- and post-synaptic segmental spinal mechanisms (Knikou 2008). In addition, a variant of an H-reflex can be elicited during a maximal isometric contraction to estimate the level of supraspinal drive (Del Balso and Cafarelli 2007; Aagaard 2003). Knowledge of the effects of these inputs on the synaptic efficiency is important because these mechanisms modulate the effectiveness of the synaptic transmission which in turn results in changes in motor output.

While there are many measures of muscle output and function, the ability to rapidly activate a muscle has been posited to be the most important functional measure (Aagaard 2003). This is based on the tenet that during deleterious situations (e.g., non-contact ACL injury) an individual is unlikely to have enough time to generate maximal force (Aagaard 2003). Therefore, a quicker and more rapid muscle activation may decrease the potential for injury. Two commonly used measures of rapid muscle activation are electromechanical delay (EMD) and rate of force development (RFD). There have been conflicting reports as to RFD and EMD sex differences, with studies using different muscle groups and methods (Behm and Sale 1994; Bell and Jacobs 1986; Hakkinen 1993; Komi and Karlsson 1978). Perhaps most important is that there are no studies that have comprehensively measured and compared a combination of spinal control mechanisms and muscle output and function in males and females. Importantly, all of these measures display activity-dependent plasticity (Aagaard et al. 2002; Del Balso and Cafarelli 2007; Earles et al. 2002; Kipp et al. 2011).

Therefore, the aim of this study was to collect a unique combination of spinal motor control variables, which encompass several segmental spinal mechanisms (i.e., inputs to the Ia-alpha motor neuron synapse), and two functional motor output variables (i.e., outputs of the Ia-alpha motor neuron synapse). Specifically, the spinal motor control variables were: (1) the gain of the unconditioned soleus H-reflex, (2) gain of both intrinsic and extrinsic pre-synaptic inhibition, (3) the amount of post-synaptic, and (4) the level of supraspinal drive. Whereas the rapid muscle activation variables were the electromechanical delay and the maximal RFD normalized to body mass.

Methods

Participants

Forty-one participants (20 females and 21 males) were recruited to participate in this study. Participants ranged in age between 18 and 35 and were physically active for a minimum of 30 min at least three times a week. Participants were free from: (a) current injury of the back, upper extremity, or lower extremity, (b) lower extremity injury in the past 6 months, and (c) history of lower extremity ligament surgery. To control for hormonal fluctuations across the menstrual cycle, females were tested on days one, two, or three of their menstrual cycle. Four male and three female participants were unable to complete the testing protocol so their data were omitted. Therefore, the total number of participants was 17 males (23.0 ± 4.3 years, 177.5 ± 5.4 cm, 77.5 ± 13.2 kg) and 17 females (24.7 ± 2.9 years, 165.3 ± 5.9 cm, 62.4 ± 8.8 kg).

Procedures

Participants read and signed the informed consent form approved by the University's Institutional Review Board. Participants completed a health history and training history questionnaire to determine eligibility for participation. Height was obtained using a wall-mounted stadiometer and weight was determined by a standard scale. Leg dominance was determined via the preferred leg with which the participant: (a) kicked a ball, (b) recovered from a balance perturbation, and (c) stepped up on a 10-inch box (Hoffman et al. 1998). The leg used in the majority of the three tests was considered the dominant leg and was used for all subsequent testing.

Dynamometer positioning

Participants were seated on the chair of the Biodex System 3 dynamometer (Biodex Medical Systems Inc, Shirley, NY, USA) in a semi-recumbent position. The knee was flexed to 60° and ankle in anatomical/neutral position. The foot was secured to the ankle attachment's foot plate preventing any movement of the foot from the plate. The non-test leg was in a comfortable, relaxed sitting position with the foot supported. This positioning was used for all subsequent testing.

Electromyography preparation

The soleus, tibialis anterior, and lateral mallelous were prepared for the application of lubricated surface EMG electrodes (Ag/AgCl). The EMG electrodes were placed longitudinally over the muscle with an interelectrode distance of 2 cm for each respective muscle. The EMG of the reflex and voluntary muscle contractions was collected and stored on a personal computer equipped with a Biopac MP100 data collection system (Biopac Systems Inc, Goletta, CA, USA). The EMG was sampled at 2,000 Hz.

Stimulating electrode placement

To elicit the soleus H-reflex, a stimulating electrode (2 cm^2) was placed over the tibial nerve in the popliteal fossa for current delivery. A dispersal pad (3 cm^2) was placed superior to the patella on the distal thigh. To elicit extrinsic pre-synaptic inhibition of the soleus, a stimulating electrode (1 cm^2) was placed over the common peroneal nerve distal to the fibular head for current delivery and a dispersal pad (3 cm^2) was placed just anterior

to the fibular head. This targeted the deep peroneal branch of the common peroneal nerve, ensuring stimulation of the tibialis anterior and limiting stimulation to the peroneal group.

H-reflex protocol

H-reflex and M-wave recruitment curves for the soleus were measured by stimulating the tibial nerve in the popliteal fossa. Stimulation was produced by a Grass S88 stimulator (Grass Technologies, West Warwick, RI, USA). A series of increasing intensity electrical stimuli (1 ms duration pulse) beginning near the threshold of the H-reflex and continuing to M_{max} were applied. There was a 10 s interstimulus latency period. The peak-to-peak H-reflex and M-wave amplitudes were measured online and were normalized to M_{max}. Stimulus intensity was normalized to the maximum stimulus. To measure the gain of the H-reflex and M-wave recruitment curves, the first derivative of each was calculated (Christie et al. 2004). The recruitment curves were imported into a LabView 8.5 (National Instruments Corporation, Austin, TX, USA) custom-made program. A 4th order polynomial curve was fit to each curve and then the curves were linearly interpolated to 100 data points and the first derivative was calculated. Figure 1 provides a representative recruitment curve from one participant.
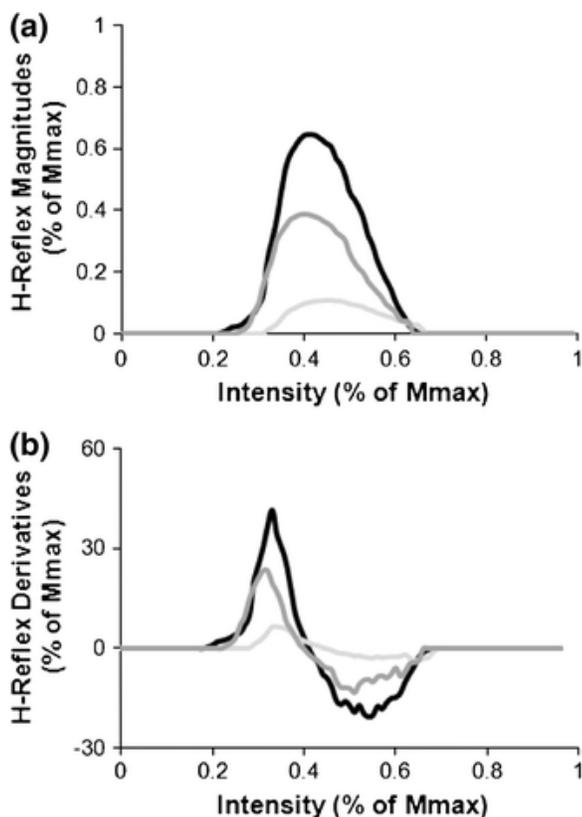
Fig. 1 H-reflex, EPI, and IPI data. An example of **a** normalized recruitment curves and **b** derivatives of the normalized recruitment curves (*black line* H-reflex, *dark gray* EPI, *light gray* IPI). M-wave data are removed from the figures for clarity

Pre-synaptic inhibition protocols

To test intrinsic pre-synaptic inhibition, the paired pulse technique was utilized. Two stimuli of the same intensity with a 100 ms interstimulus interval were given to the tibial nerve in the popliteal fossa. The double stimulation produced two H-reflexes, with the second H-reflex being depressed relative to the first H-reflex. The depression of the second reflex is the amount of inhibition due to the influence of reflex activation history. The same procedures for mapping the recruitment curve employed with the H-reflex were used for intrinsic pre-synaptic inhibition.

The procedure for measuring extrinsic pre-synaptic inhibition involved conditioning the H-reflex by stimulating the tibialis anterior prior to stimulating the soleus muscles. There was a 100 ms interstimulus interval between the conditioning and test reflex stimulations. The intensity of the conditioning stimulation was 50% of the tibialis anterior M-wave. However, the intensity of the test reflex followed the same procedure as the H-reflex and paired pulse protocols, i.e., stimulations began at or near H-reflex threshold and progressively increased until M_{max} was attained.

The recruitment curves for both types of pre-synaptic inhibition were analyzed using the same procedures as the H-reflex recruitment curve. Peak-to-peak amplitudes were obtained and were normalized to M_{max}. Stimulus intensity was normalized to the maximum stimulus. The first derivative of the pre-synaptic inhibition curves was calculated by importing the recruitment curves into a LabView 8.5 (National Instruments Corporation, Austin, TX, USA) and fitting a 4th order polynomial curve. The curves were then linearly interpolated to 100 data points and the first derivative was calculated.

Post-synaptic inhibition protocol
Post-synaptic inhibition was assessed using a recurrent inhibition protocol. In this conditioning protocol, the first stimulus, S1, was set at 25% of the soleus M_{max}. The second stimulus, S2, was set at M_{max}. A total of 20 trials were obtained. Ten trials were S1 alone and 10 trials were S1 followed 10 ms later by S2. The trials were counterbalanced. The peak-to-peak amplitudes of the H-reflexes elicited either by S1 alone or S1 conditioned by S2 were analyzed. The percent difference between the amplitudes was considered the amount of recurrent inhibition, i.e.,

$$(1 - \frac{Testreflex}{Conditionedreflex}) \times 100\%$$

Electro-mechanical delay and rate of force development protocol
Participants were instructed to plantarflex his or her ankle as fast and hard as they could once a light was illuminated. The light was attached to the wall (3 m) in front of the participant. Three trials with 60 s rest between each trial were performed. Electro-mechanical delay was determined by calculating the time between the onset of soleus EMG activity and onset of force production. RFD was calculated by determining the slope of the force–time curve from the onset of force production to the maximal force production. The RFD was then normalized to body mass for each participant. Both EMG and force production onsets were determined by the cumulative sum technique (Ellaway 1978).

V-wave protocol
V-waves were measured using the same procedures used during the RFD. Participants were instructed to plantarflex as fast and hard as they could. Once they reached 90 percent of their maximum force development, a supramaximal electrical stimulus (1 ms square pulse) was applied to the tibial nerve. Maximum force was determined by the mean of the maximum amplitude of the three trials of rate of development. Five trials were completed with 60 s rest between trials. The peak-to-peak amplitude of the M-wave and the V-wave were measured on-line. The ratio of V-wave to M-wave was considered the amount of supraspinal efferent neural drive.

Statistical analysis
A one-way MANOVA was used to compare differences of H-reflex gain, gain of intrinsic pre-synaptic inhibition, gain of extrinsic pre-synaptic inhibition, level of post-synaptic inhibition, level of supraspinal neural drive, RFD, and electromechanical delay between the sexes. Alpha level was set at 0.05 a priori. All statistical procedures were performed in SPSS 18.0 (SPSS Inc, Chicago, IL, USA).

Results

The Wilks Lambda multivariate test of overall differences among groups was statistically significant (p = 0.031) with a partial η^2 = 0.420. (See Table 1) Univariate between-subjects tests revealed males demonstrated more RI than the females (p = 0.042; partial η^2 = 0.12) (See Fig. 2). However, the sexes did not differ on the gain of the H-reflex (p = 0.773; partial η^2 = 0.003), IPI (p = 0.778; partial η^2 = 0.003), EPI (p = 0.668; partial η^2 = 0.006) nor on V-waves (p = 0.526; partial η^2 = 0.13). Additionally, muscle activation measures, RFD (p = 0.427; partial η^2 = 0.20) and EMD (p = 0.278; partial η^2 = 0.037), were also not significantly different between the sexes.

Table 1 Group means and standard deviations

	H-reflex derivative	IPI derivative	EPI derivative	Recurrent inhibition*	V_{Max}:M_{max}	Max RFD/kg (N kg^{-1} ms^{-1})	EMD (ms)	H_{Max}:M_{max}
Males	9.80 ± 3.71	2.23 ± 2.27	8.39 ± 4.15	0.86 ± 0.21	0.22 ± 0.21	4.93 ± 1.84	46.35 ± 29.76	0.65 ± 0.17
Females	10.38 ± 4.58	2.14 ± 2.23	9.79 ± 6.15	0.68 ± 0.30	0.27 ± 0.17	4.34 ± 1.60	58.50 ± 23.47	0.61 ± 0.12

1. * Significant differences between males and females $p < 0.05$
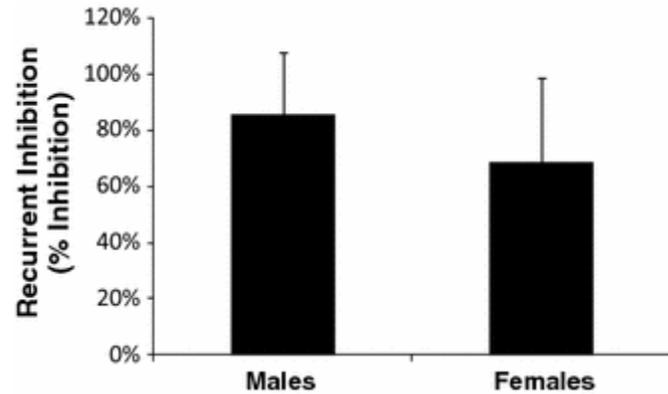
Fig. 2 Recurrent inhibition between the sexes. Males significantly greater than females ($p = 0.042$)

Discussion

Sex differences in the prevalence of certain lower extremity injuries continue to exist (Agel et al. 2005). These differences may in part result from the fact that males and females move differently during certain functional tasks (Griffin et al. 2006). However, the underlying spinal control mechanisms that influence motor neuron output and muscle activation have not been fully identified. We attempted to elucidate sex differences by examining modulators of motor neuron pool output and measures of rapid muscle activation.

Our results reveal that males and females differ in modulation of motor neuron pool output. Specifically, males had significantly greater recurrent inhibition, a post-synaptic modulator of motor neuron output, than females. The RI pathway involves a collateral from the alpha motor neuron to a Renshaw cell that when activated provides RI to the same or synergistic alpha motor neurons (Knikou 2008). Greater levels of RI reduce the sensitivity of neurons to changes in excitatory drive and decrease the discharge frequency of the alpha motor neuron (Knikou 2008). However, RI is not simply a negative feedback loop (Mattei et al. 2003). It has also been found that RI synchronizes motor neuron discharges during voluntary contractions (Mattei et al. 2003). RI also displays context dependence that can be observed with different levels of muscle contraction. Specifically, RI is greater during weak tonic contractions, whereas RI levels are lower during strong tonic contractions (Hultborn and Pierrot-Deseilligny 1979). To further highlight the context dependence, RI is smaller with soleus muscle contraction but is greater with tibialis anterior muscle contraction (Pierrot-Deseilligny et al. 1977). Due to this context dependence it has been posited that RI acts as a variable gain controller of motor neuron pool output and is engaged in selection of the appropriate muscle synergy especially during equilibrium threatening tasks (Knikou 2008).

In the current study, the males' level of RI was 86 ± 21% of the unconditioned H-reflex whereas the females' level of RI was 68 ± 30% of the unconditioned H-reflex. While no previous studies have investigated differences in RI between males and females, differences in RI between power- and endurance-trained individuals have been examined (Earles et al. 2002). The level of RI was reported to be greater in the power-trained individuals than endurance-trained individuals. It is difficult, however, to directly compare the results of that study with our results, because different stimulation intensities were used. Nonetheless, these authors suggest that differences in RI occur because power-trained athletes habitually try to fully activate the motor neuron pool during performance. It could also be that since RI is lessened during strong contractions, the power-trained athletes may have improved control of motor neuron output.

Interestingly, the males in our study showed greater levels of RI similar to the power-trained group in other reports. Based on these comparable results, it appears that the males in our study were more similar to power-trained individuals. This is not the first report of similarities in spinal control variables between males and power-trained individuals. Hoffman reported that males had lower H_{max}:M_{max} when compared to women (Hoffman 2010). Smaller H_{max}:M_{max} has also been reported in power-trained individuals when compared to endurance-trained individuals (Zehr 2002). We did not, however, specifically examine H_{max}:M_{max} in this study. Instead we chose to focus on the gain of the H-reflex recruitment curve to obtain a more complete picture of the recruitment of the entire motor neuron pool. This approach has been suggested as a better alternative to investigate the gain or the excitability of the motor neuron pool (Christie et al. 2004).

Taking this findings together, it appears that male's spinal control mechanisms are similar to power-trained individuals. Since both of these measures display activity-dependent plasticity one possible explanation is that males in both this study and the Hoffman study may have a history of participation in activities requiring power. Although we did not obtain a full history of physical activity from the participants, this explanation is a little counterintuitive when one considers the results from our measures of rapid muscle activation. Specifically, if the males had participated in more power related activities, it could be expected that max RFD, a component of

powerful muscle contractions, should also differ between the sexes. However, our results did not reveal any differences between anthropometrically normalized max RFD between the sexes. This leads to the conclusion that males and females are modulating spinal control differently, independent of rapid muscle activation characteristics.

A general limitation of the current study was that most variables were measured at rest. It is known that modulation of Ia-alpha motor neuron synapse differs when a person is at rest as compared to during movement, i.e., modulation displays context dependence. Regardless, our goal was to examine a large and novel combination of spinal control variables and functional motor outputs to provide a more complete profile of spinal modulation in males and females. Since most of these variables are difficult to assess during movement, we chose to perform all of the measures in the same recumbent position so as to minimize any possible changes due to context dependence. Based on this limitation, it remains to be determined if differences in RI, or any of the other spinal control mechanisms, exist during more functional tasks. Until more appropriate methods are developed the results of this study provide a starting point for future study. A pertinent step may be to study these variables in an environment or task that is more similar to an injurious situations.

Conclusions

Males and females have different rates of activity-related knee dysfunction owing in part to differences in functional movement patterns. Despite this knowledge, the underlying spinal control mechanisms that influence motor neuron output and muscle activation have not been fully identified. Therefore, in this study, we evaluated known modulators of motor neuron pool output and measures of rapid muscle activation in males and females. We found that recurrent inhibition, a post-synaptic spinal control mechanism, is greater in the males compared to females. Previous researchers have reported that power-trained individuals also have greater RI compared to endurance-trained individuals. Although this is the first study to report on RI differences between males and females, it is not the first study to report that males have spinal control profiles similar to power-trained athletes. Interestingly, the RI differences were independent of the rapid muscle activation measures. Taken in combination, these results are an important step in understanding spinal level motor control differences in males and females and may provide direction in design of training and rehabilitation programs.

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Acknowledgments

Conflict of interest

The authors report no conflict of interest.