CONTRIBUTION OF LOAD- AND LENGTH-RELATED MANIPULATIONS TO MUSCLE RESPONSES DURING FORCE PERTURBATIONS

by

Taryn Klarner

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ABSTRACT

Adding resistance to the legs during walking increases swing phase muscle activity, presumably through load-sensitive flexor muscle feedback pathways. However, increased muscle activity could also be due to the changes in lower limb kinematics that accompany resistance. Thus, the purpose of this study is to evaluate the contribution of resistance and knee pattern manipulations to muscle responses during force perturbations. The natural kinematic pattern associated with resistance was determined as subjects walked with the Lokomat applying resistances of 0%, 5% and 10% of their maximum voluntary contraction (MVC) to the hip and knee joints of both legs. Walking with increased resistance causes decreased knee flexion during the swing phase and decreased stride frequency. Knee joint data and stride frequencies at these resistance levels were used to create three biofeedback traces, representing three different knee pattern conditions, to be used in the experimental block. Subjects then walked at 9 different combinations of resistance (0%, 5% and 10% MVC) and knee pattern (fast, medium and slow). Leg muscle activity and joint kinematics were recorded and analyzed. Results indicate that both resistance and knee pattern perturbations independently contribute to ongoing swing phase activity in the quadriceps. Analysis of effect sizes indicate that resistance contributes more than the knee pattern manipulation to quadriceps muscle activity. Information arising from both load sensitive and length sensitive afferents could be involved in mediating these responses.

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INTRODUCTION

Biomechanical basis of walking

Walking, or gait, is one of the main forms of locomotion for legged animals. In the simplest terms, walking movements can be modeled as an inverted pendulum where the body moves over a stiff limb, repositioning the center of gravity, while the other limb advances to a new site of support (Cavagna and Margaria, 1966). Since humans have two legs, the movements associated with gait are bilaterally symmetrical and each leg acts as its own inverted pendulum. Forces generated at the ground cause the body and joints to rotate while activity produced in the muscles acts to resist and dissipate these kinetic forces. All of these events must be precisely controlled in order to keep the center of gravity over the base of support to ensure the maintenance of balance.

The cyclic movements associated with walking involve a chain of kinematic and kinetic events where each action flows smoothly into the next. Considering gait is an ongoing event, it is useful to identify discrete moments in time that can be used to divide walking into cycles. Most commonly, heel contact with the ground signifies the start of one gait cycle. The end of that gait cycle occurs when that same heel contacts the ground again. One gait cycle, or the time between successive heel contacts with the same foot, is called a stride. The period of time where the foot is on the ground is called the stance phase and the period of time the foot is in the air is called the swing phase. The stance and swing phase typically last for approximately 60% and 40% of the gait cycle, respectively (Murray et al., 1964).

Heel contact, signifying the start of the stance phase, is associated with a breaking force acting though heel to control the speed of progression. This is accompanied by hip flexion, knee extension and ankle dorsiflexion. Following this initial heel contact, the support limb begins to accept the full amount of body

weight as it is transferred forward. During this loading period, the heel acts as a rocker to transfer momentum forward. This is limited by ankle plantar flexion as the forefoot contacts the ground. Body weight acceptance on to the stance leg is also accompanied by slight knee flexion. Balance on this limb during mid stance is crucial as it will be the only point of contact with the ground as the other limb is in swing phase. Hip and knee extension as well as ankle dorsiflexion is coupled with the balance period during mid-stance. As the body weight passes over the support foot, the heel beings to rise, leaving the forefoot in contact with the ground. Ground reaction forces generated at this point in the gait cycle increase forward propulsion through the action of hip and knee extension and ankle plantarflexion. Increased hip extension leaves the limb trailing and stance is complete as the knee slightly flexes lifting the forefoot off the ground (Winter, 1991).

The entire period the foot is not in contact with the ground is called the swing phase. During the initial part of the swing phase, the hip moves from extension to flexion advancing the limb forward and the knee increasingly flexes. The ankle joint will also partially dorsiflex to ensure the toe clears the ground. As the leg swings through by the action of active hip flexion, interaction torques generated about the hip and knee joints cause the knee to extend (Phillips et al., 1983). Limb advancement is completed as the hip extends and the ankle moves into a near-neutral position and the heel makes contact with the ground. This marks the end of the swing phase and the end of a gait cycle or one stride.

The basic kinematic patterns associated with walking are quite stereotypical between subjects (Isacson et al., 1986) and even across different walking frequencies (Winter, 1983). At slow, medium and fast walking cadences, the angular displacements of the hip, knee and ankle joints hardly change (Winter, 1991). However, as cadence decreases, hip flexion and knee flexion during the swing phase will decrease. Perhaps to make up for the decrease in hip and knee flexion during the swing phase at slow walking cadences, ankle

dorsiflexion during the swing phase increases (Winter, 1991). While little difference is observed in joint positions at different walking cadences, large changes in joint angular velocities are apparent. Slow walking cadences result in decreased hip, knee and ankle joint angular velocities at all points in the gait cycle (Winter, 1983). Indeed, joint angular velocity is almost directly proportional to the cadence at which the subjects walked.

The basic locomotor pattern is divided into extension and flexion

Although the joint kinematic pattern during gait is complex, the locomotor pattern can be fundamentally described as an alternating pattern between flexion and extension. It is commonly accepted that a set of interneurons residing in the spinal cord underlies this basic pattern of flexion and extension generated during walking**.** Over a century ago, Charles Sherrington discovered that without the brain and brainstem, locomotor movements could still be evoked (Sherrington, 1906). A central pattern generator (CPG) has been identified and studied in numerous rhythmic motor systems including walking, swimming, feeding, flying, and respiration (Grillner and Wallen, 1985). It has also been demonstrated that CPG output can be modified from sensory receptors found within the peripheral nervous system and other regions within the central nervous system including supraspinal centers (Zehr and Stein, 1999, Nielsen, 2003, Pearson, 2004). Input from both descending commands and sensory afferents are required to initiate and regulate the motor output for stepping generated by a CPG.

The basic design of a CPG is based on two half-centers representing two systems of flexor and extensor neurons that mutually inhibit each other. This was based on work by Brown (1911) who developed a widely accepted model called the ‘half center model’. Brown saw that after cats were acutely spinalized and deafferented (decerebrate and unanaesthized) bursting was evident in alternating pairs of antagonist muscles in the hind legs. These bursts occur not only without

higher level input, but without sensory input. Brown went on to further postulate that the switching of activity depends on fatigue occurring in inhibitory interneurons (Brown, 1924).

The majority of evidence in favour of a CPG comes from experiments conducted in animals. It has been shown in quadrupedal mammals that spinal networks have the capability of generating basic locomotor patterns (Grillner and Wallen, 1985). After a complete spinal cord transection in the cat, hind limb stepping recovers after a few weeks with intense daily treadmill training and cutaneous stimulation of the perineal region (Pearson and Rossignol, 1991). Electromyographical (EMG) recordings from hindlimb muscles in spinal cats are generally similar to those from intact cats and many of the normal reflex responses are apparent in the spinal preparation. This compelling evidence supports the notion that a central network of neurons is capable of producing motor patterns resembling walking without input from the brain or brainstem. These results also highlight the importance of sensory afferent information in facilitating gait recovery.

To emulate a nervous system closer to that of humans, studies have used monkeys to model locomotion. In macaque monkeys with complete spinal transection no convincing evidence was initially found to support the notion that a central pattern generator exists. In macaque monkeys with incomplete spinal injuries, however, stepping movements could be elicited, particularly if the locomotor centers of the brain (mesencephalic locomotor region, posterior subthalamic region and in the midbrain tegmentum) were stimulated (Eidelberg et al., 1981). In marmoset monkeys, Fedirchuk et al. (1998) was also successful in eliciting CPG activity with clonidine and NMDA agonists injected intrathecally, but the activity was not as robust as seen in cats. This suggests that primates might depend more on supraspinal input to effectively entrain CPG output.

Although there is evidence for a locomotor central pattern generator from several mammalian species (Grillner and Wallen, 1985, Nishimaru and Kudo, 2000, Burke, 2001), there is only indirect evidence supporting the notion that similar neural circuits underlie the control of human locomotion. People with a clinically complete spinal cord injury are unable to recover walking (Behrman and Harkema, 2000). This is in stark contrast to findings from cats with complete spinal transections that were able to recover walking function (Pearson and Rossignol, 1991). However, there is some indirect evidence of CPG-mediated locomotion in humans (Bussel et al., 1988, Calancie et al., 1994, Dimitrijevic et al., 1998). In a case study of a patient with a complete cervical spinal cord injury, rhythmic activity developed in the extensor muscles resulting in symmetrical and bilateral movement of the trunk and lower limbs. This demonstrates that in humans rhythmic movements could be produced in a spinal cord devoid of supraspinal inputs. During extensor activation, elicitation of flexor activity by peripheral stimulation of flexor reflex afferents induced alternating flexor and extensor bursting (Bussel et al., 1988). Dimitrijevic et al (1998) also showed that tonic electrical stimulation of the lumbar spinal cord in patients with complete cervical spinal cord injury resulted in phasic bursts of activity in lower limb muscles. Indirect evidence for a CPG in humans with a neurologically incomplete injury of the cervical spinal cord also exists. Although the subject had no ability to generate voluntary lower leg muscle activity, 'forceful and patterned' bursts of activity in antagonist muscles in the subject's legs were recorded when lying supine. All activity ceased when he rolled over, sat up, or bent the hip to 90 degrees (Calancie et al., 1994).

Indirect evidence for a locomotor central pattern generator also exists from studies of the automatic stepping response in human infants. Suspending an infant (who is unable to walking and bear weight on their own) over a treadmill can elicit rhythmic stepping movements (Yang et al., 1998). This suggests that some of the basic neuronal circuitry for locomotion is present in humans before the onset of voluntary stepping. Stepping movements have also been observed

in anencephalic infants, suggesting that locomotor control centers could exist below the level of the brain stem (Forssberg, 1992). Finally, the fact that the descending pathways from the cerebellum and motor cortex are not fully mature in a human infant (Khater-Boidin and Duron, 1991, Yang et al., 2004) further supports the notion that infant stepping responses are mediated by walking centers located in the brainstem or spinal cord.

These studies show that while direct evidence from animal models supports the notion that a CPG is involved in the control of locomotion, there is only indirect evidence for a locomotor CPG in humans. Nevertheless, the concept that a network of neurons located in the spinal cord could be responsible for rhythmic activity during locomotion provides a conceptual framework for understanding how the basic alternating pattern between leg flexors and extensors is generated during walking. However, it is clear that there is a more complex control system underlying human bipedal walking involving supraspinal and peripheral sensory feedback pathways.

Descending control during locomotion

Inputs from supraspinal centers are required to initiate and regulate the motor pattern required for stepping (Zehr and Stein, 1999, Nielsen, 2003, Pearson, 2004). To significantly modulate muscle activity during walking, intact corticospinal transmission is essential (Nielsen, 2003). Descending inputs are also required to successfully steer around obstacle (Hess et al., 2003), to adapt to dynamic external conditions (Drew, 1988), and when transitioning between a walk and run (Shik et al., 1969, Grillner and Zangger, 1975). With the help of the visual system, descending inputs are also required to appropriately anticipate when and where gait modifications are necessary (Drew et al., 1996, Schubert et al., 1999). Supraspinal inputs could have a higher functional relevance to bipeds compared to quadrupeds due to the increased need for balance control in bipedal human gait (Yang and Gorassini, 2006).

Only limited evidence exists in humans where several brain imaging and noninvasive electrophysiological techniques have been adopted in order to better understand supraspinal control of walking in humans. To make inferences about which brain region is active during voluntarily controlled movements, research has been conducted that investigates cerebral blood flow as an indicator of brain activity. Voluntary cycling, compared to passive cycling induced by the experimenter, yielded a larger increase in cerebral blood flow to the leg representation of the primary motor cortex imaged with positron emission tomography (Christensen et al., 2000). This suggests that there is a larger involvement of supraspinal structures (particularly the motor cortex) during voluntary repetitive, bicycling similar to walking. Supporting this finding, during treadmill walking in humans, single photon emission tomography revealed a significant increase in cerebral blood flow to the leg representation area in the sensorimotor cortex, cerebellum and frontal cortex (Fukuyama et al., 1997).

It has been shown that motor cortical areas contribute to generating the motor program during human walking via the corticospinal tract. Transcranial magnetic stimulation was applied to the motor cortex during walking while evoked responses were measured in the muscles of the lower limbs (Schubert et al., 1997). Phase-dependent amplitude modulation was present in tibialis anterior and medial gastrocnemius and the response was not correlated to with gait-associated modulation of the EMG activity. The role of the corticospinal tract was also studied in a single subject who incurred a selective bilateral pyramidal tract (corticospinal tract) lesion. The subject was unable to walk for five months following the injury highlighting the importance of the pyramidal tract in locomotor control (Nathan, 1994). The importance of the pyramidal tract in the control of walking was also demonstrated in a study of the functional recovery of walking following chronic spinal cord injury (Thomas and Gorassini, 2005). After several months of intensive locomotor training, the response to transcranial magnetic stimulation (measured by motor evoked potentials in the tibialis anterior)

increased. This increase in corticospinal tract connectivity following training was associated with improvements in the distance covered in a 6 minute walk test and in the recovery of locomotor EMG activity.

The corticospinal tract, descending from the motor cortex, could be more closely linked with the flexor muscles during walking (Capaday et al., 1999). During walking and during a voluntary task the motor cortex was activated transcranially. The voluntary task involved subjects sitting with their foot strapped in place while performing isometric dorsi- and plantarflexion contractions. During walking, measurements of motor evoked potentials (MEPs) revealed that during the late stance phase, MEPs in the tibialis anterior (normally inactive in this phase) were enhanced relative to their size during voluntary ankle plantarflexion at the same level of background EMG activity. In contrast, soleus MEPs were larger during voluntary plantarflexion than during the stance phase of walking. These investigators concluded that during walking the corticospinal tract is more closely involved in the motor circuits controlling the flexors (tibialis anterior) than it is with the circuits controlling the ankle extensors (soleus). Functionally, these results suggest that the motor cortex attends more to flexor activity during walking to terminate stance and to facilitate swing phase activity (Capaday et al., 1999).

Descending motor cortical pathways also contribute to locomotor control during skilled walking or when precise control is needed (Nielsen, 2003). Without the motor cortex, cats are capable of walking on a treadmill (Armstrong, 1988). However, when obstacles need to be avoided or in more complicated walking activities, such as walking on a horizontal ladder, the motor cortex plays a crucial role (Rossignol et al., 1999). Adjustments are made by increasing flexor muscle activity and changing the spatial and temporal patterns of muscle firing. Recordings from descending pyramidal tracts also reveal an increase in discharge rate of firing during gait adjustments (Drew et al., 1996).

Studies in humans show facilitation in the involvement of the corticospinal pathway if locomotion requires more precise control (Bonnard et al., 2002). Using a mechanical constraint, which affected the upper-leg muscles, a significant increase in rectus femoris and biceps femoris MEPs were observed compared to those recorded during unconstrained walking. These results demonstrate the importance of corticospinal involvement during skilled walking tasks where fine control is needed, even in proximal upper-leg muscles. The co-facilitation of MEPs evoked in both the rectus femoris and biceps femoris could also indicate a possible parallel excitatory pathway. These results suggest that perhaps during walking with the upper leg constraint, reciprocal inhibition is diminished, by pre-synaptic inhibition, and there is an increased reliance on excitatory heteronymous projections between the muscles of the proximal leg.

The cerebellum is also involved in motor learning and locomotor adaptations during walking (Nielsen, 2003, Morton and Bastian, 2004). In walking cats, spike potentials from Purkinje cells in the lateral vermis of the cerebellum were recorded during stable treadmill walking and during perturbed walking where the contralateral forelimb suddenly experienced increased belt speed. During this perturbation, climbing fiber discharge rate significantly increased during late swing in the ipsilateral leg (Yanagihara and Udo, 1994). These results unveil the involvement of the cerebellar vermal purkinje cells in locomotor adaptations. Individuals with cerebellar damage have difficulties with movement co-ordination and prediction. They are able to make reactive changes during normal walking, but are unable to learn predictive strategies to split-belt treadmill walking perturbations (Morton and Bastian, 2006). In another study involving cerebellar patients, it was found that although they could adapt to unexpected changes in treadmill belt speed by minimizing their postural sway and changing step length, they could not establish a motor program that was consistent from trial to trial or resembled the strategy employed by normal subjects (Rand et al., 1998). These results suggest that the cerebellum is a key structure involved in the formation of predictive control strategies. Predictions made by the cerebellum are

based on rapid integration of the consequences of the motor command, information from the motor cortex and updates via sensory feedback (Wolpert and Miall, 1996).

Online regulation of locomotion

Sensory information continuously acts to modify the motor output via feedback networks in order to ensure balance and successful stepping (Pearson, 1976). Although the generation of the fundamental rhythm associated with gait does not depend on peripheral afferent inputs (Grillner and Zangger, 1979, Grillner and Zangger, 1984), it is clear that input from sensory organs is important for regulating walking, provides crucial information necessary for motor control and is functionally significant in a number of different ways (Zehr and Stein, 1999). For example, in cats with a complete spinal cord transection at the T12-L1 level, sparing sensory afferents below the level of the injury, short term motor learning is possible. Following gait retraining interventions where cats were exercised at full body weight support at maximal velocity for 30 minutes on a treadmill 5 days/week, spinal cats were able to regain gait function. This indicates that motor learning at the level of the spinal cord is facilitated by sensory afferents. Conversely, a reversal was seen when spinal cats with full locomotor capacity underwent standing training and consequently lost walking ability (Hodgson et al., 1994).

Sensory feedback may act to increase the output of motor neuron pools via the alpha motor neuron. This generates features of the stepping motor program from peripheral cues and controls the level of activity in the muscles involved in walking. Afferent sensory feedback plays a crucial role in error detection and is of increased significance when it is necessary to make adjustments to the basic locomotor rhythm in response to changing environmental demands. Sensory inputs also provide critical signals regulating the duration of muscle activity thus controlling phase transitions.

Sensory feedback contribution to extensor muscle activity

We have previously seen that locomotor patterns can be generated centrally (Brown, 1911), and after suppressing all sensory inflow in a spinal cat a fundamental rhythmic locomotor pattern can still be produced (Grillner and Zangger, 1979). However, sensory signals provide crucial cues required to generate features of the stepping motor program associated with extension (Pearson, 2004, Duysens et al., 1998). Sensory feedback also acts to regulate the duration of extensor activation (Pearson, 2004).

Much of what we know about the contribution of muscle afferents to the level of muscle activity during locomotion comes from animal models. Proprioceptive inputs from group I afferents contribute to ankle extensor activity during stance (Stein et al., 2000). Long trains of stimulation were delivered to afferents arising from the lateral gastrocnemius, soleus, plantaris, vastus lateralis and vastus intermedius at the start of the stance phase in decerebrate cats. This direct electrical stimulation of group I afferents arising from leg extensor muscles resulted in an increase in the amplitude and duration of extensor muscle activity during the stance phase of locomotion (Whelan et al., 1995). A similar conclusion was reached by loading and unloading ankle and knee extensor muscles during walking in a decerebrate cat (Hiebert and Pearson, 1999). To evaluate the contribution of proprioceptive information arising from ankle extensors, cats stepped on a trap door which opened into a hole while walking on the treadmill. During this simulated unloading, a 70% decrease in ankle extensor activity was experienced. In the same study, the hindquarters of cats were raised or lowered during treadmill walking, effectively unloading and loading the knee extensors, respectively. Raising the hindquarters during treadmill walking resulted in a strong reduction in knee extensor muscle activity; the opposite occurred when the hindquarters were lowered (Hiebert and Pearson, 1999). These data support the notion that sensory input acting on extensor motoneurons greatly affects the level of activity in the leg extensors during stance.

Similar to cats, proprioceptive input from leg extensor muscles contributes to extensor activity during human walking. It has been shown that spindle primaries contribute to extensor activity during early stance (Yang et al., 1991). A pneumatic actuator, placed under the forefoot was used to induce unexpected artificial stretch in the soleus muscle simulating soleus loading. This mechanical dorsiflexion of the foot induced stretch reflex activity in this muscle and it was concluded that 30-60% of soleus activation arises from muscle spindle primaries. Normally silent during early stance, a near-linear increase in velocity of stretch and the response of the soleus as reflected in the EMG was found. Therefore the velocity sensitive component contributes to the difference in reflex gain. A second piece of evidence to support the notion that afferent signals from ankle extensors contributes to extensor activity in human walking is from studying the effects of ankle unloading during the stance phase (Sinkjaer et al., 2000). Forced unloading by ankle extension by a portable stretch device capable of rotating the ankle joint during stance caused a 50% decrease in soleus activity. To eliminate the possibility that the decrease in soleus activation was caused by reciprocal inhibition from the stretch induced in ankle flexors, lidocaine was locally injected into the common peroneal nerve, which innervates the ankle dorsiflexors. The onset and decrease in soleus activation was unchanged following lidocaine injection.

Other evidence supports the notion that afferent feedback is involved in modulating extensor activity (af Klint et al., 2008). Within a step, afferent feedback from the triceps surae group modulates extensor activity to contribute to smooth and ongoing gait. When participants walked on an inclined support surface that could be tilted either up or down (±3°, 2°, 0° degrees in the sagittal plane), there was an increase in triceps surae muscle activity when the platform was inclined and a decrease when the platform was tilted down. In a similar experimental setup involving a subject who lacked sensory inputs from the neck down due to a rare neuropathy, no modulation of ankle extensor activity was

recorded during the different platform inclination conditions (af Klint et al., 2008). These findings demonstrate the importance of proprioceptive input from ankle extensors in producing extensor activity during stance in human walking.

Afferent reflexes associated with extensor activity could be especially important when walking is difficult. Changes in muscle spindle sensitivity have been studied for different walking contexts. In the cat, sensitivity of gamma drive and Ia fibers is low during level over ground walking, but increased in walking on uneven ground or when walking is difficult or unfamiliar (Hulliger, 1993). This increase in afferent sensitivity resulting in increased control of locomotion is required to make adjustments to account for changes in environmental demands (Sorensen et al., 2002). Ia afferent recordings in cats reveal increased discharge rates during novel or difficult walking tasks compared to routine over ground locomotion (Prochazka et al., 1988). Task modulation of the soleus H-reflex during the stance phase in humans has also been documented with different types of walking. Specifically, the H-reflex was attenuated during narrow beam walking compared to treadmill walking. This suggests a decrease in reflex excitability threshold when balance control and stability are highly necessary (Llewellyn et al., 1990).

Feedback mechanisms from extensor afferents facilitate locomotor adaptations (Pearson, 2004). Consistent with this position is the finding that following the transection of motor nerves to lateral gastrocnemius, soleus and plantaris in walking cats, leaving the medial gastrocnemius (MG) as the only ankle extensor, adaptive changes in motor activity occur on different time scales (Pearson et al., 1999). Initially, a large increase in MG activity is seen in ankle flexion (yield) during early stance and during ankle plantarflexion at the end of the stance phase. Functional recovery of these two components of MG bursts appeared to be independent because the ankle yield deficit recovered after 1 week, whereas improvements in ankle extension at end stance recovered after 3 days. Sensory feedback from the MG muscle spindles during end stance acts as

an error signal to rescale the magnitude of the early MG burst component. Therefore, feedback is thought to drive feedforward strategies (Pearson et al., 1999). Indeed, immobilizing the leg, therefore diminishing sensory feedback from the MG during late stance, prevented the increase in the initial component of the MG EMG.

Afferent input from extensor muscles could be associated with the termination of the stance phase. Unloading of the leg at the end of stance causes a decrease in the discharge rate of load sensitive afferents which contribute to initiating flexor activity associated with the onset of swing in the quadruped (Pearson, 1995). In cats, brief electrical stimulation of group I afferents from knee and ankle extensors prolongs extensor activity and delays the following flexor burst associated with the onset of swing (Conway et al., 1987). A second piece of evidence supporting the notion that unloading the leg at end stance triggers the onset of swing comes from mechanically loading (or stretching) the triceps surae in decerebrate cats during treadmill walking. This results in a sudden disappearance of ankle flexor bursts that only returns after the experimenters stopped stretching the triceps surae (Duysens and Pearson, 1980). These data support the notion that in order to initiate ankle flexion associated with swing, ankle unloading must occur. This change in loading would be preferentially signaled by proprioceptors arising from ankle extensors.

In the soleus, the H-reflex amplitude is highest during late stance suggesting the soleus' functional relevance to end stance control (Capaday and Stein, 1986). Indeed, the increase in soleus activity during stance could be due to an increase in excitability via facilitation along Ia reflex pathways (Verschueren et al., 2002) Sensory feedback arising from muscle spindles is also involved in phase transitions (Hiebert et al., 1996). In spinal and decerebrate cats, manually imposing movement around the hip joint, by a decrease in leg extension, resets and entrains the locomotor rhythm (Andersson and Grillner, 1983). Manually stretching the hip flexor muscle, iliopsoas, during the early part of the stance

phase in decerebrate cats caused an early initiation of flexor activity (Hiebert et al., 1996). The contralateral step cycle was also affected by stretching iliopsoas in the ipsilateral leg where flexor activity was shortened and extension occurred earlier. This supports the hypothesis that muscle spindle afferents in hip flexor muscles contribute to the termination of stance, initiation of swing, and are capable of resetting the locomotor rhythm (Hiebert et al., 1996).

Sensory feedback contribution to flexor muscle activity

In the case of leg flexors during the swing phase of walking, proprioceptive feedback also modulates the amount of activity recorded from these muscles. The concept that non-cutaneous inputs influence the swing phase was first proposed by Orlovskii and Shik in 1965 following their experiments involving treadmill locomotion in dogs. A 30 ms delay existed between the application of a braking force to the swinging paw and the observed swing phase correction. The short latency of this response suggests that a corrective mechanism exists in the lower levels of the central nervous system to ensure a consistently patterned swing phase to promote safe paw placement (Orlovskii and Shik, 1965).

In decerebrate walking cats devoid of cutaneous input and other afferent inputs from surrounding hindlimb musculature the role of flexor afferents was evaluated. By assisting hip flexion by either manual perturbation or with a mechanical device, a decrease in activity was recorded from the iliopsoas and sartorius muscles (Lam and Pearson, 2001) Conversely, resisting hip flexion caused an increase in iliopsoas and sartorius recruitment. One possible neural mechanism mediating flexor enhancement could arise from flexor muscle afferents which detect the change in flexor muscle length due to the perturbation.

The contribution of flexor muscles during the swing phase has also been demonstrated by applying direct electrical stimulation to flexor muscle afferents in

fictive cats (Hiebert et al., 1996, Quevedo et al., 2000). Stimulation of afferents at intensities that preferentially activate group I and II afferents from iliopsoas and sartorius muscles during fictive locomotion facilitated and enhanced ongoing flexor activity during the swing phase (McCrea, 2000). Ongoing flexor activity was also enhanced following stimulation at group I intensity in the extensor digitorum longus and peroneus longus muscles (Stecina et al., 2005). Activation of group I afferents from the sartorius muscle during the flexor phase in a fictive cat model also caused a simultaneous increase in step cycle duration (Perreault et al., 1995). These results suggest that flexor group I afferents can access a locomotor CPG and entrain its rhythmic output. Sartorius flexor group II afferents can also entrain rhythm generating networks by resetting the locomotor rhythm to extension (Perreault et al., 1995). Activating afferents from the sartorius muscle also causes generation of flexor bursts in other leg flexor muscles. Direct electrical stimulation of sartorius muscle afferents was conducted and its effect on iliopsoas and tibialis anterior activation was evaluated (Lam and Pearson, 2002). Activating group I sartorius afferents in decerebrate walking cats caused an increase in the duration of iliopsoas and tibialis anterior bursts and an increase in the magnitude of iliopsoas bursts during swing activity.

Direct recordings of spindle afferents from the sartorius muscle show that spindles are active during the swing phase of walking in unrestrained cats revealing their involvement in normal locomotion (Loeb et al., 1985b). Floating electrodes were implanted in the fifth lumbosacral dorsal root ganglion and used to record thigh muscle spindle activity during unrestrained walking in cats. It was found that spindles from knee extensors, the vastus lateralis and medialis, were active in passive stretch during the flexion phase of swing. Muscle spindles from the sartorius, an anterior biarticular muscle crossing both the hip and knee joints, were active during the swing phase where rapid muscle shortening occurred. These results, however, must be interpreted carefully due to the mechanical influence of intrafusal muscle fibers on muscle spindle sensitivity.

In order to make some qualitative and quantitative analysis of the effects of fusimotor drive on spindle activation, a lidocaine blockade to the femoral nerve was used to progressively block gamma motoneuron activity (Loeb and Hoffer, 1985). A large decrease in afferent activity in primary and secondary endings from both the monoarticular and biarticular hip flexor muscles was recorded. These results support the notion that muscle spindle sensitivity is highly influenced by fusimotor activity, both when the muscle is silent and when the muscle is active. Decreased activity of primary and secondary afferents occurred at different stages of the progressive fusimotor blockade suggesting different sources of control of fusimotor activity (Loeb and Hoffer, 1985). Fusimotor drive is also suggested to be controlled independent from extrafusal recruitment and the extent of fusimotor influence on muscle spindle sensitivity depends on the mechanical events occurring at that time (Loeb and Duysens, 1979).

Length sensitive feedback pathways can modulate the amount of activity from the quadriceps muscles during the swing phase of walking. The effects of an external stimulus (electrically induced twitches of the antagonist hamstrings muscle) were examined in the quadriceps. Primary and secondary afferents from the sartorius muscle discharged rapidly during the twitch showing highly sensitive short latency responses (Loeb et al., 1985a). This is consistent with the notion that spindles play a role in detecting small mechanical perturbations. In humans, a potential monosynaptic connection was identified between the quadriceps and knee extensor antagonists by recording stretch reflexes following mechanical knee flexion perturbations (Mrachacz-Kersting et al., 2004). Short latency responses were measured in the quadriceps to stretch and short latency responses were recorded in the medial hamstring and biceps femoris. The responses in the hamstrings were similarly modulated as compared to the quadriceps responses during the gait cycle. This suggests the existence of a possible functional excitatory monosynaptic connection between the knee extensors and flexors. The effectiveness of these projections during human walking could provide increased knee stability prior to heel contact.

Flexor afferent feedback could act to increase activation of these muscles especially during the swing phase (Garrett and Luckwill, 1983, Lam et al., 2006, Noble and Prentice, 2006). Subjects who walked on a treadmill experienced a sudden unexpected resistance to the leg during swing by use of a mechanical apparatus. This caused an increase in quadriceps activity which the authors presumed to arise from the increase in hip flexor load signaled by quadriceps load afferents (Garrett and Luckwill, 1983). In a similar experimental design, recent work has suggested that feedback mechanisms are involved in the adaptation of walking to a novel force condition (Lam et al., 2006). This condition involves a velocity dependent resistance imposed by the Lokomat, a gait training device, which acts to restrict hip and knee flexion during the swing phase of walking. A 12 degree reduction in knee flexion angle during the swing phase is apparent in steps taken against resistance. Although hip flexion angles were also reduced during the swing phase, this decrease was not statistically significant compared to control steps. To cope with the decreased early swing flexion and late swing extension of the knee, the rectus femoris muscles are immediately recruited. This adaptation was hypothesized to be associated with a feedback mechanism because the elevated swing phase activity only appeared during resisted steps and did not persist when the swing phase disturbance was removed (Lam et al., 2006).

In subjects with an incomplete spinal cord injury the addition of lower extremity ankle weights or the application of Lokomat applied force perturbation to swing phase activity resulted in an increase in muscle activity (Lam et al., 2008). Human infants also show increased flexor muscle activation at the hip and knee following disturbances to swing phase activity (Lam et al., 2003). The specific afferent feedback pathways responsible for mediating this increase in flexor activity are unknown in humans.

RATIONALE

It has been well established that feedback pathways are capable of producing and modifying the motor output associated with gait (Pearson, 2004). In particular, afferent feedback is critical for the control of extensor activity during gait and in the transition from stance to swing (Duysens and Pearson, 1980, Whelan et al., 1995). A growing body of evidence suggests that afferent feedback is also important in the control of swing phase activity (Perreault et al., 1995, McCrea, 2000, Lam and Pearson, 2002, Pearson, 2004). Resistance to swing phase movements during walking, whether using Lokomat-applied resistance (Lam et al., 2006) or a mechanical apparatus (Garrett and Luckwill, 1983), will not only induce load-related changes, but also length- related changes, given the changes in lower limb joint kinematics associated with resistance. Thus it is unclear the extent to which load- and length-related manipulations contribute to the muscle responses observed during resisted walking.

Purpose

The purpose of this study is to evaluate the contribution of load and length related manipulations on the muscle responses associated with swing phase resistance.

Hypothesis

It is hypothesized that perturbations that manipulate either load or length will independently contribute to the magnitude of muscle activity during walking. Based on past research, it is hypothesized that increasing load and decreasing range of motion and velocity during swing will increase the magnitude of muscle activity in the quadriceps muscles.

METHODS

Subjects

Participants with no known neurological conditions were recruited to participate in this study (N=20). An equal number of males and females between the ages of 22 and 37 years old were included. The mean height and weight of the participants were 173.66 cm (SD 6.64 cm) and 69 kg (SD 9.46 kg), respectively. All participants gave their informed consent and all procedures were approved by the UBC Behavioural Research Ethics Board.

Data recording procedures

Muscle activity was recorded by surface electromyography (EMG) electrodes from these muscles of the right leg: rectus femoris (RF), vastus medialis (VM), vastus lateralis (VL), medial hamstrings (MH), biceps femoris (BF), medial gastrocnemius (MG), and the tibialis anterior (TA). Skin cleaning techniques, including shaving, abrasion and cleaning the skin with alcohol pads, was employed to optimize signal clarity. EMG electrodes were placed over the muscle bellies, parallel to the muscles fibers. EMG data were amplified, high-pass filtered at 20 Hz and low-pass filtered at 450 Hz and converted on-line to digital form at 1000Hz.

Ankle joint sagittal plane kinematics from the right leg were recorded with an electro-goniometer aligned over the ankle joint (Biometrics Ltd., United Kingdom). Sagittal plane hip and knee joint kinematics from both legs were collected from position sensors at the Lokomat hip and knee joints (Hocoma AG, Volketswil Switzerland). Force sensitive resistors (FSRs; Interlink Electronics, Camarillo CA) were affixed to the insole of the participant's left and right shoes. Three FSRs were positioned under the heel, the first metatarsal head and the fifth metatarsal head. Kinematic data and FSR data were sampled at 1000 Hz and stored to a PC for offline analysis.

Lokomat

The lower limb lengths of the participants were measured to ensure a proper fit within the Lokomat robotic gait device (Hocoma AG, Volketswil Switzerland). This system incorporates a body weight support system suspended over a treadmill with a pair of robotic actuators which attach to the legs. The entire device sits on a flexible parallelogram frame which is counterbalanced by a large spring. Subjects' legs were strapped into the exoskeleton with Velcro cuffs around the mid-thigh, upper shank and lower shank while a chest strap provided trunk support.

The Lokomat was programmed to apply a velocity-dependent torque against left and right leg hip and knee movements, defined by:

$$\begin{bmatrix} \overline{M}_H \\ \overline{M}_K \end{bmatrix} = - \begin{bmatrix} B_H & 0 \\ 0 & B_K \end{bmatrix} \begin{bmatrix} \theta_H \\ \theta_K \end{bmatrix}$$

where M is the instantaneous amount of torque applied, B is the viscous (or damping) coefficient, and θ is the instantaneous angular velocity of the hip (H) and knee (K) joints (Lam et al., 2006). B values, to apply the target velocity dependent resistance, were calculated by dividing the desired percentage of the participant's maximal voluntary contraction (MVC) torque of the hip and knee joint as determined within the Lokomat device (Bolliger et al., 2008) by the peak swing phase angular velocity of either the hip or knee joint:

$$B_{HorK(Nm \bullet \sec/ rad)} = \frac{FlexorTorque_{HorK(Nm)}}{AngularVelocitySwing_{HorK(rad/\sec)}}$$

Experimental protocol

Participants walked on the treadmill with the Lokomat for several minutes to familiarize themselves with the device. Belt speed was set to 2.0km/h for the experiment. The natural kinematic pattern associated with resistance was

determined as subjects walked with the Lokomat applying resistances of 0%, 5% and 10% MVC to the hip and knee joints of both legs. Adding resistance resulted in changes in knee joint kinematics as well as stride frequency. Knee joint angles from each step collected in these initial trials were averaged and normalized to average stride time in seconds. The standard deviation of knee joint angle across the gait cycle was also calculated, averaged, normalized for each step and used to create a target window around the knee joint angle. These data, representing three different knee patterns, were used to create the three different biofeedback traces to be used in the experimental block (Fig. 1). The kinematic trajectories as well as auditory tones corresponding to the time of right heel contact were provided to the subject to ensure they maintained the corresponding trajectory and cadence. Biofeedback traces as well as online knee joint data were displayed on screen for the subjects in real time.

To evaluate the independent effects of resistance and knee pattern, subjects then walked in 9 blocks of trials each one consisting of one of the 9 possible combinations of resistance (0%, 5%, 10% MVC) and knee pattern (fast, medium and slow as defined by the initial control trials). The B value to apply the velocity dependent resistance was adjusted across the different conditions of kinematic speed so that the total torque applied was conserved. Biofeedback was provided for each of the 9 trials to help subjects match the different knee patterns across different levels of resistance, to each of the fast, medium and slow conditions (Fig. 1). The order of the trials was randomized and each trial lasted for 150 seconds. Breaks were provided between each trial to avoid fatigue. Subjects were instructed to walk as normally as possible while matching their stride frequency and knee joint excursions (within the window defined by 1 standard deviation around the mean) to the target trajectory displayed on screen.

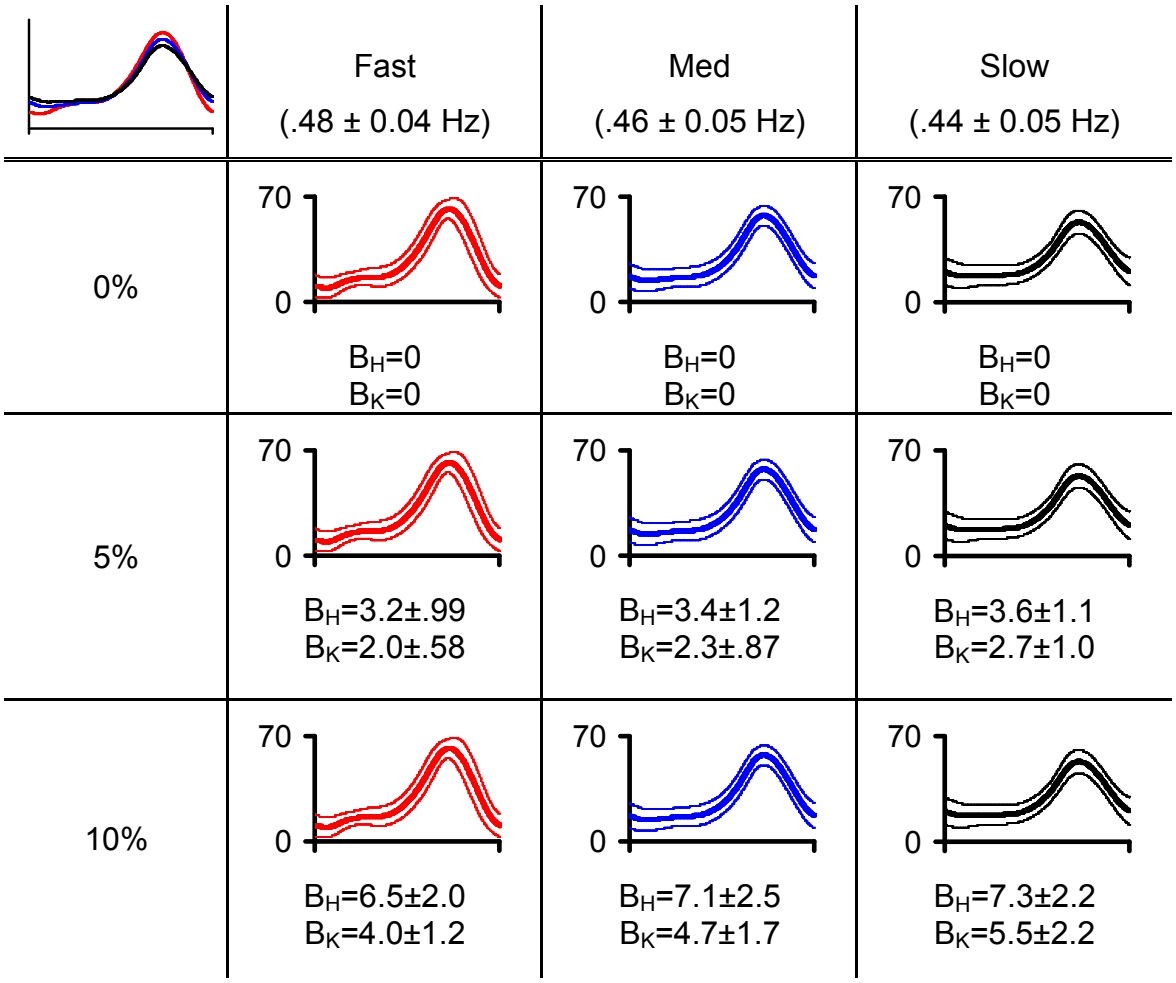

Figure 1: Experimental Conditions
Nine experimental conditions each one is a combination of resistance (0%, 5% and 10%) and knee pattern (fast (red), medium (blue) and slow (black)). Stride frequencies (Hz) corresponding to the three knee patterns are listed. Biofeedback trace given for each condition shows knee angle ± 1 standard deviation for a stride. B values (Nm·sec/rad) for each condition to apply the velocity dependent resistance to the hip (H) and knee (K) are also listed.

Data analysis

FSR signals were used to indicate periods of stance (foot contact) and swing (no foot contact). One step cycle was determined as the time between consecutive foot contacts and the stride frequency was determined by the number of step cycles per second. EMG and kinematic data were full-wave rectified and filtered (low pass filter cut off frequencies were 100Hz for EMG and 6Hz for kinematics). EMG and kinematic data were then averaged and normalized in time to 100% of the step cycle. Only steps that matched the kinematic trajectory of the biofeedback trace for that condition were included in the analysis. In order to determine these 'matched' steps, the subject had to maintain the trajectory of their knee angle within the one standard deviation for 80% of the time between toe-off (TO) and the maximum knee joint flexion angle during swing.

Kinematic data were quantified by measuring the peak extension or flexion angle of the hip, knee, and ankle joints during the swing phase in each of the 9 trials. Hip and knee joint angular velocity was quantified by measuring the peak value of hip or knee flexion and extension velocity. Torque applied to the hip or knee was quantified by calculating the peak value corresponding to hip flexion or knee flexion torque during the swing phase for each of the 9 trials.

For comparisons between subjects, EMG data were normalized to the peak value obtained from the 0% resistance and fast knee pattern condition. EMG activity was then quantified by taking the root mean square (rms) of the filtered and rectified EMG activity within a specified window of interest in each of the 9 trials for each muscle. Windows of interest were determined visually and are similar to times where changes in the locomotor patterns occur as reported by Lam et al. (2006). Quadriceps and ankle flexor activity was quantified during the stance phase lasting from 0% to 60% of the gait cycle and during the swing phase lasting from 60% to 100% of the gait cycle. Hamstrings activity was

quantified during windows corresponding to areas where muscle activity was seen to change. Hamstrings data were quantified between 0% to 50% of the gait cycle representing early and mid stance phase, between 50% to 70% of the gait cycle representing end stance and pre-swing phase, and between 70% to 100% of the gait cycle representing mid to end swing phase. The same windows of quantification were used for each participant.

Using the known joint angles during the flexion and extension movements, the muscle-tendon lengths of the RF, VM, VL, MH and BF were estimated using previously established models (Hawkins and Hull, 1990). These data were then differentiated to approximate the rate of change of length of these muscles. Muscle-tendon lengths and the rate of change of muscle lengths were quantified by determining the maximum length or velocity accompanying knee flexion or extension.

Statistics

Repeated measures analysis of variance (ANOVA) were used to determine the main and interaction effects of resistance and knee pattern on maximum hip, knee, and ankle joint angles, maximum hip or knee torque, EMG rms values, stride frequencies, and the maximum muscle-tendon lengths and muscle-tendon length velocities (SPSS 11.0, SPSS, Chicago, IL). For all statistical evaluations, the level of significance was set to an alpha value of .05. The F statistic and P-values for main effects are reported. For post hoc comparisons of each main effect, a Bonferroni adjustment was used to correct for the 3 possible contrasts setting the new adjusted alpha value to .017. P-values for post hoc comparisons are reported as the adjusted value, significance is set at $p<0.05$.

RESULTS

Values and corresponding standard errors of each of the graphed dependent variables can be found in the Appendix.

Effects of biofeedback

The use of the biofeedback successfully allowed us to manipulate knee joint kinematics and stride frequency independently during each of the 9 experimental trials. The auditory cues provided helped subjects maintain stride frequencies of 0.46 Hz (SD 0.04 Hz), 0.44 Hz (SD 0.04 Hz), and 0.43 Hz (SD 0.05 Hz) for the fast, medium and slow knee pattern conditions, respectively. There was a significant main effect of knee pattern on stride frequency ($F_{(2,38)}$=8.65, p=0.001) where stride frequency was different across the knee pattern conditions regardless of the level of resistance. Knee joint kinematics were also constrained with the biofeedback between the three different knee pattern conditions. Maximum swing phase knee angle reached 63.7° (SD 0.31°) in the fast knee pattern condition, 57.4° (SD 0.75°) in the medium knee pattern condition and 53.5° (SD 0.56°) in the slow knee pattern condition. There were significant differences between all three knee pattern conditions; results reported below.

Kinematics

Figure 2 shows the average hip (Fig. 2A), knee (Fig. 2B), and ankle angle (Fig. 2C) for a stride. There was a main effect on peak hip extension across the 3 levels of resistance ($F_{(1.24,23.58)}$=7.896, p=0.007, Fig. 2D). Post hoc tests revealed a significant increase in extension between the 0 and 10% conditions (p=0.022). Peak hip flexion during the swing phase was also significantly affected by both resistance ($F_{(1.44,27.34)}$=40.933, p=0.000) and knee pattern ($F_{(2,38)}$=22.623, p=0.000) (Fig. 2G). Peak hip flexion increased with increasing resistance

(between 0 and 10% (p=0.000), 0 and 5% (p=0.000), and 5 and 10% (p=0.000)) and decreased in the slow (p=0.000) or medium (p=0.000) compared to the fast knee pattern conditions.

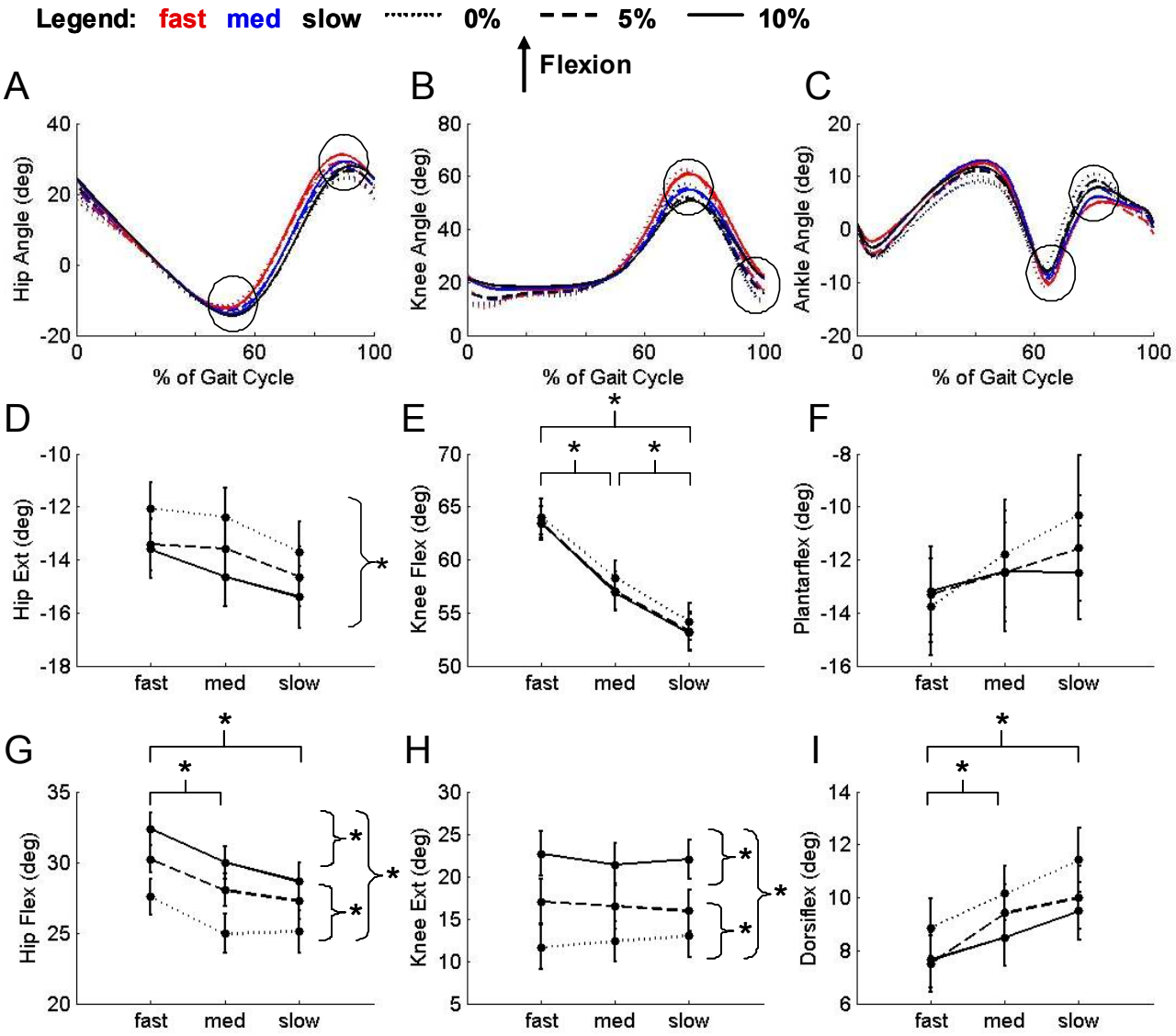

Figure 2: Kinematics
Sagittal plane kinematics for hip, knee and ankle joint angle for a stride averaged across all subjects. Each line color represents a different knee pattern condition. Each line style represents a different resistance conditions. Line plots in the middle and bottom panels show data quantified in each black circle (max ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

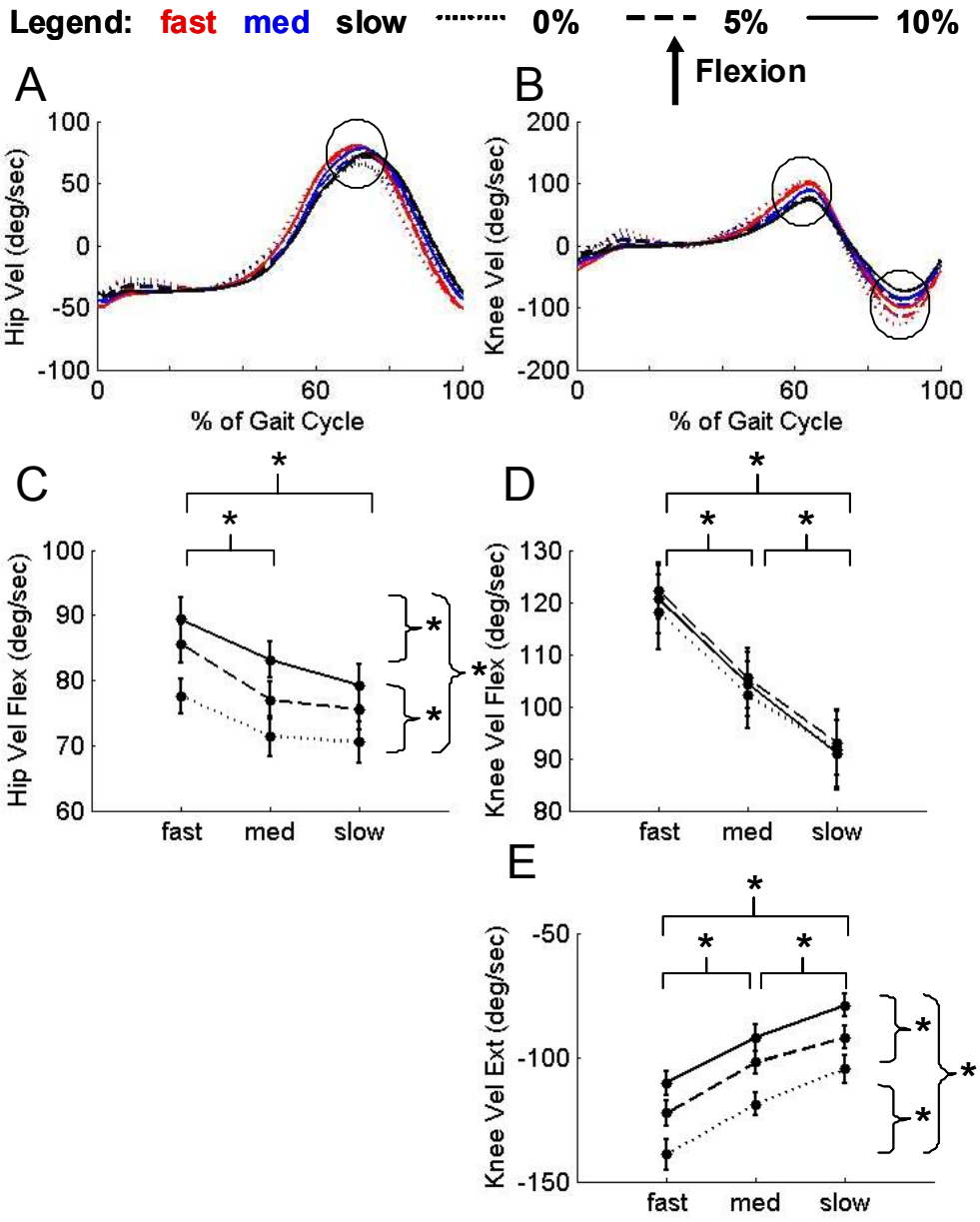

Figure 3: Angular Velocity
Sagittal plane hip and knee angular velocity for a stride averaged across all subjects. Each line color represents a different knee pattern condition. Each line style represents a different resistance conditions. Line plots in the middle and bottom panels show data quantified in each black circle (max ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

Peak knee flexion changed with knee pattern regardless of the level of applied resistance ($F_{(2,38)}$=63.03, p=0.000) (Fig. 2E). There was a significant difference in peak knee flexion across all knee pattern conditions (between fast and slow p=0.000, fast and medium p=0.000, and medium and slow p=.000). Peak knee extension increased as resistance increased ($F_{(1.23,23.31)}$=52.38, p=0.000) (Fig. 2H). Post hoc tests reveal a difference across all three levels of resistance: between 0 and 10% (p=0.000), 0 and 5% (p=0.001), and 5 and 10% (p=0.000).

Peak ankle dorsiflexion angle was significantly affected by knee pattern ($F_{(1.45, 24.65)}$=11.62, p=0.011) (Fig. 2I). Peak ankle dorsiflexion angle was greatest in the slow knee pattern compared to the fast knee pattern condition (p=0.004) and in the medium compared to the fast knee pattern condition (p=0.022). There was no significant effect on ankle plantarflexion angle across the 9 trials (Fig. 2F).

Figure 3 shows the sagittal plane hip (Fig. 3A), and knee (Fig. 3A), angular velocity for a stride. Peak hip flexion velocity changed with resistance ($F_{(1.28, 24.35)}$=21.03, p=.000) and knee pattern ($F_{(1.48,28.05)}$=11.03, p=.001) (Fig. 3C). Hip flexion velocity was different between all resistance conditions and decreased between the fast to slow (p=.006) and between the fast to medium (p=.006) condition. Peak swing phase knee flexion velocity was statistically different between all knee pattern conditions ($F_{(2,38)}$=30.09, p=.000) (Fig. 3D). Knee velocity was greatest in the fast knee pattern condition compared to the medium (p=0.000) and slow knee pattern conditions (p=0.000). Knee velocity was also greater in the medium compared to the slow knee pattern condition (p=0.004). Peak swing phase knee extension velocity decreased with increasing resistance ($F_{(1.26, 23.99)}$=38.70, p=.000) and knee pattern condition ($F_{(2,38)}$=44.67, p=.000) (Fig. 3E). Extension velocity was greatest with 0% resistance compared to and 10% (p=0.000) and 5% (p=0.001), and was greater with 5% compared to 10%

(p=0.000). Extension velocity was also greatest in the fast knee pattern condition compared to the slow (p=0.000) and medium (p=0.000) conditions, and greater in the medium condition compared to the slow (p=0.000) knee pattern condition.

Torque

Figure 4 shows the average sagittal plane hip torque (Fig. 4A) and knee torque (Fig. 4B) applied by the Lokomat across a stride. The maximum torque experienced by the hip and knee during the swing phase was conserved across changes in knee pattern. Peak hip and knee flexor torque during swing increased as resistance increased ($F_{(1.07,20.29)}$=196.41, p=0.000 and $F_{(1.06,20.19)}$=177.27, p=0.000, for the hip and knee, respectively) (Fig. 4C & D). There was no significant main effect of knee pattern on peak hip or knee flexor torque.

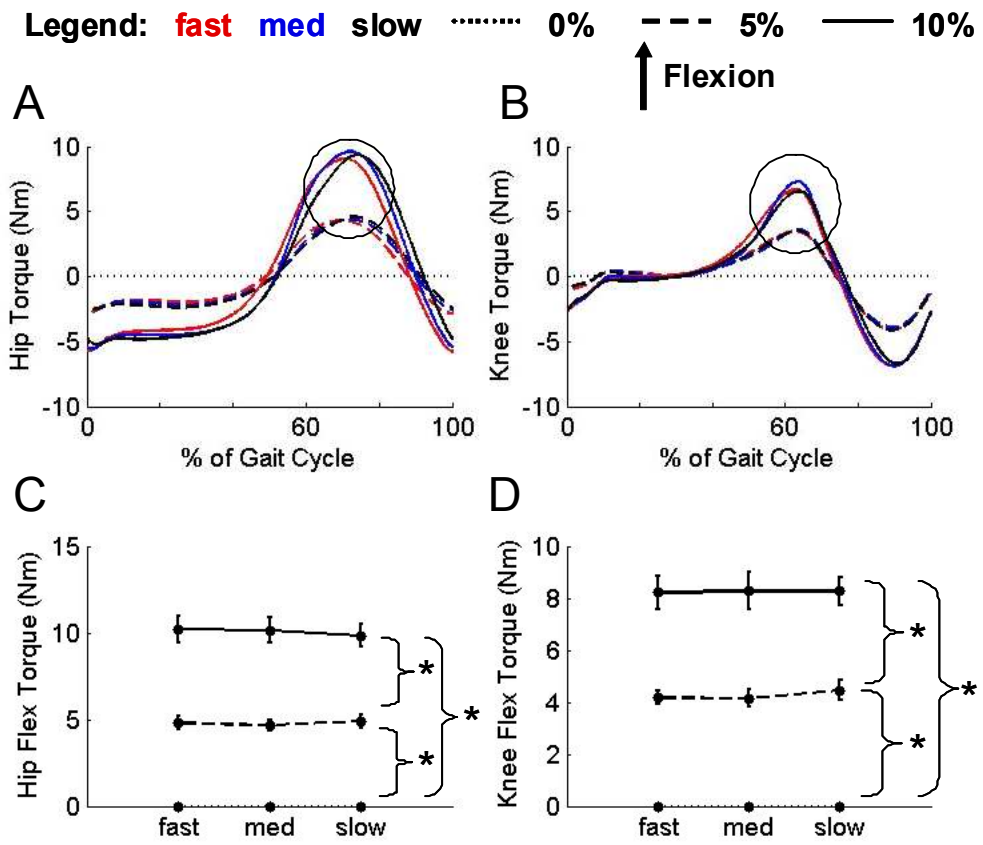

Figure 4: Torque
Sagittal plane hip and knee torque applied by the Lokomat for a stride averaged across all subjects. Each line color represents a different knee pattern condition. Each line style represents a different resistance conditions. Line plots show data quantified in each black circle (max ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance.

EMG

Quadriceps response

Muscle activity for the RF, VM and VL averaged across all subjects for each condition is shown in Figure 5 (Fig. 5A-C). During the swing phase, quadriceps activity is affected by both resistance and knee pattern. RF activity increased with increasing resistance ($F_{(1.17,22.21)}$=20.08, p=0.000). RF activity also increased in the medium and slow compared to the fast knee pattern condition ($F_{(2,38)}$=6.62, p=0.003) (Fig. 5D). Post hoc tests revealed differences between 0 and 10% (p=0.001), 0 and 5% (p=0.001), and 5 and 10% resistance (p=0.037). Significant differences in RF activity were also found between the fast and medium (p=0.026) and fast and slow knee pattern conditions (p=0.015). VM activity also changed with resistance ($F_{(1.13,21.49)}$=9.416, p=0.004) and knee pattern ($F_{(1.53,29.02)}$=3.708, p=0.048) (Fig. 5E). Post hoc tests revealed an increase in activity between 0 and 10% resistance (p=0.014) and 5 and 10% resistance (p=0.024) as well as between the slow and fast knee pattern conditions (p=0.046). There were no significant main or interaction effects of either resistance or knee pattern in the VL (Fig. 5F). Effect sizes of main effects on quadriceps activity are reported in Table 1.

Estimated quadriceps muscle-tendon lengths and velocities are shown in Figure 6. RF length was affected by resistance ($F_{(1.55,29.51)}$=33.31, p=0.000) and knee pattern ($F_{(1.213,23.05)}$=30.98, p=0.000) (Fig. 6A & G). Post hoc tests revealed a decrease in length across all levels of resistance (decreased between 0 and 10% p=0.000, 0 and 5% p=0.001, and 5 and 10% p=0.001) and all three knee patterns (decreased between fast and slow p=0.000, fast and medium p=0.001, and medium and slow p=.000). VM length was affected by resistance ($F_{(2,38)}$=4.19, p=0.023) and knee pattern ($F_{(1.34,25.36)}$=43.99, p=0.000) (Fig. 6B & H). Post hoc tests revealed a decrease between 0 and 10% resistance (p=0.020) and all three knee patterns (decreased between fast and slow p=0.001, fast and medium p=0.000, and medium and slow p=0.000). VL length was affected by

resistance ($F_{(2,38)}$=4.16, p=0.023) and knee pattern ($F_{(1.23,25.27)}$=43.25, p=0.000) (Fig. 6C & I). Post hoc tests revealed a decrease between 0 and 10% resistance (p=0.021) and all three knee patterns (decreased between fast and slow p=0.000, fast and medium p=0.000, and medium and slow p=0.000).

Main effects due to both resistance and knee pattern were found for peak shortening and lengthening velocities of the quadriceps muscles. Peak lengthening velocity was affected by resistance (RF: $F_{(1.44,27.29)}$=4.39, p=0.033; VM: $F_{(1.48,28.09)}$=5.49, p=0.016; VL: $F_{(1.48,28.15)}$=5.665, p=0.014) and knee pattern (RF: $F_{(2,38)}$=13.09, p=0.000; VM: $F_{(2,38)}$=16.01, p=0.001; VL: $F_{(2,38)}$=15.97, p=0.000) (Fig.6J-L). Post hoc tests revealed statistical differences for peak lengthening velocity across levels of resistance for the RF (between 5 and 10%, p=0.033), VM (between 0 and 5%, p=0.037) and VL (between 0 and 5%, p=0.035). For the effect of knee pattern on RF, a decrease in lengthening velocity was found between the fast and medium knee pattern conditions (p=0.016) and fast and slow knee pattern conditions (p=0.001). For the VM and VL, post hoc differences were found between all knee pattern conditions (VM lengthening decreased between fast and slow p=0.000, fast and medium p=0.016, and medium and slow p=0.016; VL lengthening decreased between fast and slow p=0.000, fast and medium p=0.000, and medium and slow p=0.000).

Quadriceps shortening velocity were affected by resistance (RF: $F_{(1.28,24.36)}$=40.01, p=0.000; VM: $F_{(1.20,22.75)}$=45.13, p=0.000; VL: $F_{(1.20,22.71)}$=45.34, p=0.000) and knee pattern (RF: $F_{(1.30,24.61)}$=11.00, p=0.001; VM: $F_{(2,38)}$=25.45, p=0.000; VL: $F_{(2,38)}$=25.09, p=0.000) (Fig. 6M-O). Post hoc tests revealed a decrease in shortening between all levels of resistance (RF shortening decreased between 0 and 10% p=0.000, 0 and 5% p=0.000, and 5 and 10% p=0.001; VM shortening decreased between 0 and 10% p=0.000, 0 and 5% p=0.000, and 5 and 10% p=0.000; VL shortening decreased between 0 and 10% p=0.000, 0 and 5% p=0.000, and 5 and 10% p=0.000). For the effect of knee pattern in the RF, a significant decrease was found between the fast and slow

(p=0.003) and medium and slow knee pattern conditions (p=0.000). For the VM and VL, post hoc differences were found between all knee pattern conditions (VM shortening velocity decreased between fast and slow p=0.000, fast and medium p=0.008, and medium and slow p=0.001; VL shortening velocity decreased between fast and slow p=0.000, fast and medium p=0.008, and medium and slow p=0.001).

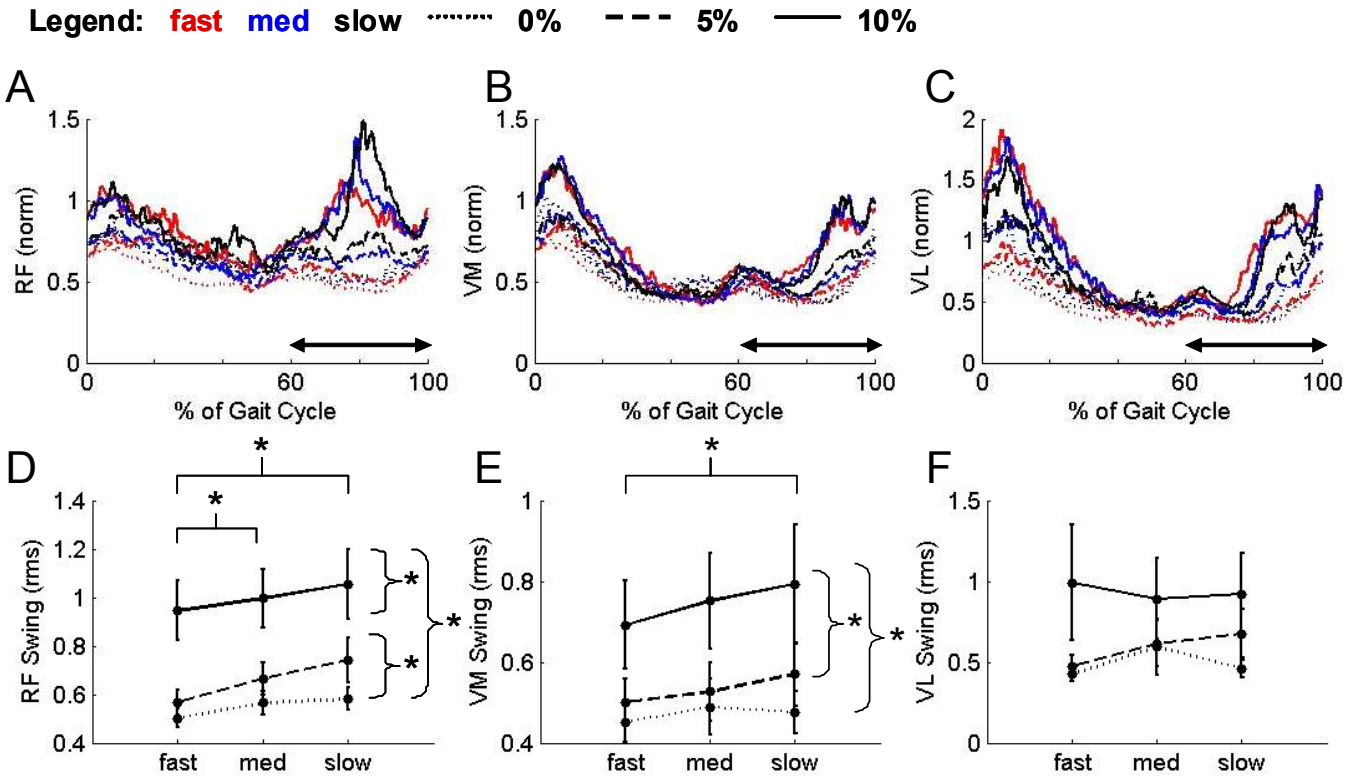

Figure 5: Quadriceps EMG
Quadriceps (rectus femoris RF; vastus medialis VM; vastus lateralis VL) muscle activity for a stride averaged across all subjects. Each line color represents a different knee pattern condition. Each line style represents a different resistance conditions. Line plots show data quantified within the period of the gait cycle indicated by the horizontal arrow (mean rms ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

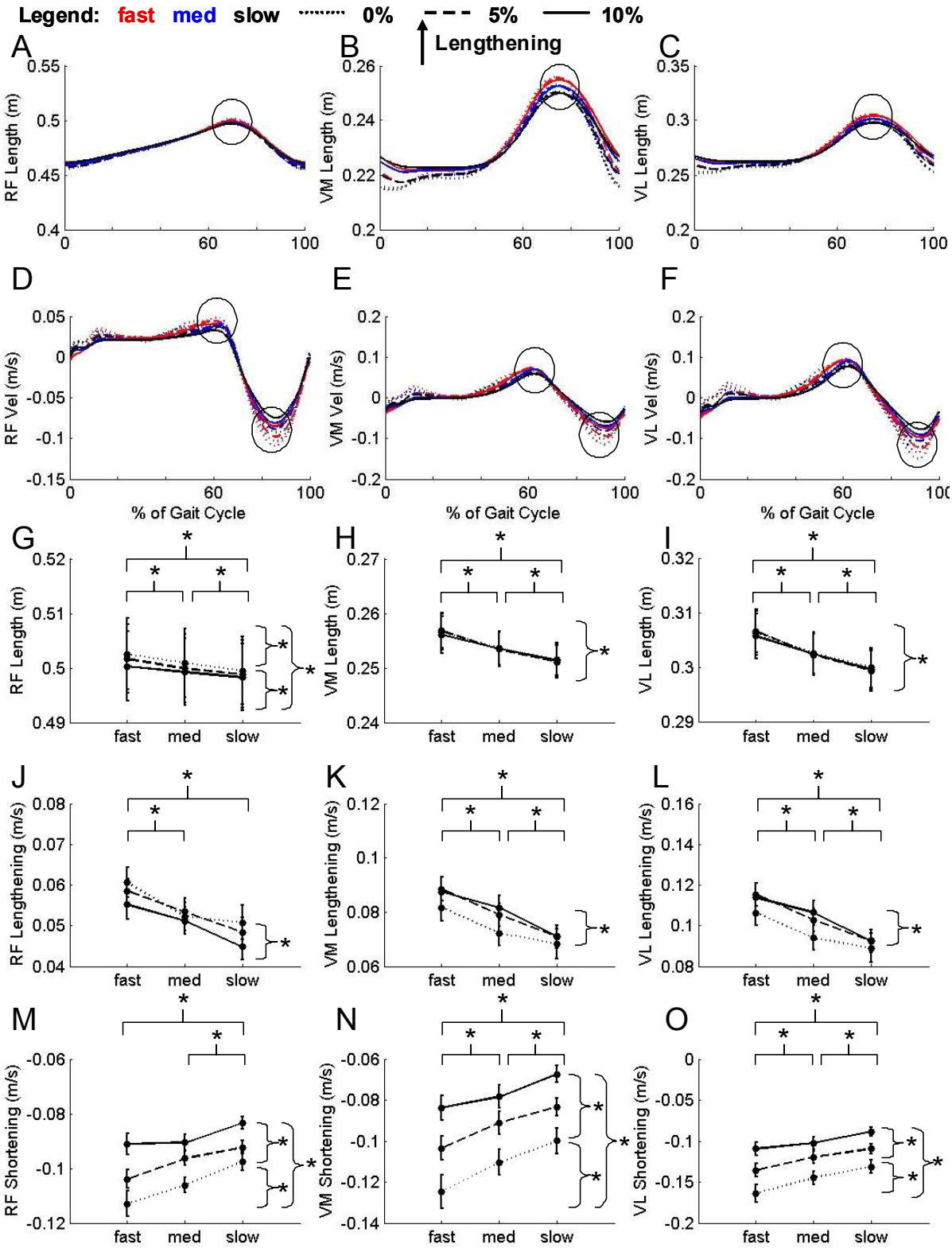

Figure 6: Quadriceps Length

Quadriceps (rectus femoris RF; vastus medialis VM; vastus lateralis VL) muscle tendon length and velocity for a stride averaged across all subjects. Each line color represents a different knee pattern condition. Each line style represents a different resistance conditions. Line plots show data quantified in each black circle (max ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

Hamstrings response

Muscle activity for the MH and BF averaged across all subjects for each condition is shown in Figure 7. Early stance phase hamstrings activity increased with increasing resistance (MH: $F_{(1.39,26.36)}$=6.19, p=0.012; BF: $F_{(1.081,20.54)}$=6.46, p=0.017) (Fig. 7C & D). Post hoc tests revealed a difference between 0 and 10% for MH (p=0.040) and between 0 and 10% (p=0.048) and 0 and 5% (p=0.014) for the BF. End stance phase hamstrings activity also increased with increasing resistance (MH: $F_{(2,38)}$=15.07, p=0.000; BF: $F_{(1.47,27.89)}$=4.96, p=0.022) (Fig. 7E & F). Post hoc tests revealed a difference between the 0 and 10% conditions (MH p=0.000; BF p=0.033) and 5 and 10% conditions (MH p=0.002; BF p=0.050). End swing phase hamstrings activity increased between the slow and fast knee pattern conditions (MH: $F_{(2,38)}$=6.82, p=0.003; BF: $F_{(2,38)}$=3.69, p=0.034) (Fig. 7G & H). Post hoc tests revealed an increase in activity in the fast vs. slow knee pattern condition for the MH (p=0.008) and BF (p=0.004). Effect sizes of main effects on hamstrings activity are reported in Table 1.

Estimated hamstrings muscle-tendon lengths and velocities are shown in Figure 8 (Fig. 8 A-D). Peak length at end swing decreased with increasing resistance for the MH ($F_{(1.29,24.53)}$=26.801, p=0.000) and for the BF ($F_{(1.36,25.79)}$=13.47, p=0.000) (Fig. 8E & F). Post hoc tests revealed a difference between the 0 and 10% conditions (MH: p=0.000; BF: p=0.002) and 5 and 10% conditions (MH: p=0.000; BF: p=0.000).

Main effects of resistance ($F_{(1.29,24.55)}$=38.016, p=0.000) and knee pattern ($F_{(1.27,24.15)}$=7.61, p=0.007) were found for lengthening velocities of the MH (Fig. 8G). Post hoc tests revealed a slower lengthening velocity between all resistance conditions (decreased between 0 and 10% p=0.000, 0 and 5% p=0.000, and 5 and 10% p=0.002) and decreased between the fast vs. slow knee pattern conditions (p=0.015) and medium vs. slow knee pattern conditions (p=0.000). For the BF, there was a main effect of resistance ($F_{(1.32,25.00)}$=25.417, p=0.000) (Fig.

8H). Post hoc tests revealed a decrease in lengthening velocity between the 0 and 10% conditions (p=0.000) and 5 and 10% conditions (p=0.000).

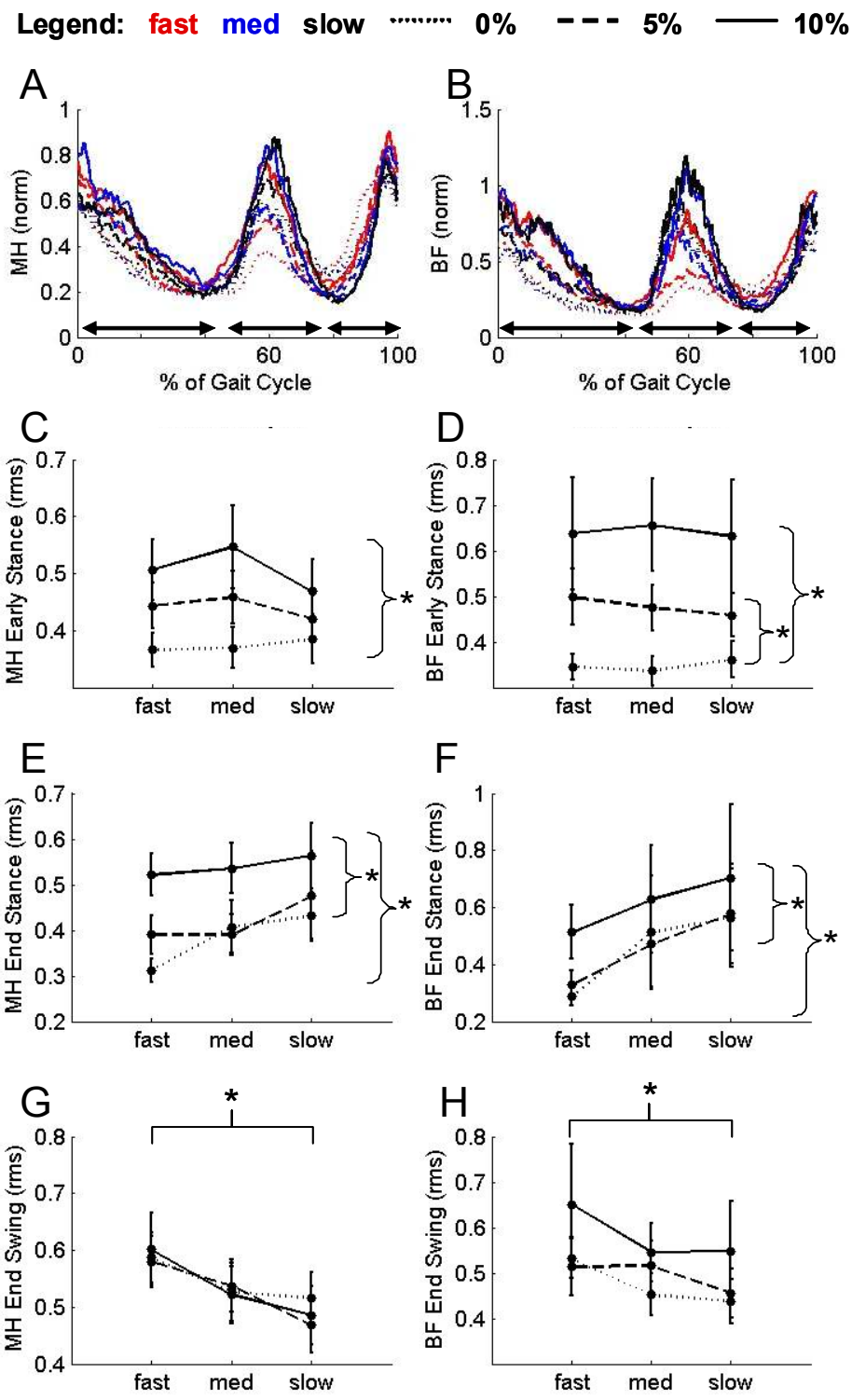

Figure 7: Hamstrings EMG

Hamstrings (medial hamstring MH; biceps femoris BF) muscle activity for a stride averaged across all subjects. Each line color represents a different knee pattern condition indicated by the legend. Each line style represents a different resistance conditions indicated by the legend. Line plots show data quantified within each arrow (rms ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

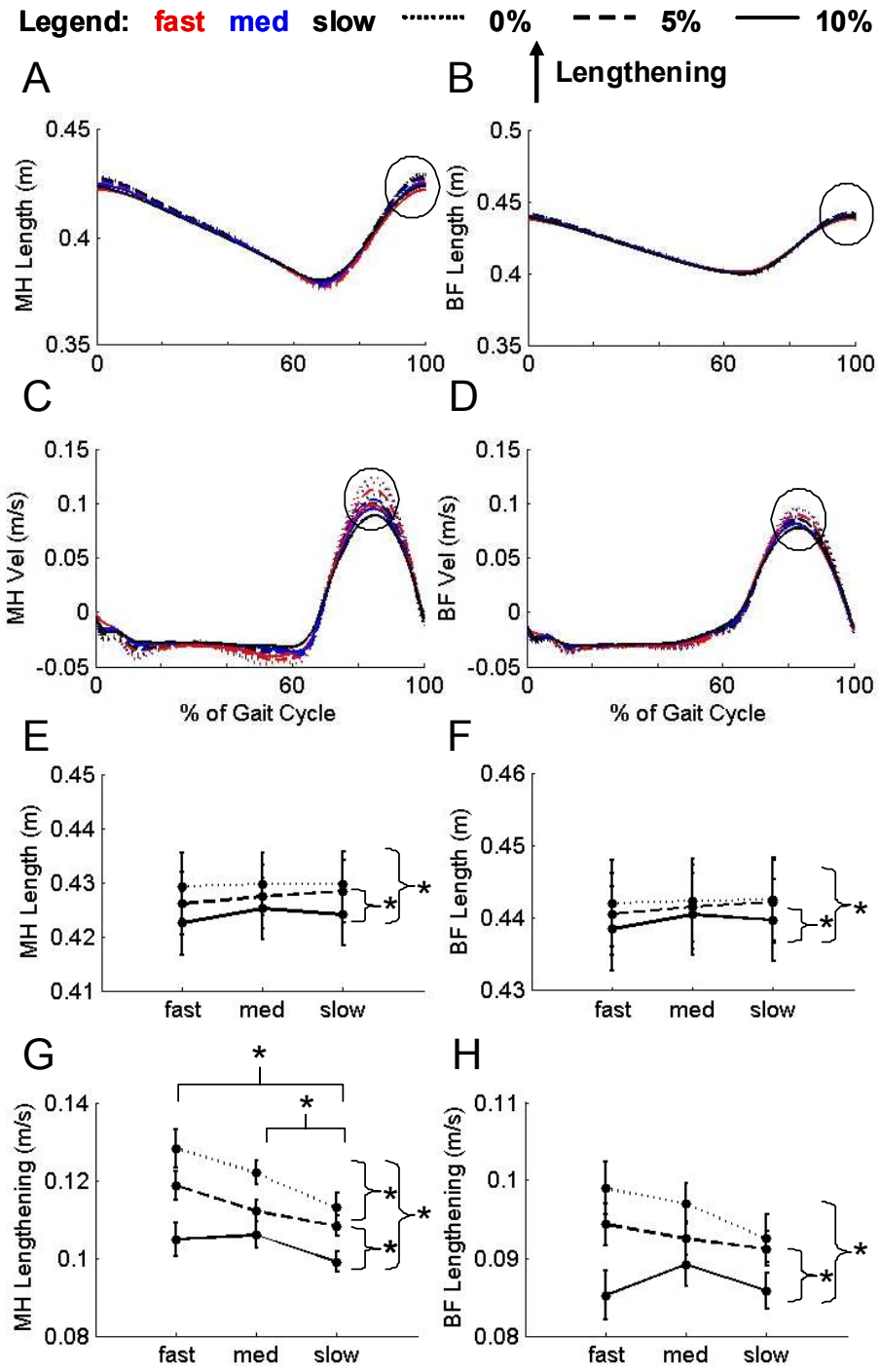

Figure 8: Hamstrings Length

Hamstrings (medial hamstring MH; biceps femoris BF) muscle tendon length and velocity for a stride averaged across all subjects. Each line color represents a different knee pattern condition indicated by the legend. Each line style represents a different resistance conditions indicated by the legend. Line plots show data quantified in each black circle (max ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

Ankle muscle response

Muscle activity for the MG and TA averaged across all subjects for each condition is shown in Figure 9. End stance phase activity of the MG increased as resistance increased ($F_{(1.30,23.34)}$=7.16, p=0.009) (Fig. 9C). Post hoc tests revealed a difference between the 0 and 10% conditions (p=0.031) and between the 5 and 10% conditions (p=0.002). Swing phase activity of the TA increased between knee pattern conditions ($F_{(1.41,26.62)}$=7.614, p=0.006) (Fig. 9D). Post hoc tests revealed an increase between fast and slow knee pattern conditions (p=0.016). Effect sizes of main effects on ankle muscles activity are reported in Table 1.

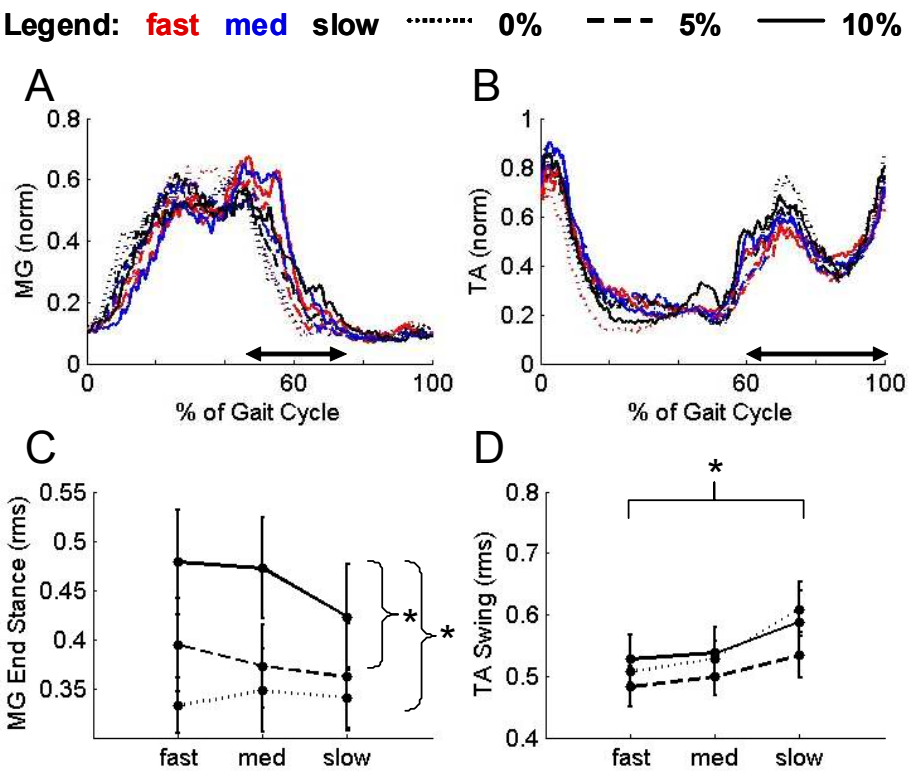

Figure 9: Ankle Muscle EMG
Ankle (medial gastrocnemius MG; tibialis anterior TA) muscle activity for a stride averaged across all subjects. Each line color represents a different knee pattern condition indicated by the legend. Each line style represents a different resistance conditions indicated by the legend. Line plots show data quantified within each arrow (rms ± s.e.m.). Curly brackets with asterisks show significant main effects of resistance and straight brackets with asterisks show significant main effects of knee pattern.

Table 1: Effect Size

	Resistance	Knee Pattern
Quadriceps		
RF - swing	0.514	0.258
VM - swing	0.331	0.163
VL - swing	-	-
Hamstrings		
MH - stance	0.246	-
MH - end stance	0.442	-
MH- swing	-	0.264
BF - stance	0.254	-
BF- end stance	0.207	-
BF- swing	-	0.163
Ankle Muscles		
MG - end stance	0.285	-
TA - swing	-	0.286

DISCUSSION

In this study we have shown that both changes in resistance and knee pattern can independently modulate muscle activity. Changes in resistance were applied with the Lokomat, a robotic gait device, and changes in knee pattern were facilitated with the use of online biofeedback. Increasing the torque applied to the joints or walking with a slow knee pattern both contribute independently to swing phase quadriceps activity. In the hamstrings, resistance and knee pattern also contribute to ongoing activity, but during different phases of the gait cycle. The muscles surrounding the ankle joint are also modulated by the two manipulations. The functional and neurological relevance of these results are discussed.

Locomotor adaptations to resistance and knee pattern

The results here show that increased resistance applied to the legs causes an increase in muscle activity. These results confirm earlier findings that adding weight to the legs of decerebrate cats, (Lam and Pearson, 2001), neurologically intact people, (Garrett and Luckwill, 1983, Stephens and Yang, 1999, Lam et al., 2003, Lam et al., 2006) and those with spinal cord injury (Lam et al., 2008) causes increased muscle activity. These results have been attributed to an increase in hip flexor load signaled by quadriceps load afferents (Garrett and Luckwill, 1983). It has also been suggested that these results could also arise from changes in lower limb kinematics associated with resistance perturbations; however no study has systematically tested this hypothesis.

Indeed, it is shown here that different knee patterns, corresponding to the natural changes in kinematics accompanying resistance, are also capable of modulating ongoing muscle activity. When participants adopt the slow pattern, with the help of biofeedback, these changes in kinematics are enough to independently increase swing phase quadriceps activity regardless of the amount

of added resistance. Therefore the muscle activity associated with swing phase force perturbations arise, in part, from the changes in kinematics due to resistance.

Hip and ankle kinematics, as well as knee joint kinematics, were affected by the resistance and knee pattern perturbations. Increased hip flexion due to the increase in resistance could be part of a compensatory mechanism to cope with the decrease in knee flexion. This strategy would be appropriate to ensure the foot clears the ground. The effect of the knee pattern perturbation on hip and ankle flexion could be due to the differences in stride frequency across knee pattern conditions. Consistent with this is the finding that dorsiflexion increases and hip flexion decreases as walking cadence decreases (Winter, 1991). This is the same as the findings reported here.

The findings that both resistance and knee pattern perturbations independently contribute to swing phase quadriceps activity supports the initial hypothesis. Both of these manipulations enhance ongoing quadriceps activity. The relative contribution of these two manipulations was also evaluated by comparing the effect size of each significant main effect. For the quadriceps muscles, the main effect size for resistance was higher compared to the main effect size for knee pattern. This suggests a stronger contribution from the resistance manipulation to quadriceps activity compared to the contribution from the knee pattern manipulation.

The effects of resistance and knee pattern manipulations on hamstrings muscle activity have confirmed and extended previous studies that examined these manipulations during walking. Hamstrings activity during the early stance phase is enhanced as resistance increased. Torque applied during this phase is similar to adding weight to the body since resistance acts on hip extension and knee flexion. Adding load to the body's center of mass with a removable weight was shown to increase extensor amplitude in humans (Stephens and Yang,

1999). Conversely removing load, with body weight supported walking, causes a reduction in burst amplitude of the muscles that are active during stance (Finch et al., 1991). These findings, as well as the ones reported here, support the notion that resistance perturbations enhance extensor activity during the stance phase, presumably to provide increased support to the body (Stephens and Yang, 1999).

The manipulation of increasing resistance in this investigation also caused an increase in hamstrings activity during end-stance. Functionally, activation of the hamstrings at the end of stance, during the preparatory period before swing phase, is appropriate to assist with knee flexion to cope with resistance (Lam et al., 2006). A similar result is found in cats that step over obstacles (McFadyen et al., 1999). As for the results reported here, the amplitude of hamstrings modulation is scaled by the amount of added resistance. This is similar to the modulation of hamstrings activity as humans step over progressively taller objects (Patla and Rietdyk, 1993). The increase in hamstrings activity due to resistance could have also accounted for the increase in hip extension at the end of the stance phase.

Hamstrings muscle activity, quantified at the end of the swing phase, was significantly affected by the knee pattern perturbation. Hamstrings activity increased in the fast knee pattern condition compared to the slow knee pattern condition. The fast knee pattern condition is associated with a faster stride frequency translating to increased angular velocity. It is therefore appropriate for hamstrings activity to be increased in the fast knee pattern condition, compared to the slow condition, due to the increase in speed. This is consistent with the notion that the hamstrings at the end of swing are reflexively activated. This is supported by the finding that in fictive cat preparations (deafferented and spinalized), activity of the hamstrings at end swing is often small or absent (Grillner and Zangger, 1984, Pearson and Rossignol, 1991, Smith et al., 1993). This suggests a potential role of afferent feedback in producing muscle activity as

part of the motor pattern for walking. Furthermore, tendon taps, eliciting stretch reflex activity, vary as a function of the step cycle and are highest at end swing (Crommert, 1996, Faist et al., 1999). This suggests a possible facilitation in the stretch reflex pathway during the swing phase of the gait cycle to produce biceps femoris activation to help decelerate the leg.

The perturbations of resistance and knee pattern affect the muscles surrounding the ankle joint. In the case of the ankle flexors, walking in the slow knee pattern condition caused an increase in TA activity associated with an increase in ankle dorsiflexion. This could be a part of a compensatory mechanism where a decrease in hip and knee flexion during the swing phase yields an increase in ankle dorsiflexion to ensure foot clearance and heel contact. Considering the importance of successful heel contact, this strategy could be mediated by descending commands from brain centers. It has been shown that descending tracts from the motor cortex are closely linked with the tibialis anterior, but more so during the stance phase (Capaday et al., 1999). Direct involvement of the motor cortex in the control of ankle muscles during walking has been demonstrated by transcranial magnetic stimulation (TMS) (Petersen et al., 2001). Following TMS where corticospinal contributions were 'knocked out' using low intensity, sub-threshold stimulation of the motor cortex, suppression of EMG activity was seen. Recordings from the tibialis anterior and soleus during walking revealed a decrease in activity following motor cortex 'knock out' with TMS highlighting the role of descending inputs in ankle flexor activity. Furthermore, spinal cord injured patients display a loss of descending inputs to ankle dorsiflexors causing foot drop (Barthelemy et al., 2010). Subjects who displayed a large degree of foot drop had decreased MEPs recorded from the TA at rest. This suggests that descending inputs, from the corticospinal tract, are important during the swing phase to ensure the foot does not drag on the ground and is ready for the subsequent stance phase.

For the MG, added resistance enhanced end stance phase activity. Increased activity at this point, could aid propulsion of the leg into the swing phase. In an experiment where body segment energetics were simulated, the potential contribution of the plantarflexors to swing phase initiation were evaluated. At the end of stance, the gastrocnemii muscles were found to accelerate the trunk forward and deliver almost all of their energy to accelerate the leg to initiate swing (Neptune et al., 2001). The results in the present study indicate that plantarflexor activity was associated with increased resistance; therefore the increase in MG activity could be associated with a strategy to cope with resistance.

A similar effect of resistance on end stance phase activity in the MG was found in the hamstrings. During this time in the gait cycle, these muscles increased in activity as resistance increased. Functionally, increased hamstrings activity results in hip extension and knee flexion. Increases in MG activity will also assist in knee flexion, as well as plantarflex the ankle. Considering both muscles were seen to respond to resistance in a similar way and both perform similar actions, a potential functional group between the MG and the hamstrings could exist. Support for this concept comes from imaging spatiotemporal activation of alpha motoneurons in the cat lumbosacral spinal cord during walking (Yakovenko et al., 2002). Recordings from hip extensors and knee and toe flexors, posterior biceps, gracilis, posterior biceps, posterior semimembranosus, semitendinosus and flexor digitorum muscles, reveal their involvement at end stance when the foot is lifted off the ground. All of these muscles, located in the most caudal part of the lumbosacral enlargement, are excited concurrently during locomotion (Yakovenko et al., 2002).

Potential contribution of afferent input

The manipulations of resistance and knee pattern modulate muscle activity. It has previously been suggested that Lokomat- induced changes in quadriceps activity are mediated by afferent reflex pathways (Lam et al., 2006), therefore the changes in muscle activity reported here could also be modulated by afferent pathways. There has been some speculation about the source changing transmission along afferent reflex pathways, although no definitive conclusions have been made. Evidence for disynaptic flexor group I afferents to flexor motoneurons comes from studies of fictive locomotion in decerebrate cats (Degtyarenko et al., 1998, Quevedo et al., 2000, Lam and Pearson, 2002). Stimulating RF nerves at group I strength, preferentially activating golgi tendon organs and muscle spindles, in decerebrate cats produced significant effects especially during mid-flexion (Frigon et al., 2010). Similarly, sartorius and iliopsoas nerve stimulation at group I strength also increased flexor activity and prolonged the flexion phase (Perreault et al., 1995, McCrea, 2000). These results confirm the importance of group I flexor afferents, golgi tendon organs and muscle spindles, from flexor muscles in enhancing flexor activity.

Lokomat applied resistance adds a velocity dependent torque to the hip and knee joints which was shown to enhance muscle activity. The changes in muscle activity could be mediated by changes in firing of load sensitive afferents arising from golgi tendon organs. In static postures, golgi tendon reflexes are associated with a negative force feedback loop, however during locomotion, there is evidence to suggest that a switch is made to a positive force feedback action (Prochazka et al., 1997, Donelan and Pearson, 2004). In one example, investigators changed the level of body weight support provided to subjects during over ground treadmill walking. To assess the nature of the load-related sensory feedback contribution to soleus activity, sudden ankle joint dorsiflexion perturbations were induced at early and mid stance (af Klint et al., 2010). Medium latency responses, thought to be mediated by mainly group II afferents

(Schieppati and Nardone, 1997, Grey et al., 2001), were significantly modulated by changes in body weight support. Tizanidine, a drug documented to reduce group II transmission but not affect group I transmission (Jankowska et al., 1998), was used and did not produce a significant decrease in the unload response (af Klint et al., 2010). Because of these reasons, it was concluded by the authors that load- related afferent feedback contributes to the background locomotor activity during the stance phase.

During the swing phase, although no direct recordings from group Ib afferents from flexor muscles have been made, there is indirect evidence to suggest group I load afferents are involved in enhancing flexor muscle activity. Short latency reflexes following electrical excitation of motoneurons were recorded from hindlimb motoneurones with microneurography during fictive locomotion. Motoneurons innervating ankle, knee or hip flexors showed oligosynaptic excitatory potentials following stimulation at group I strength suggesting group Ib afferent contribution (Quevedo et al., 2000). These results were only apparent during locomotion and excitation was largest during the swing phase. Group I stimulation activates both golgi tendon organs and muscle spindles however. Therefore it is hard to independently associate enhancement of activity from just load-sensitive afferents.

Given the changes in lower limb kinematics, length sensitive afferents arising from muscle spindles are also hypothesized to contribute flexor muscle activity (Quevedo et al., 2000, Lam and Pearson, 2001). Direct recordings of muscle spindle activity from sartorius muscles reveal their involvement in normal locomotion in unrestrained cats (Loeb et al., 1985b). During the swing phase, spindle discharge increases, especially from the biarticular muscles. As flexor muscles shorten spindle afferents act to facilitate homonymous swing phase activity (Hiebert et al., 1996, Quevedo et al., 2000). This is further supported by the fact that stimulation of hip flexors at group I strength increased muscle amplitude and duration (Hiebert et al., 1996, Lam and Pearson, 2002). During

slow shortening contractions, compared to fast contractions, more spindles discharge in the tibialis anterior. Furthermore, if shortening contractions are opposed by an external load, even higher discharge rates are recorded (Burke et al., 1978).

Muscle spindles are sensitive to both length and rate of change of length and undergo shortening velocities proportionally to the cadence at which we walk (Winter, 1991). Muscle spindles discharge more rapidly during the dynamic phase of stretch then they do at the new length (Matthews, 1933). These findings have implications to the velocity sensory role of spindle receptors. The increase in spindle sensitivity to velocity of shortening, compared to position, could be due to the influence of gamma drive on spindle sensitivity. Dynamic gamma motoneurons innervate only bag I spindle fibers making the dynamic fiber more receptive to velocity changes (Emonet-Denand et al., 1977). Considering the spindle is sensitive to muscle fiber length, dynamic activation during slow contractions, increases to keep the spindle tight and sensitive to irregularities in movement (Burke et al., 1978). High sensitivity of muscle spindles has significant physiological relevance in the reflexive control of movement.

Limitations

The results from the knee pattern perturbation should be interpreted cautiously. This manipulation consists of two variables; one of knee angle and one of stride frequency. The knee pattern perturbation is based on the natural changes in kinematics induced by walking with resistance where walking with increased resistance caused a decrease in knee flexion (Lam et al., 2006) and a decrease in stride frequency. It has been shown that hip and knee flexion changes naturally as cadence changes (Grieve and Gear, 1966, Winter, 1991). Therefore, allowing the natural stride frequencies accompanying resistance proportionally influences changes in joint angular velocity (Winter, 1983). For

these reasons, both knee joint kinematics and stride frequency were included in the knee pattern manipulation.

In the experimental trials, subjects were only instructed to match the biofeedback traces during the initial swing phase. Thus, the degree of knee extension at the end of swing and into stance was not controlled. Further, there were also small changes in hip joint kinematics. The changes in EMG activity were consistent with what is known about sensory modulation of muscle activity during walking. However, EMG changes occurring during the end of swing and during the stance phase, where kinematics were not controlled, cannot be fully attributed to the manipulations used.

The assumption that resistance and knee pattern manipulations influenced sensory afferent output should be taken cautiously because there was no direct measure of actual golgi tendon organ or muscle spindle activity. For golgi tendon organs, implanted force transducers in the muscle tendon would be required to confirm this theory. However, it has been shown that golgi tendon organs increase their response to actively generated forces compared to passive stretch (Eccles et al., 1957). Resistance applied by the Lokomat imposes a load which requires active generation of muscle force to overcome therefore it could be possible that load afferents mediate muscle responses to resistance. Load on a single muscle fiber of around 30-90 millinewtons can activate golgi tendon organs (Stuart et al., 1970, Binder et al., 1977). The resistance perturbation used here involves forces of 5-10 Nm at the hip and knee, exceeding what is required to activate single load related sensory afferents.

It is also only assumed that the knee pattern perturbation did in fact change quadriceps muscle lengths thereby affecting spindle afferents. To fully assess changes in muscle length, ultrasound imaging of quadriceps muscles should be performed to assess what actual length changes occur. Nevertheless, we estimated approximately a 1 cm change in quadriceps muscle-tendon length.

In the sartorius, small sinusoidal changes of length, up to only about 0.1 mm, is all that is required to activate primary spindle endings (Matthews and Stein, 1969). Therefore, length sensitive afferents could have potentially been affected by the knee pattern manipulation.

Other sources of input mediating changes in muscle responses to resistance and knee pattern perturbations need to also be considered. Along with group I afferent excitation, other afferent inputs and descending inputs could be responsible for the changes in muscle activity reported here. Indeed, stimulation of afferents at group II strength increased activity and duration in both extensor and flexor muscles (McCrea, 2000). Non-spindle group II afferents, flexor reflex afferents (Burke, 1999) may have also contributed to facilitating flexor burst activity. Stimulation of flexor reflex afferents during the late flexion phase causes a prolongation of that phase (Schomburg et al., 1998). Cutaneous receptors could also independently mediate changes in muscle activity considering the mechanical imposition of the Lokomat. To test this theory, the skin underlying the Lokomat cuffs could be anesthetized to estimate the contribution of cutaneous afferent feedback.

Joint receptors located at the hip or knee joint capsule could also be a possible source of afferent input. Although, joint receptors are present to provide mainly joint position information, and not joint velocity, and most joint receptors fire in a very limited way (Proske et al., 1988). Joint receptors respond mainly at the extremes of joint movement and respond mainly to joint pressure (e.g. caused by swelling) (Aloisis and Rossi, 1988, Proske et al., 1988). Joint receptor response is largely ambiguous to movement and knee ligaments need to be heavily stretched before any measurable muscle response can be detected (Rossi and Grigg, 1982). For these reasons, it is concluded that joint afferents do not substantially contribute to the muscle responses seen here.

Descending inputs are required to regulate gait and we cannot discount the influence of descending commands (Capaday et al., 1999, Bonnard et al., 2002). Although, the quadriceps response to resistance manifests immediately (Lam et al., 2006) and is therefore associated more with a reflexive strategy. The use of biofeedback could have also influenced descending inputs because subjects had to attend more closely to walking. However, only data from conditions where biofeedback was used were included in the analysis, therefore biofeedback equally affected all conditions.

CONCLUSION

In conclusion, the results of this study demonstrate that both resistance and knee pattern perturbations modulate muscle activity. Previous investigations of resistance manipulations could not account for the changes in kinematics associated with resistance. Both resistance and knee pattern enhance swing phase activity in the quadriceps muscles. Resistance may contribute more to swing phase quadriceps activity as demonstrated by a larger main effect of resistance compared to knee pattern. Information arising from both load sensitive and length sensitive afferents could be involved in mediating these responses.

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APPENDIX

Walking Characteristics

Table 2: Stride Frequency (Hz)

	fast		med		slow	
0%	0.463	± 0.010	0.449	± 0.011	0.437	± 0.013
5%	0.460	± 0.009	0.445	± 0.010	0.433	± 0.012
10%	0.460	± 0.009	0.445	± 0.010	0.435	± 0.012

Table 3: Stride Time (sec)

	fast		med		slow	
0%	2.193	± 0.046	2.261	± 0.055	2.333	± 0.070
5%	2.203	± 0.042	2.276	± 0.052	2.350	± 0.069
10%	2.203	± 0.044	2.277	± 0.054	2.341	± 0.069

Table 4: Stance Phase Duration (%)

	fast		med		slow	
0%	59.855	± 0.771	59.844	± 1.029	59.220	± 0.928
5%	59.720	± 1.017	60.435	± 0.993	59.631	± 0.995
10%	59.346	± 1.083	60.494	± 0.933	59.611	± 1.097

Kinematics

Table 5: Maximum Hip Extension (deg)

	fast		med		slow	
0%	-12.063	± 0.959	-12.390	± 1.101	-13.707	± 1.128
5%	-13.418	± 0.991	-13.582	± 1.068	-14.636	± 1.139
10%	-13.602	± 1.112	-14.656	± 1.116	-15.404	± 1.173

Table 6: Maximum Hip Flexion (deg)

	fast		med		slow	
0%	27.560	± 1.286	24.955	± 1.354	25.085	± 1.489
5%	30.220	± 0.957	28.020	± 1.148	27.248	± 1.254
10%	32.353	± 1.158	29.970	± 1.167	28.647	± 1.286

Table 7: Maximum Knee Flexion (deg)

	fast		med		slow	
0%	64.013	± 1.691	58.282	± 1.654	54.155	± 1.721
5%	63.522	± 1.480	57.065	± 1.820	53.281	± 1.780
10%	63.429	± 1.548	56.904	± 1.711	53.106	± 1.739

Table 8: Maximum Knee Extension (deg)

	fast		med		slow	
0%	11.637	± 2.651	12.322	± 2.378	12.994	± 2.605
5%	17.048	± 2.646	16.481	± 2.724	15.960	± 2.378
10%	22.676	± 2.671	21.382	± 2.503	21.990	± 2.262

Table 9: Maximum Ankle Plantarflexion (deg)

	fast		med		slow	
0%	-13.779	± 1.812	-11.779	± 2.038	-10.310	± 2.240
5%	-13.308	± 1.797	-12.475	± 1.871	-11.568	± 2.004
10%	-13.174	± 1.673	-12.432	± 2.287	-12.481	± 1.761

Table 10: Maximum Ankle Dorsiflexion (deg)

	fast		med		slow	
0%	8.860	± 1.078	10.152	± 1.033	11.424	± 1.206
5%	7.494	± 1.064	9.410	± 1.062	9.989	± 1.182
10%	7.643	± 1.059	8.493	± 1.067	9.489	± 1.088

Table 11: Maximum Hip Flexion Velocity (deg/sec)

	fast		med		slow	
0%	77.593	± 2.700	71.386	± 3.127	70.516	± 3.169
5%	85.606	± 2.915	76.975	± 2.912	75.544	± 3.171
10%	89.369	± 3.340	83.156	± 2.843	79.223	± 3.209

Table 12: Maximum Knee Flexion Velocity (deg/sec)

	fast		med		slow	
0%	118.072	± 7.084	102.159	± 6.313	91.581	± 7.488
5%	122.145	± 5.339	105.401	± 5.755	93.036	± 6.278
10%	120.594	± 6.566	104.283	± 6.229	90.886	± 6.354

Table 13: Maximum Knee Extension Velocity (deg/sec)

	fast		med		slow	
0%	-139.185	± 6.010	-118.957	± 4.621	-104.797	± 5.660
5%	-122.552	± 4.884	-102.015	± 4.460	-92.087	± 4.518
10%	-110.375	± 4.772	-92.110	± 5.461	-79.063	± 4.528

Resistance

Table 14: Hip B Value (Nm sec/rad)

	fast		med		slow	
0%	0.000	± 0.000	0.000	± 0.000	0.000	± 0.000
5%	3.224	± 0.992	3.430	± 1.250	3.594	± 1.133
10%	6.500	± 1.967	7.103	± 2.514	7.300	± 2.243

Table 15: Knee B Value (Nm sec/rad)

	fast		med		slow	
0%	0.000	± 0.000	0.000	± 0.000	0.000	± 0.000
5%	2.008	± 0.584	2.337	± 0.869	2.772	± 1.084
10%	4.035	± 1.199	4.720	± 1.720	5.540	± 2.160

Table 16: Maximum Hip Flexor Torque (Nm)

	fast		med		slow	
0%	0.000	± 0.000	0.000	± 0.000	0.000	± 0.000
5%	4.807	± 0.351	4.654	± 0.322	4.903	± 0.391
10%	10.213	± 0.775	10.142	± 0.751	9.834	± 0.651

Table 17: Maximum Knee Flexor Torque (Nm)

	fast		med		slow	
0%	0.000	± 0.000	0.000	± 0.000	0.000	± 0.000
5%	4.167	± 0.267	4.142	± 0.339	4.459	± 0.379
10%	8.214	± 0.634	8.282	± 0.717	8.271	± 0.541

EMG

Quadriceps

Table 18: RF Swing Phase (norm)

	fast		med		slow	
0%	0.502	± 0.039	0.565	± 0.050	0.580	± 0.047
5%	0.567	± 0.051	0.665	± 0.067	0.742	± 0.091
10%	0.946	± 0.126	0.995	± 0.122	1.054	± 0.142

Table 19: VM Swing Phase (norm)

	fast		med		slow	
0%	0.451	± 0.049	0.489	± 0.069	0.476	± 0.053
5%	0.500	± 0.059	0.527	± 0.072	0.569	± 0.080
10%	0.691	± 0.109	0.752	± 0.118	0.793	± 0.148

Table 20: VL Swing Phase (norm)

	fast		med		slow	
0%	0.426	± 0.048	0.594	± 0.171	0.459	± 0.055
5%	0.477	± 0.066	0.613	± 0.143	0.676	± 0.150
10%	0.992	± 0.359	0.892	± 0.252	0.921	± 0.253

Hamstrings

Table 21: MH Stance Phase (norm)

	fast		med		slow	
0%	0.366	± 0.029	0.369	± 0.036	0.385	± 0.043
5%	0.443	± 0.040	0.458	± 0.046	0.420	± 0.041
10%	0.506	± 0.053	0.547	± 0.073	0.469	± 0.055

Table 22: MH End Stance Phase (norm)

	fast		med		slow	
0%	0.312	± 0.025	0.407	± 0.058	0.431	± 0.051
5%	0.390	± 0.042	0.390	± 0.046	0.475	± 0.098
10%	0.522	± 0.045	0.536	± 0.055	0.563	± 0.072

Table 23: MH Swing Phase (norm)

	fast		med		slow	
0%	0.587	± 0.045	0.527	± 0.051	0.515	± 0.045
5%	0.580	± 0.045	0.537	± 0.047	0.468	± 0.048
10%	0.601	± 0.063	0.522	± 0.050	0.486	± 0.051

Table 24: BF Stance Phase (norm)

	fast		med		slow	
0%	0.345	± 0.028	0.336	± 0.032	0.361	± 0.040
5%	0.499	± 0.062	0.475	± 0.050	0.458	± 0.048
10%	0.637	± 0.124	0.656	± 0.101	0.631	± 0.125

Table 25: BF End Stance Phase (norm)

	fast		med		slow	
0%	0.287	± 0.033	0.512	± 0.200	0.563	± 0.174
5%	0.328	± 0.051	0.472	± 0.152	0.578	± 0.175
10%	0.513	± 0.094	0.628	± 0.190	0.703	± 0.256

Table 26: BF Swing Phase (norm)

	fast		med		slow	
0%	0.531	± 0.044	0.453	± 0.046	0.438	± 0.049
5%	0.514	± 0.064	0.516	± 0.055	0.455	± 0.055
10%	0.651	± 0.133	0.545	± 0.064	0.549	± 0.109

Ankle muscles

Table 27: MG End Stance Phase (norm)

	fast		med		slow	
0%	0.332	± 0.028	0.348	± 0.042	0.341	± 0.031
5%	0.395	± 0.047	0.373	± 0.042	0.362	± 0.054
10%	0.478	± 0.053	0.472	± 0.052	0.422	± 0.054

Table 28: TA Swing Phase (norm)

	fast		med		slow	
0%	0.507	± 0.026	0.529	± 0.028	0.609	± 0.044
5%	0.483	± 0.033	0.499	± 0.031	0.534	± 0.037
10%	0.528	± 0.039	0.538	± 0.042	0.589	± 0.051

Quadriceps muscle-tendon length and velocity

Table 29: Maximum RF Muscle-Tendon Length (m)

	fast		med		slow	
0%	0.503	± 0.007	0.501	± 0.006	0.499	± 0.006
5%	0.502	± 0.006	0.500	± 0.006	0.499	± 0.006
10%	0.500	± 0.006	0.499	± 0.006	0.498	± 0.006

Table 30: Maximum RF Velocity of Lengthening (m/sec)

	fast		med		slow	
0%	0.061	± 0.004	0.052	± 0.003	0.051	± 0.004
5%	0.059	± 0.003	0.053	± 0.003	0.048	± 0.004
10%	0.055	± 0.004	0.051	± 0.003	0.045	± 0.003

Table 31: Maximum RF Velocity of Shortening (m/sec)

	fast		med		slow	
0%	0.113	± 0.005	0.106	± 0.003	0.097	± 0.003
5%	0.104	± 0.003	0.096	± 0.003	0.092	± 0.002
10%	0.091	± 0.004	0.091	± 0.003	0.083	± 0.002

Table 32: Maximum VM Muscle-Tendon Length (m)

	fast		med		slow	
0%	0.257	± 0.003	0.254	± 0.003	0.252	± 0.003
5%	0.257	± 0.003	0.253	± 0.003	0.251	± 0.003
10%	0.256	± 0.003	0.254	± 0.003	0.251	± 0.003

Table 33: Maximum VM Velocity of Lengthening (m/sec)

	fast		med		slow	
0%	0.082	± 0.005	0.072	± 0.005	0.068	± 0.005
5%	0.089	± 0.004	0.079	± 0.004	0.071	± 0.004
10%	0.087	± 0.005	0.082	± 0.004	0.071	± 0.004

Table 34: Maximum VM Velocity of Shortening (m/sec)

	fast		med		slow	
0%	0.125	± 0.008	0.110	± 0.006	0.100	± 0.006
5%	0.104	± 0.006	0.091	± 0.006	0.083	± 0.004
10%	0.084	± 0.006	0.078	± 0.006	0.067	± 0.004

Table 35: Maximum VL Muscle-Tendon Length (m)

	fast		med		slow	
0%	0.306	± 0.004	0.303	± 0.004	0.300	± 0.004
5%	0.307	± 0.004	0.302	± 0.004	0.299	± 0.004
10%	0.306	± 0.004	0.303	± 0.004	0.300	± 0.004

Table 36: Maximum VL Velocity of Lengthening (m/sec)

	fast		med		slow	
0%	0.106	± 0.006	0.094	± 0.006	0.089	± 0.007
5%	0.115	± 0.006	0.103	± 0.006	0.092	± 0.006
10%	0.114	± 0.007	0.106	± 0.006	0.093	± 0.005

Table 37: Maximum VL Velocity of Shortening (m/sec)

	fast		med		slow	
0%	0.164	± 0.011	0.145	± 0.008	0.131	± 0.008
5%	0.136	± 0.008	0.120	± 0.007	0.109	± 0.006
10%	0.109	± 0.008	0.102	± 0.007	0.088	± 0.005

Hamstrings muscle-tendon length and velocity

Table 38: Maximum MH Muscle-Tendon Length (m)

	fast		med		slow	
0%	0.429	± 0.006	0.430	± 0.006	0.430	± 0.006
5%	0.426	± 0.006	0.427	± 0.006	0.428	± 0.006
10%	0.422	± 0.006	0.425	± 0.006	0.424	± 0.006

Table 39: Maximum MH Velocity of Lengthening (m/sec)

	fast		med		slow	
0%	0.128	± 0.005	0.122	± 0.003	0.113	± 0.004
5%	0.119	± 0.004	0.112	± 0.003	0.108	± 0.003
10%	0.105	± 0.004	0.106	± 0.003	0.099	± 0.003

Table 40: Maximum BF Muscle-Tendon Length (m)

	fast		med		slow	
0%	0.442	± 0.006	0.442	± 0.006	0.443	± 0.006
5%	0.441	± 0.006	0.442	± 0.006	0.442	± 0.006
10%	0.439	± 0.006	0.441	± 0.006	0.440	± 0.006

Table 41: Maximum BF Velocity of Lengthening (m/sec)

	fast		med		slow	
0%	0.099	± 0.003	0.097	± 0.003	0.093	± 0.003
5%	0.094	± 0.003	0.093	± 0.002	0.091	± 0.002
10%	0.085	± 0.003	0.089	± 0.003	0.086	± 0.002

UBC Ethics Board Certificates

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CERTIFICATE OF APPROVAL - AMENDMENT & RENEWAL

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC BREB NUMBER:
Tania Lam	UBC/Education/Human Kinetics	H08-01300

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
Vancouver Coastal Health (VCHRI/VCHA)	Vancouver General Hospital
UBC	Vancouver (excludes UBC Hospital)

Other locations where the research will be conducted:
Data collection for this will also take place at the Blusson Spinal Cord Centre (818 West 10th Ave).

CO-INVESTIGATOR(S):
Adina Houldin
Taryn Klarner

SPONSORING AGENCIES:
Natural Sciences and Engineering Research Council of Canada (NSERC)

PROJECT TITLE:
Generalization of internal models of the legs for walking

CERTIFICATE EXPIRY DATE: May 11, 2011

AMENDMENT(S):	RENEWAL AND AMENDMENT APPROVAL DATE: May 11, 2010	
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The application for continuing ethical review and the amendment(s) for the above-named project have been reviewed and the procedures were found to be acceptable on ethical grounds for research involving human subjects.

Approval is issued on behalf of the Behavioural Research Ethics Board and signed electronically by one of the following:

Dr. M. Judith Lynam, Chair
Dr. Ken Craig, Chair
Dr. Jim Rupert, Associate Chair
Dr. Laurie Ford, Associate Chair
Dr. Anita Ho, Associate Chair