Interlimb transfer of motor adaptations between the legs during treadmill walking

by

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ABSTRACT

Adaptations in kinematic and kinetic measurements have been demonstrated to occur in response to dynamic perturbations in the environment via feedback (e.g., reflexes) and feedforward (anticipatory) mediated mechanisms. Generalization of motor adaptations has been found to occur between the limbs, a process called interlimb transfer. Few studies have explored this phenomenon in the lower limbs and none have yet to elucidate whether the response to manipulation of the dynamic properties of one limb during a walking task will transfer to the other limb. This study aimed to determine whether locomotor adaptations to a velocity-dependent force field in one (trained) leg will transfer to the contralateral (test) leg during unipedal walking. It is expected that neuromuscular adaptations to force perturbations in the trained leg during walking will transfer to the contralateral test leg via generalization of anticipatory adaptive strategies. Twenty able-bodied, right leg dominant, adults walked unipedally in the Lokomat robotic gait orthosis, which applied velocity-dependent resistance to the legs. The amount of resistance was scaled to 10% percent of each individual's maximum voluntary contraction of the hip flexors. Electromyography and kinematics of the lower limb were recorded. All subjects were tested for transfer of motor adaptations from the right leg to the left leg. Catch trials, consisting of the unexpected removal of resistance, were presented after the first step with resistance and after a period of adaptation to determine if there were any after-effects. The time course of adaptation in hip kinematics showed no significant differences between the legs. Catch trials of the lower limb kinematics were compared within and between the legs using a 2 by 2 repeated measures ANOVA. There was a main effect for time ($p < 0.001$) and an interaction effect for time and leg ($p = 0.011$). Post-hoc tests reveal no differences in the size of the

after-effects between the legs during the catch trials. Motor adaptations to resistance against right unipedal walking did not generalize to left unipedal walking. The results of this study will add to our current understanding of the neural mechanisms that drive the basic walking pattern.

PREFACE

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To my family, your unconditional love and support are what pushed me through every challenge I faced. I am blessed with two incredible parents whose belief in me is unwavering. You both have a genuine passion for learning that taught me to enjoy the pursuit of knowledge. To my brother Evan, thank you for your insight and intelligent sense of humour and to my sister Julia, for your limitless encouragement and advice.

This was more than just a degree, it was a life experience.

To my parents

INTRODUCTION

Overview

Feedback-mediated mechanisms (reflexes) aid the central nervous system in adjusting to sensory perturbations during walking. A strong body of evidence suggests that proprioceptive input helps to initiate and drive the locomotor pattern (Conway et al. 1987; Grillner and Rossignol 1978; Hiebert and Pearson 1999). With sustained exposure to a perturbation, the nervous system will also develop feedforward anticipatory motor adaptations to efficiently respond to the impending disturbance. An internal model of limb dynamics is a proposed mechanism for this type of movement planning (Shadmehr and Mussa-Ivaldi 1994). This model is thought to be created and updated through kinematic and kinetic adjustments that accommodate movement error (Kawato 1999). The internal model then stores the updated movement plan and may use it for variations on the movement for which it was originally intended (Shadmehr and Mussa-Ivaldi 1994). This generalization of an adaptation from one task to another allows for efficiency in motor planning.

Sustained exposure to a force-field resistance against limb movement has been demonstrated to evoke anticipatory motor adaptations. For example, resistance applied to hip and knee motion during walking will increase flexor muscle activity during the swing phase of walking in cats and human infants and adults (Lam et al. 2006; Lam and Pearson 2001; Lam et al. 2003). Previous research has found that able-bodied adults will adapt to the resistance within 5 steps (Lam et al. 2006). After-effects that occur

following the unexpected removal of the resistance manifest as a high-step and reveal the possible formation of an internal model (Lam et al. 2006).

Upper limb motor tasks have shown that adaptations to a force (e.g. applied through a hand-held manipulandum) that interjects a movement trajectory will generalize to similar force perturbations in the same limb (Morton et al. 2001). It has also been demonstrated that generalizations of the same upper limb manipulandum tasks develop in the opposite limb, indicating that interlimb transfer of feedforward anticipatory adaptations has occurred (Criscimagna-Hemminger et al. 2003). To date, no studies have determined whether interlimb transfer of neuromuscular adaptations during unipedal resisted treadmill walking will occur. Given the strong interlimb coordination necessary for bipedal walking, it is therefore possible that this type of transfer may also be present in the lower limbs during walking.

Literature Review

The development of an anticipatory motor program in the presence of a novel force perturbation is described in the literature in the context of so-called 'internal models' of limb dynamics in the central nervous system (CNS) (Kawato 1999; Shadmehr and Mussa-Ivaldi 1994). This model is the basis of a motor learning concept that describes a set of issued motor commands, which are based on the physical properties of the limbs (the 'internal model'), employed to execute as well as predict movement trajectories (Kawato 1999; Shadmehr and Mussa-Ivaldi 1994). The intended motor

output is compared with the actual response and a discrepancy between the two is determined. Adaptations to fix this discrepancy develop. Internal models are therefore thought to be updated through adjustments to erroneous movement as the CNS 'learns' the new dynamics of the limb and/or movement environment. Indeed, by transiently increasing error (incorrect trajectory) during walking, movement adaptations are accelerated (Emken and Reinkensmeyer 2005). Much of the evidence for internal model formation has been demonstrated with upper limb movement tasks. Subjects are typically asked to move the hand towards various targets in the workspace using a manipulandum. In the presence of a force field perturbation delivered by the manipulandum, the trajectory will be directed off-course. After several trials, the pattern and velocity of the arm trajectory will return to the baseline straight path. These observations can be explained by the idea that an internal model was created by sensory feedback from the force field and resulted in an adapted motor plan of anticipated limb dynamics (Shadmehr and Mussa-Ivaldi 1994).

Verification of the formation of an internal model is evidenced by after-effects following the unexpected removal of the force. After-effects are characterized by a movement trajectory that is opposite to that seen during the adaptation period. In the case of the arm manipulandum task, the after-effect is the arm trajectory again directed off-course from the baseline straight path, but in the directly opposite movement pattern as the one acquired during the presence of the force field perturbation (Shadmehr and Mussa-Ivaldi 1994). The after-effect reveals that the nervous system has anticipated the presence of the force (updated its model of the movement environment) and developed

a new motor program for the required movement (Shadmehr and Mussa-Ivaldi 1994). During walking tasks, these after-effects have been shown to occur following the removal of a velocity-dependent force applied to the legs in a direction that resists forward walking and manifest as a high-stepping pattern (Lam et al. 2006). Infant studies have also demonstrated the presence of after-effects upon removal of leg weights during treadmill walking, suggesting that feedforward mechanisms are present even prior to full neural maturation (Lam et al. 2003; Pang et al. 2003).

Immediate, short-term adaptations contribute to the storage of a motor program

Internal models are thought to develop from both feedback and feedforward mediated adaptations. The nervous system uses sensory feedback to accommodate novel perturbations within the environment during walking (Pearson 2004). This type of feedback is instructive to the nervous system for generating a model of limb dynamics. Walking is a movement task that requires adaptability, efficiency and balance for navigation through the environment. The ability to adapt to or avoid obstacles, such as pebbles on the ground, is obviously advantageous for safe navigation through different environments. The nervous system uses sensory input to initiate, adapt and maintain a smooth walking pattern. There are two main types of proprioceptive sensory feedback that have been shown to drive the basic walking pattern: hip position and limb load. The position, or angle, of the hip is a robust signal for the transitions from swing-to-stance (McVea et al. 2005) and stance-swing (Grillner and Rossignol 1978). The load exerted by body weight over the limb can even prevent or prolong the period spent in stance

through the strong load sensory signals sent to the extensors (Conway et al. 1987; Duysens and Pearson 1980). These two key components of walking regulation indicate on-going changes that must be addressed by the process of adaptation. The different forms of sensory information provide essential feedback to the CNS of the overall adaptations to be corrected in the gait pattern, as well as any subtle adjustments (af Klint et al. 2008).

In able-bodied adult humans, the application of a velocity-dependent resistance against hip and knee joint motion has been shown to result in an immediate increase in the activity of the rectus femoris (RF) during the swing phase of locomotion. The RF activity remains stable for the duration of resistance, but this response disappears immediately once the resistance is removed, suggesting that feedback mechanisms are in place to respond to transient environmental perturbations (Lam et al. 2006). Consistent with cat and infant models of walking, the response to the resistance is likely mediated via feedback-mediated mechanisms (Lam and Pearson 2001; Lam et al. 2003). Lam and Pearson (2001) demonstrated the effects of sensory feedback by resisting flexor movement during the swing phase of walking in cats. With both manual resistance and a mechanical blocking device, resisted treadmill walking resulted in an increase in flexor muscle activation. It was proposed that the slowed rate of muscle shortening as a result of resistance during the swing phase led to an increase in muscle spindle and golgi tendon activation. The opposite effect was shown, i.e., a decrease in flexor amplitude, when the flexors were assisted during the swing phase. Assisting hip flexion during swing shortens the burst duration of the hip flexor muscle (IP) and this is positively

correlated with an advanced onset of ankle extensor activity (MG) at the end of swing (Lam and Pearson 2001; McVea et al. 2005). The immature human nervous system can also adapt to the presence of sustained sensory input and mechanical disturbance to the limbs. In one study, infant subjects were held over a treadmill to elicit a rhythmic walking pattern along with the addition of weights strapped to the limbs for added resistance (Lam et al. 2003). The immediate increase in hip and knee flexor torque that accompanied the applied resistance supports the idea that feedback pathways via sensory afferents, similar to the loading of the limb during stance phase, are mediating this reflexive response (Lam et al. 2003). These studies emphasize that mechanical perturbations applied during the swing phase of walking will modulate flexor activity.

Longer-term motor adaptations solidify memory storage

Sensory feedback mechanisms have been demonstrated to contribute to longer-lasting adaptations throughout the gait cycle. For example, feedback processes may be sufficient for 'on-line' adjustments to perturbations, but feedforward processes allow the nervous system to respond to sensory stimuli more effectively. Perturbations can be predicted (anticipated) in advance to conserve time and improve accuracy. In this way, relayed motor commands will then fire according to anticipated movements. Evidence of this type of preparation has been supported by the observation that it takes several steps for the biceps femoris (BF) and medial hamstrings (MH) to increase activity with the application of robot-applied velocity-dependent resistance (Lam et al. 2006). As mentioned above, to compensate for the resistance against the swing phase, RF is

immediately recruited to flex the hip with the application of resistance. Changes in BF and MH occur more gradually and only after some experience with the resistance. The change in hamstring muscle activity is thought to further help compensate for the swing phase resistance by promoting a greater degree of knee flexion at the beginning of the swing phase. The development of this adaptive response in the BF and MH also persists for a period of time following the removal of the resistance. The persistence of this response during catch trials and washout period supports the idea the locomotor program had been recalibrated.

Spinal circuits contribute to the adaptability of walking, but supraspinal input is also necessary to modulate the basic walking movement and to provide a more sophisticated level of control. The cerebellum has been implicated as a prominent structure for predictive motor control (Bastian 2006). As a result, individuals with cerebellar damage are unable to accurately form anticipatory motor commands to perturbations (Bastian 2006). Cerebellar damaged patients do not display after-effects following removal of load during a hand lifting task (Diedrichsen et al. 2005). Feedback control, however, is generally preserved (Bastian 2006). Also preserved were stride length and swing and stance timing during split-belt walking, parameters that are indicators of feedback control (Morton and Bastian 2006). However, adaptations in step length and timing of double support walking over a split-belt treadmill, which are associated with feedforward processing, are not present or diminished in individuals with cerebellar damage (Morton and Bastian 2006). This provides additional support for cerebellar involvement in predictive movement strategies (Morton and Bastian 2006).

More specifically, it is hypothesized that medial cerebellar structures (vermis, fastigial nuclei) and flocculonodular lobe of the cerebellum may be responsible for predictive control of gait and balance (Morton and Bastian 2004).

Motor memory can be characterized on a continuum from short-term to long-term storage. Longer term memory storage has been demonstrated to develop over a period of time after the initial movement acquisition and can be defined in terms of whether the movement is susceptible to an interfering stimulus (e.g., a different movement) (Shadmehr and Brashers-Krug 1997). If the presence of a disruptive stimulus does not interfere with movement recall, longer-term memory storage is thought to be established. It was determined that after approximately 5-6 hours post-perturbation during an arm manipulandum task, the formed internal model becomes impervious to interference (Shadmehr and Brashers-Krug 1997). This finding is associated with a reorganization of the neural representation of the motor task (Shadmehr and Holcomb 1997). When long-term motor memory becomes stable, this would be an example of a process called consolidation.

Fortin and Bouyer (2009) demonstrated retention of a motor program in response to walking against an elastic force-field. Subjects walked over a treadmill with an elastic that connects the front of the treadmill to the foot, which pulled the foot upward and forward during the swing phase. The subjects walked in 1 of 6 conditions of varied time exposure to the elastic force (1, 3, 5, 10, 20, 30 min.). Velocity error during the swing phase was calculated to evaluate performance. Kinematic and EMG parameters of the

medial and lateral hamstrings (MH and LH, respectively) were also tracked. The exposure duration was found to have a significant effect on after-effect duration, but not on the magnitude of the after-effect. Conversely, increases in absolute force applied to the legs led to an increased after-effect magnitude and recall of the stored motor program – demonstrated by a decrease in velocity error and earlier onset of MH and LH activity – 24 hours after the initial 49 strides (< 1 min) against force-field exposure. Exposure durations >49 strides did not appear to impact retention of motor programs 24 hours post-training, indicating that brief periods of exposure to a force-field during a walking adaptation task can lead to recall of the formed motor program as much as one day later. This study provides insight into the potential for motor memory storage during short bouts of locomotor training.

Can stored adaptations of one task be applied to another? Generalization of motor adaptations

As previously mentioned, it has been established that the nervous system is capable of adapting to sensory perturbations and further, storing them for future use. These stored adaptations developed for a specific task can also be used for variations of that task. For example, a city bike and a road bike may feel slightly different to ride, but if one knows how to ride a regular bike he/she can generalize this motor skill to the movement required for riding the thinner wheels of the road bike. The nervous system's ability to generalize a formed motor program from one task to another permits flexibility in novel environments. The motor program of one arm may be generalized to operate in the

contralateral arm. The contralateral arm can be thought of as the road bike in the example above. The adaptation in one arm has already been acquired (e.g. bike riding), therefore the novel yet similar task of the contralateral arm perturbation can be performed without the initial adaptation period (e.g. the road bike). Both scenarios involve a generalization of an acquired motor adaptation from one task to another.

An example of a phenomenon which relates to generalization of adaptations between limbs is 'cross-education', wherein activity or training of one side of the body affects performance on the contralateral side. This phenomenon has been demonstrated in studies investigating the effects of contralateral strength training intended to prevent loss of strength in the weaker limb (Lee and Carroll 2007). A meta-analysis of cross-education studies found an average increase in strength of 7.6% in the contralateral untrained limb following unilateral limb training (Carroll et al. 2006). Adaptations present in the contralateral untrained limb appear to be proportional to the increases in the strength of the trained limb (Hortobagyi 2005).

Cross adaptation demonstrates that the adaptations in one limb can improve performance (e.g., strength) in the untrained limb. These neuromuscular adaptations have been shown to occur across a single joint. Will this phenomenon occur during a more complex movement task involving multiple joints and distinct trajectories? Generalizations have been demonstrated to occur across movement amplitudes (Mattar and Ostry 2007), arm configurations in different work spaces (Malfait et al. 2002),

bipedal versus unipedal tasks (Wang and Sainburg 2009) and sitting versus standing (Ahmed and Wolpert 2009).

Generalizations have also been demonstrated to occur across non-homologous limbs (Savin and Morton 2008). To test for generalization of adaptations between the upper and lower limbs during a trajectory task, subjects were divided into 3 groups based on the direction of generalization that was being tested. Each experimental period involved wearing prism goggles, which shifted the visual field laterally to the right (17 degrees), while performing a pointing task to a target. Group 1 began with a seated arm pointing task and was tested for generalization to seated leg pointing. Group 2 was tested for the opposite direction of generalization (leg → arm). Group 3 tested for standing leg pointing to standing arm pointing. Error number during each condition (determined by the distance between the target location and finger or foot, as well as body position) was used as the main outcome variable. To verify that a generalization between the two distinct tasks occurred, statistical tests were used to compare the pointing errors between the Generalization period and late Baseline. There was a statistically significant difference found between the two tasks in Group 1. However, there were no significant differences between the two tasks in Groups 2 and 3. These findings indicated that generalization of a prism adaptation pointing task occurred from the arms to legs but not from the legs to the arms. The authors speculated that the legs have access to the stored motor plan of the arms, but not vice versa. From an evolutionary perspective, the hindlimbs of quadrupedal forward walking mammals must encounter the same obstacles as the forelimbs do, but the same situation does not occur in the

reverse (McVea and Pearson 2007) and this could explain the unidirectional transfer of stored motor plans reported in this study. The results of this study are in contrast to previous findings of the same authors during a similar paradigm. Subjects demonstrated generalization of a prism adaptation from walking (legs) to a pointing task (arms) (Morton and Bastian 2004). In this case, the locomotor circuits, visual information and the presence of arm swinging involved in walking appeared to be the factors that differentiated the two studies.

Similar to cross education and the studies above, interlimb transfer is a motor learning concept that can be used to assess generalizations of motor adaptations. Interlimb transfer describes the transfer of adaptations resulting from movement task dynamics in one limb to the contralateral untrained limb. In the context of the internal model framework, interlimb transfer can be thought of as a transfer of a stored motor program from one limb to the other.

Interlimb transfer has been evaluated during a simple grasp orientation experiment (Frak et al. 2006). Thirty right-handed adults made reaching movements to grasp a cylinder in front of them 10 times consecutively with one arm followed by the same sequence with the other arm. Subjects were divided into two groups (15 each) to perform the grasping task from right hand (R) followed by left hand (L), and *vice versa*. Grasp orientation was defined by the distance from the index finger and thumb used to grasp the object. The results demonstrated an interaction effect between the sequence the hands were presented (RL vs. LR) and laterality (R and L), indicating that

presentation order is dependent on laterality. Specifically, during LR sequence the L mirrors the R (average grasp orientation = 32 degrees for both hands), however during RL sequencing the R orientation (26 degrees) does not mirror the L orientation (17 degrees). This experiment demonstrates transfer of fine motor movement from R to L during a complex upper limb prehension task.

Interlimb transfer of the upper limbs was also described during an arm manipulandum task in which a force-field perturbation was applied to generate motor adaptations (Criscimagna-Hemminger et al. 2003). Both directions of transfer were tested i.e., dominant arm to non-dominant (D → ND) and vice versa, in 36 healthy adults and 1 split brain (cut corpus callosum) subject. Transfer of adaptation was determined by an Adaptation Index (defined by an improvement in arm position movement error) that was greater in the second hand (transferred hand) compared to the control group. The authors found that transfer only occurred in the D→ND groups, but not *vice versa*. The split brain subject also demonstrated this effect, indicating that inter-hemispheric connections are not necessarily involved in the transfer of motor adaptations between the limbs. More likely, the small percentage of corticospinal tract projections which remain ipsilateral appear to be involved in the transfer of adaptations from D→ND limb.

The findings from this study led Malfait and Ostry (2004) to examine whether the transfer of adaptation from one limb to the other was partly due to the involvement of the sudden presence of a load perturbation. The authors devised an experiment to test whether interlimb transfer would occur with a sudden vs. a gradual introduction of a

force-field during a horizontal plane arm movement task. Interlimb transfer appeared to occur only during conditions that involved an unexpected and immediate application of a force to the arms from 0-15 Nm/s, compared to the gradual introduction of this force over a period of 145 trials. This experiment confirmed the results of the study previously described and added insight into the cognitive strategies that may be involved in the transfer of motor adaptations from one context (arm) to another.

Also consistent with Criscimagna-Hemminger and colleagues (2003), Wang and Sainburg (2004) demonstrated asymmetric interlimb transfer from D $\rightarrow$ ND arm of a novel upper limb perturbation task. In this study, the imposed force perturbation altered the inertial dynamics of the limb by changing the centre of mass of the forearm. The device used to impose load isolated proprioceptive information about the force perturbation by excluding the presence of a shearing force between the hand and device. The subjects in this study moved one arm (either D or ND) towards one of 3 targets (10, 20, 30 degree shoulder starting positions, with elbow angle remaining constant). The opposite arm was then tested for the same effect. Inverse dynamics analysis was used to determine the changes in joint torques that compensated for the applied load. Linearity error, direction error and final position error were also main outcome measures used to determine differences between the limbs in response to load. Improvements in target trajectory were demonstrated by a decrease in linearity error of ND after training in D. To counteract the extensor torque imposed by the load, shoulder and elbow flexor torque of the ND increased to the same extent as those that appeared at the end of D training. This improvement in torque strategy following

opposite limb training did not occur in the direction of ND → D. In contrast, previous work by Sainburg and Wang (2002) demonstrated interlimb transfer of a visuomotor rotation task from ND → D. The literature suggests that discrete neural processes may underlie visuomotor (Clower et al. 1996; Ghilardi et al. 2000) versus dynamic tasks (Shadmehr and Holcomb 1997), which could explain the opposing outcomes of the two studies. In addition, the authors speculated that the dominant hemisphere is more adept at generating an internal model of inertial dynamics which becomes readily accessible to the non-dominant hemisphere during interlimb transfer.

Inter and intra-limb transfer of the arms was evident in a ball catching task with differently weighted balls (Morton et al. 2001). In this study intra-limb transfer (e.g. arm position) occurred to a greater degree (greater displacement due to impact and joint angle change) than inter-limb transfer. The success of the ball catching in the ipsilateral limb at a different arm position occurred within the first trial after the initial ball catch training. The contralateral limb did not achieve identical success as that of the trained ipsilateral limb, however subsequent trials were successful. The authors concluded that partial interlimb transfer occurred.

Robust interlimb connections in the lower limbs

The linkages that exist between the limbs provide the framework for the transfer of motor adaptations from one limb to the other. In particular, the observation that the legs coordinate in order to produce the walking pattern provides evidence that a strong

linkage between the legs exists. More robust connections are thought to exist between the lower limbs in comparison to the upper limbs (Zehr 2005). For example, the basic movement pattern of the lower limbs during walking is thought to be mediated through specialized neural circuits within the spinal cord. This collection of spinal neurons located in the spinal cord, the central pattern generator (CPG), is proposed to autonomously generate the rhythmic timing of flexor and extensor muscles of the legs. Charles Sherrington (1910) first observed that stepping could be elicited without the presence of supraspinal input. Brown (1914) demonstrated that animals with transected spinal cords and dorsal roots cut at lumbosacral level were still able to maintain the basic locomotor walking pattern. Grillner and Zangger (1975) described the source of this phenomenon as the CPG. The CPG was proposed to be composed of neurons that fire in a coordinated fashion so that the flexor half-centers of each leg fire while suppressing the extensor half-centers in the same leg (Brown 1924).

Although the locomotor rhythm between limbs clearly needs to be strongly linked for successful bipedal walking, support for independent CPGs of each leg during walking has also been described in the literature. Consistent with studies in cats and insects, infant studies have indicated that separate CPG control may exist for each leg (Yang et al. 2005). Infants were placed over a split-belt treadmill that varied the speed and direction on each side and were able to adapt within the first couple steps of each condition by adjusting the stance and swing phase durations accordingly (Yang et al. 2005). Further, a study investigating the response to split-belt treadmill training in forward (FW) and backward (BW) walking in adults, explored the neural circuitry

involved in FW vs. BW as well as between the limbs during hybrid walking (one leg simultaneously moves faster than the other) (Choi and Bastian 2007). Hybrid walking was used to evaluate the neural response to performing different tasks in separate legs. Subjects walked at baseline with tied belts followed by a period of adaptation in either FW, BW or hybrid walking. Subjects then walked FW then BW (presentation order depended on the direction of walking during the adaptation period) for the post-adaptation period with tied belts. Results showed that the adaptations did not transfer to the post-adaptation period. This lack of adaptation transfer provides support for the idea that lower limb adaptations are direction and leg specific and that the neural circuitry reflects these adaptations (Choi and Bastian 2007).

Independent CPGs may be present in each leg but the central CPG network is one example which provides support for the presence of neural connections linking the lower limbs during walking. The common neural circuitry between the lower limbs underlies interlimb coordination and it appears that this circuitry is partially laid down by birth (Choi and Bastian 2007). Infants as young as 6 months old will display interlimb coordination patterns (symmetrical, synchronous), with and without weight bearing training. The transitions between the two coordination patterns were smooth and transfer of the adaptation from weight bearing to non-weight bearing conditions occurred (Choi and Bastian 2007). Infants are capable of immediately adapting to the presence of different speeds and directions of the two legs during split-belt treadmill walking (Yang et al. 2004). These patterns have also been demonstrated in cats (Forssberg et al. 1980) and insects (Bassler and Buschges 1998). It has been proposed

that two CPGs exist in each leg to account for differences in separate leg adaptations. However, it is evident during these split-belt walking tasks that the swing phase will occur several times on the fast side only if the contralateral slow leg is in stance (Choi and Bastian 2007; Yang et al. 2005). At least one leg must remain on the treadmill at all times, satisfying the requirements for successful bipedal walking. Further, increasing the speed of one leg will result in multiple steps of that leg for every one step of the slower leg. Though CPGs may exist in each leg, there must be a strong connection between them in order for this coordination to occur.

These connections appear to be robust when the limbs are loaded as well as when just one leg is stepping. Weight bearing of the stepping limb has been shown to produce rhythmic muscle activations in the non-stepping limb in subjects with complete spinal cord injury (Ferris et al. 2004). Subjects walked in 4 different uni-lateral stepping conditions over a treadmill with body weight support: 1) uni-standing condition: one-legged standing on a board while the contralateral limb stepped; 2) uni-extended condition: extended leg with a dorsiflexed foot hanging in the air while the contralateral leg stepped; 3) uni-flexed condition: similar to the uni-extended except the non-stepping limb was flexed backward; and, 4) uni-airstepping: the only condition that did not include weight bearing of the non-stepping limb. In this condition subjects had 100 percent body weight support and the ipsilateral leg hung still while the contralateral limb was moved passively in a stepping motion. During the weight bearing conditions, it is proposed that the locomotor circuits or reflex pathways are engaged when sensory information from Golgi tendon organs and cutaneous stimulation of the foot are present. The circuits or

reflexes involved in uni-lateral stepping appear to be engaged without supraspinal input (complete SCI subjects) and depend on sensory information to be maintained and modulated. However, the presence of muscle activity in the non-stepping loaded limb in the SCI subjects is in contrast to results found previously (Dietz et al. 2002). Dietz (2002) found that muscle activation in the lower limbs was absent during unilateral stepping in the SCI group, compared to able bodied controls. The loading of the limbs, however, was 30 percent less than in the aforementioned study and it can therefore be postulated that the modulation of muscle activity in the non-stepping limb during contralateral stepping requires a certain degree of limb loading in the SCI population.

Partial interlimb transfer was also evident in the outcome of an induced slip walking paradigm (Bhatt and Pai 2008). Subjects walked across a platform composed of movable plates controlled by the experimenter. Random slip trials to the right limb interspersed between blocks of regular walking led to improvements in measures of fall prevention and loss of balance measures. To observe whether interlimb transfer of these adaptations to the slip condition was possible, one slip trial was randomly induced on the contralateral untrained limb. Reduction in slip response in the final trial (37th) of the trained limb was greater than in the contralateral limb, indicating that complete learning did not transfer. However, it was found that there was a reduction in falling response ('pre-slip stability') in the contralateral leg compared to the first slip response (trial 1) in the trained leg. Further, the adaptation was retained in the untrained limb in the following week and 3rd week post-testing sessions. This paradigm reflects a transfer

of balance and posture from one limb to the other during a whole-body balance recovery task.

Interlimb transfer during an obstacle avoidance walking task has also been shown (van Hedel et al. 2002). Healthy subjects were presented with an obstacle to one leg while treadmill walking. They were subsequently tested in the obstacle avoidance task with the contralateral leg. Foot clearance, lower limb EMG activity, and knee joint trajectory parameters of the contralateral leg all had faster adaptations (decreased leg muscle activation and optimal foot clearance) than the initial trained leg (van Hedel et al. 2002). Less adaptation during the contralateral untrained leg indicates that the motor program for obstacle avoidance was transferred to this leg to avoid 're-learning' of the task.

Few studies have demonstrated interlimb transfer during walking and no studies have examined whether the manipulation of the dynamic properties of one limb in response to resistance during a walking task, will transfer to the other limb. Given the strong interlimb linkages required for successful bipedal walking and the likely contribution of internal models to locomotor adaptations, it is expected that motor adaptations produced in one leg should be readily transferred to the other leg during a walking task.

Purpose

The purpose of this study is to determine whether locomotor adaptations to a velocity-dependent force field in one (trained) leg transfer to the contralateral (test) leg.

The specific objectives are to determine whether:

1) after-effects will appear sooner in the test leg than the trained leg

2) changes in lower limb muscle activity and kinematic patterns associated with adaptations to the force perturbation will develop faster in the test leg compared to the trained leg

Hypothesis

Consistent with previous literature, it is hypothesized that locomotor adaptations will take time to develop. Specifically, it is expected that:

1) the feedback mediated response in RF EMG will not change over the course of steps taken against resistance;

2) there will be a gradual change in BF EMG over the course of steps taken against resistance; and,

3) after-effects will appear only after several steps have been taken against resistance.

The main hypothesis of this study is that neuromuscular adaptations due to velocity-dependent force perturbations in one leg during walking will transfer to the contralateral test leg. Specifically, it is expected that:

4) after-effects in the test leg will appear larger and sooner compared to those in the trained leg

5) exposure to resistance on the contralateral test leg will result in a faster rate of adaptation of lower limb kinematic patterns than that observed in the trained leg during unipedal walking; and,

6) interlimb transfer will occur even after a washout period is provided after training.

METHODS

Subjects

Twenty able-bodied adults (13 females, 7 males) were recruited to participate in this study. Demographic information including age, height, weight, sex was collected from all subjects (Table 1). All subjects selected were screened for right leg dominance by asking them which leg is used to kick a soccer ball. Leg dominance has previously been defined as the leg used for mobility and the non-dominant leg is that which is used for support (Sadeghi et al. 2000). Subjects were excluded if considered to be an athlete in a sport which induces leg dominance e.g. soccer. Subjects with known medical condition (gait impairment, musculoskeletal disease) or cognitive disorder which could prevent them from engaging in exercise were excluded. Additional inclusion criteria were age over 19 years of age, under 6'1" in height and under 300 lbs in weight. All experimental procedures were approved by the UBC Behavioural Research Ethics Board. All subjects gave their written informed consent.

Experimental setup

Subjects were fitted to the Lokomat gait orthosis (Hocoma AG, Volketswil, Switzerland) and placed in a harness over a treadmill. The exoskeletal legs of the Lokomat were attached to the subject's legs with leg cuffs strapped to the mid-thigh, upper and lower shank. The Lokomat was programmed to apply a velocity-dependent resistance (viscous force field) against hip joint movement. The resistance is defined by the

algorithm $M = -B \times v$ where M is the instantaneous amount of torque applied, B is the viscous (or dampening) coefficient (in N.m.s/rad), and v is the instantaneous angular velocity against the hip (Lam et al. 2006). When B is set to zero, no force is applied (null field). The specific resistance level was scaled to 10% of each individual's hip flexor maximum voluntary contraction (MVC) (Bolliger et al. 2008) and the average angular velocity during the swing phase.

Subject	Gender	Age	Height (cm)	Weight (kg)
1	FM	19	170	59
2	FM	22	162	50
3	M	22	180	88
4	FM	26	155	55
5	FM	30	163	51
6	FM	22	165	64
7	FM	26	163	58
8	M	29	185	82
9	M	27	177	77
10	FM	26	170	58
11	M	28	180	72
12	FM	26	160	50
13	FM	27	170	55
14	M	31	180	75
15	M	27	180	80
16	FM	29	178	86
17	FM	25	178	63
18	M	19	175	68
19	FM	28	175	52
20	FM	19	178	76
	AVERAGE	25	172	66

Table 1. Subject demographics

To familiarize them with the apparatus, subjects walked for several minutes with the Lokomat and were instructed to walk at a 'normal' pace and pattern. Treadmill speed was set to 2.5 km/h and remained constant throughout the experiment. During baseline walking the natural walking tempo was established with a metronome and used for all testing conditions. Data were then collected during baseline (no resistance) bipedal walking with the Lokomat. Two subsequent trials of baseline unipedal walking were also collected for each leg (Base R and Base L). During unipedal walking, one leg was free to move while the other was fixed in a position of knee flexion with the hip at neutral. Velcro straps were secured around the metal struts of the Lokomat to help ensure that the hip and knee remained stationary (Figure 1). Body weight support was provided to ensure the subject remained upright during the swing phase of unipedal walking. Subjects were instructed to maintain the stationary leg quiescent. EMG feedback was provided to ensure that there was no muscle bursting activity in the stationary leg.

Subjects first performed right-side unipedal walking. The resistance was turned on and off according to the pattern depicted in Figure 2A. This pattern consisted of 1 step with resistance (R ON1) immediately followed by 1 step without resistance (catch trial, R OFF1), followed by an *adaptation period* where the resistance was applied for 100 consecutive steps (R ON2). Another catch trial then occurred R OFF2), followed by 10 steps with resistance. The treadmill was then stopped. Subjects then performed left-side unipedal walking as described for the right side and depicted in the black lines of Figure 2B. A subset of 10 subjects performed an additional pattern of walking during the left-side unipedal walking that consisted of 100 steps of undisturbed (no resistance) walking

as depicted in the thick grey lines of Figure 2B. This was done to determine whether the stored motor program can be retained after a washout of any perturbation effect has occurred. The resistance was always turned on or off during mid-stance, which is a point in the gait cycle where angular velocity is low compared to the rest of the cycle.
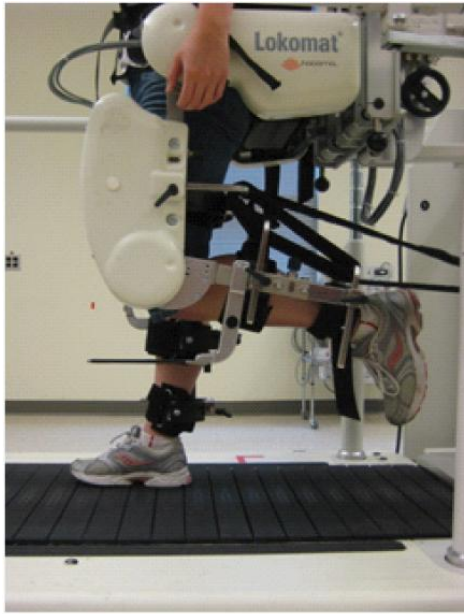
Figure 1 Photograph of unipedal walking position in the Lokomat
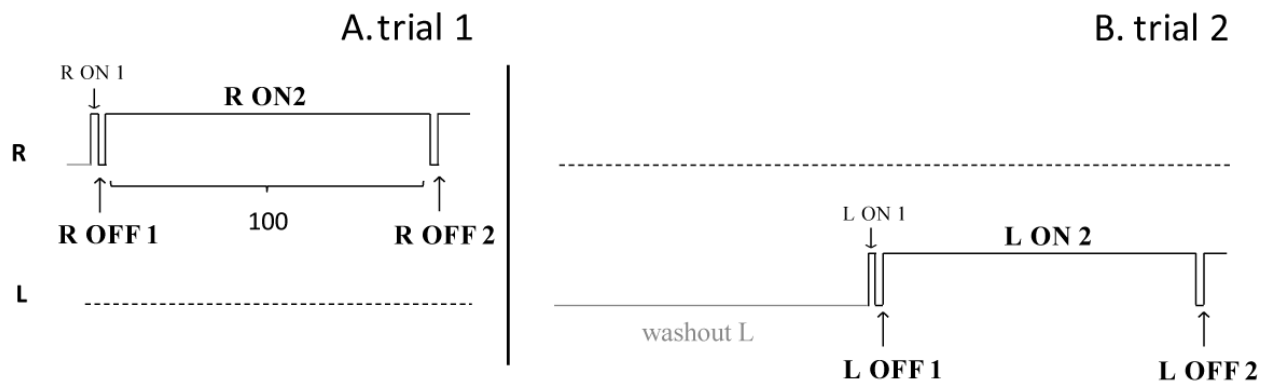
Figure 2 Experimental protocol
Sequence of resistance application (ON) and removal (OFF) for right leg (R) and left leg (L) during unipedal stepping. Lengths of thin solid lines indicate the period of stepping during each condition. Dotted lines represent zero resistance to the stationary limb. Gray lines represent supplementary stepping periods. Washout L was performed by a subset of n=10 subjects. The solid vertical line depicts the separation between trials A) and B).

Data collection

Surface electromyography (Delsys Inc, Boston MA) was used to record activity bilaterally from the rectus femoris (RF), biceps femoris (BF), tibialis anterior (TA) and the medial gastrocnemius (MG). To reduce impedance, the skin was shaved, abraded and wiped with alcohol. A ground electrode was placed over the surface of the proximal tibia of either leg. Hip and knee joint angles were collected from Lokomat position sensors. Ankle angles were recorded bipedally using goniometers (Biometrics Ltd., Cwmfelinfach, UK). Force sensitive resisters (FSRs; Interlink Electronics, Camarillo CA) were placed under the heel and great toe of each foot. Analog EMG and kinematic data were sampled at 1000 Hz and stored on a computer for off-line analysis.

An active motion capture system (Optotrak; Northern Digital Inc., Waterloo, ON) was used to record foot trajectory. An infrared-emitting marker was secured over the 5th metatarsal heads bipedally in order to track toe trajectory height and stride length during walking. Marker data were collected at 100 Hz. A custom-made switch was used to send a common 5 V pulse to all acquisition systems for off-line synchronization of the data.

Data analysis

A custom-designed program in MATLAB (MathWorks, Inc. Natick, MA) was used for all off-line data analysis. EMG and kinematic data were divided into individual strides

(stance and swing) as determined by the FSRs. EMG data were rectified, filtered (low pass: 100Hz, 4th order Butterworth) and then normalized to the peak average baseline EMG during a stride cycle. EMG data were quantified by taking the average amplitude during the swing phase of a stride cycle. Kinematic data was low pass filtered at 6 Hz and quantified by taking the peak toe trajectory height, peak hip flexion angle, peak knee flexion angle, and peak ankle dorsiflexion angle during the swing phase of a stride cycle. Unfortunately, knee angle data were unavailable from Subject 5 and ankle angle data were unavailable from Subject 4 due to equipment error. All data from the unipedal walking conditions were normalized to the respective unipedal baseline walking of that leg. The MVC of each leg and the % MVC applied to each of the legs during walking were compared to determine any differences in strength between the legs.

Peak hip flexion during the swing phase was selected to track the adaptation rate (see Results, Rate of adaptation). The time course of adaptation (TCA) was calculated by using a 3-point moving average to determine the number of steps required for peak hip flexion angle to reach the 95% confidence interval bounds of the last 10 steps against resistance (Fortin et al. 2009).

Muscles of the stationary left leg during right unipedal walking were evaluated for bursting of activity throughout the right leg experimental trial with resistance (ON2) using a fast Fourier transform (FFT). Muscles were considered to be bursting if the FFT showed a peak corresponding to step frequency (average cycle duration was 2 seconds, or a step frequency of 0.5 Hz), indicating the presence of muscle bursts at

least once per step cycle. A cross-correlation analysis was performed on antagonist bursting muscles to determine if locomotor-like bursting was present. Subjects that did not show a central large peak (no correlation) were classified as reciprocal (locomotor-like) bursters.

Statistics

All statistical analyses were conducted with a commercially available software package (SPSS 8.0; SPSS Inc, Chicago, Illinois). Descriptive statistics were calculated for age, height and weight of each subject. An alpha value of 0.05 was used for all statistical evaluations. Trends were defined by differences of $p < 0.10$. A Bonferroni correction was applied to all post-hoc analyses to account for multiple comparisons.

The L-force (MVC) values of each leg were compared with a paired t-test. The same analysis was done to compare the % MVC applied to each of the legs during walking.

The effects of the resistance were tested by a repeated measures ANOVA comparing baseline, the first step against resistance, and the average of the last 10 steps against resistance on the EMG and kinematic variables. Post-hoc comparisons were performed on the following 3 contrasts: baseline vs. 1st step against resistance; baseline vs. average of last 10 steps against resistance; 1st step vs. average of last 10 steps against resistance.

The presence of after-effects were tested by a one-way repeated measures ANOVA on lower limb kinematic variables to compare baseline values with OFF1 and OFF2 steps in each leg. To determine if there was interlimb transfer of motor adaptations, a 2 (OFF1, OFF2) by 2 (right leg, left leg) repeated measures ANOVA was used to determine whether there was a main effect of time of OFF period (after 1 step; 100 steps) and/or leg, and if an interaction between the two exists on the percent change in lower limb kinematic parameters compared to baseline. If a significant interaction effect was found, a paired t-test was used to determine where the differences lay. Post-hoc comparisons were performed for the following 4 contrasts: R OFF1 vs. R OFF2; L OFF1 vs. L OFF2; R OFF1 vs. L OFF1; R OFF2 vs. L OFF1.

The rate of adaptation (TCA) of the right vs. left leg was compared with a paired t-test.

A subset of 10 subjects performed the additional washout-L after right leg training (see Figure 2). To confirm that there were no immediate transfer effects during the washout, a paired t-test was used to compare the first step of washout-L with Baseline Uni-L. A paired t-test was also used to determine whether there were hip, knee or ankle angle or EMG changes compared to baseline during washout-L. A 2 (OFF1, OFF2) by 2 (right leg, left leg) repeated measures ANOVA, as described above, was then performed on the data collected from this subset of 10 subjects to determine if the addition of the washout period had any effect on the interlimb transfer pattern.

RESULTS

Bipedal vs. unipedal walking

To determine whether unipedal walking was a good representation of bipedal walking, comparisons between baseline bipedal walking versus unipedal walking are shown in Figure 3. There were differences in the muscle activation pattern between unipedal and bipedal walking. In particular, BF activity was markedly greater during the stance phase of unipedal walking compared to bipedal walking. Also, RF exhibited greater activity during bipedal walking. However, RF, TA and MG showed similar patterns of activation across the step cycle. It can also be appreciated from the figure that the kinematic patterns were similar (surrounding standard deviation lines of each walking condition overlap), indicating that the hip, knee and ankle joint angular trajectories were similar between unipedal and bipedal walking.

Response to resistance

The response to resistance was characterized by specific changes during the swing phase. Figure 4 illustrates the kinematic and EMG pattern of the right leg during baseline unipedal walking, the first step against resistance, and the last 10 steps against resistance. A repeated measures ANOVA revealed an effect of resistance on RF activity ($F_{(2,38)}=16.5$, $p<0.001$). An immediate increase in RF activity in the first
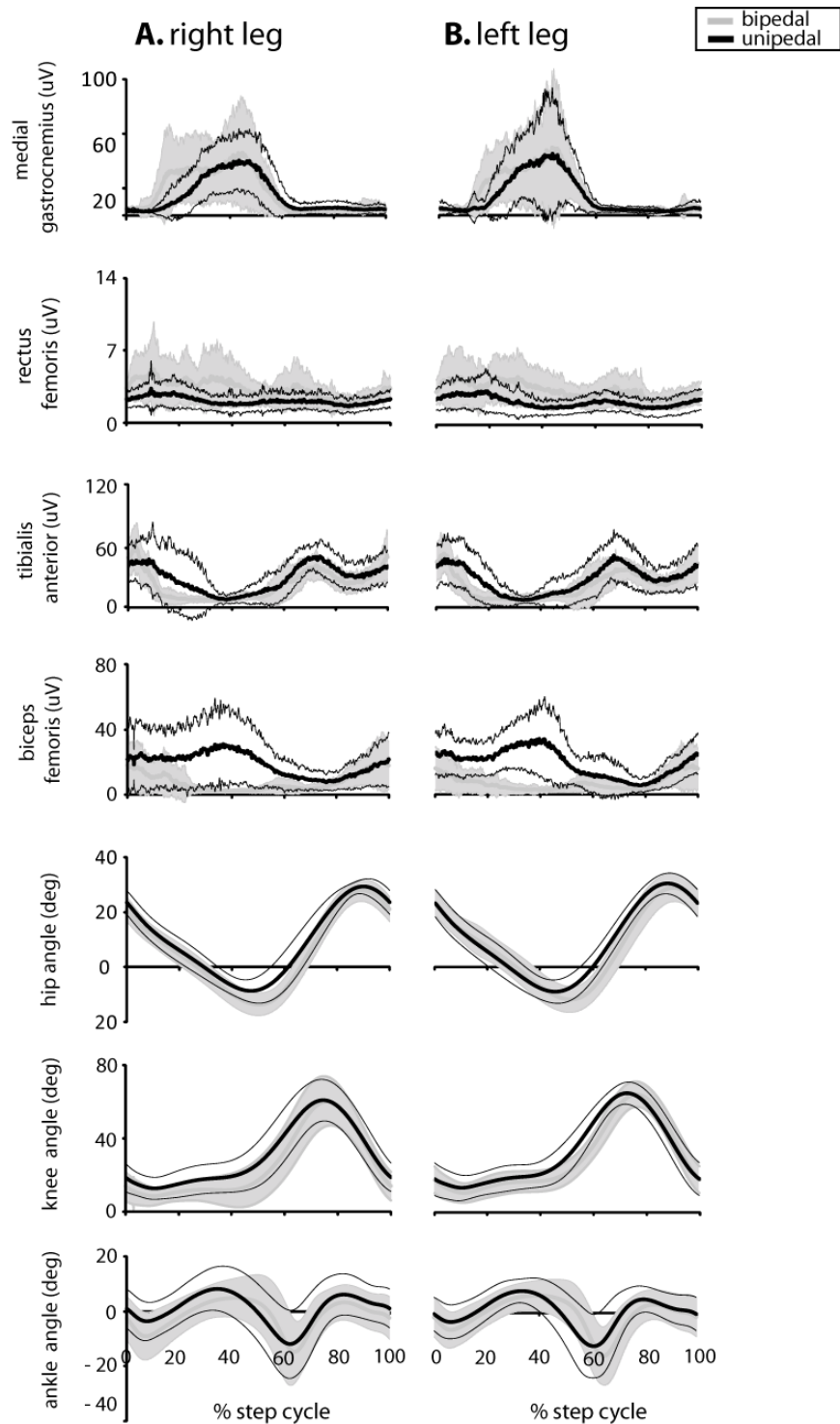
Figure 3 Bipedal vs. unipedal walking
Averaged raw electromyographic (EMG) and kinematic patterns in the (A) right and (B) left leg of all subjects during bipedal walking (gray lines and fill) and unipedal walking (black lines). The thin lines represent +/- SD across the step cycle. EMG data are plotted in uV and kinematic angles in degrees. In the kinematic plots, positive values indicate flexion. All data were normalized in time to 100% of the step cycle.
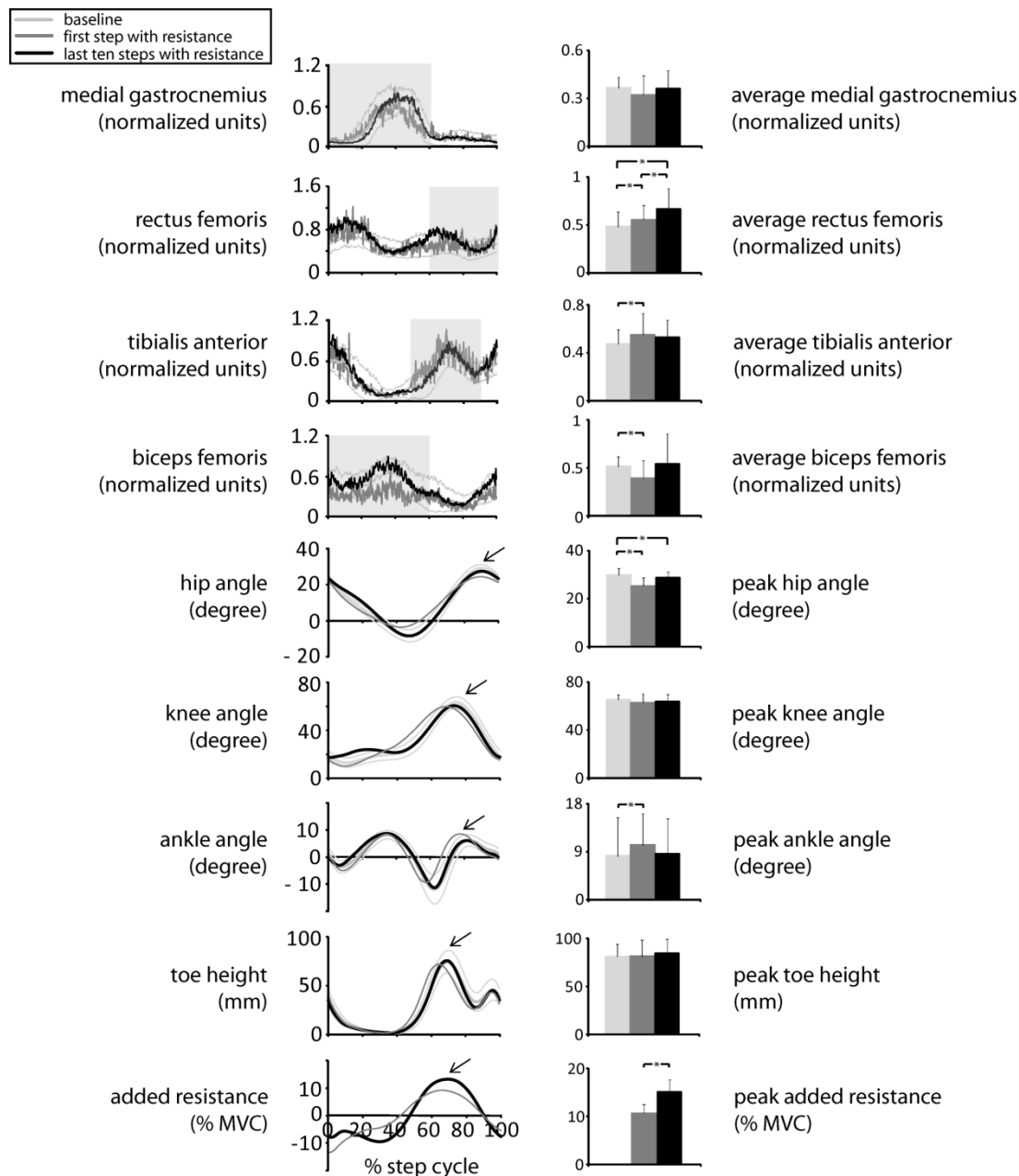
Figure 4 Electromyographic (EMG) and kinematic response to resistance
Averaged A) EMG and B) kinematic patterns of all subjects during right leg unilateral walking. Plots show the response to the first step taken with resistance (dark gray) and the last 10 steps taken with resistance (black) compared to baseline unilateral walking (light gray lines). The thin light gray lines represent +/-SD across the step cycle. The average amount of added resistance during the swing phase was 10% of each individual's maximal voluntary contraction (MVC). All EMG data from each subject were normalized to the peak averaged EMG of each muscle during baseline walking. Shaded areas in the EMG plots represent the period over which the average EMG amplitude was measured. Arrows in the kinematic plots and resistance plot represent the peak flexion angle, toe height and resistance used to quantify changes at each joint, the foot and amount of added resistance. Average EMG amplitude, peak joint flexion and resistance values are plotted in the bar graphs on the right. In the kinematic plots, positive values indicate flexion. All data were normalized in time to 100% of the step cycle. Asterisks represent statistical significance.

step against resistance compared to baseline during the swing phase was observed (p=0.012). This increase in RF persisted across the last 10 steps against resistance (p<0.001). The first step and last 10 steps against resistance of RF activity were significantly different from each other (p=0.005). There were no significant main effects of resistance in the MG (F(2,38)=1.79, p=0.18). In the BF, there was a significant main effect of resistance (F(1,27)=3.31, p=0.047) and post-hoc testing showed that there was a significant decrease in BF activity in the first step against resistance (p=0.005), but no difference between the last 10 steps against resistance and baseline (p=0.69) and a trend for a difference between the first and last 10 steps against resistance (p=0.06). There was also a significant main effect of resistance in TA activity (F(2,38)=3.80, p=0.03). Post-hoc testing showed that TA activity significantly increased in the first step against resistance (p=0.015) and a trend for a difference between the last 10 steps against resistance and baseline (p=0.06). There was no difference in TA activity between the first and last 10 steps against resistance (p=0.44). Therefore, the hip flexor muscle (RF) was the only muscle that showed an adaptive response during all steps against resistance.

There were also significant changes in lower limb joint kinematics with resistance. There was a significant main effect of resistance on peak hip flexion (F(2,38)=57.37, p<0.001). Peak hip flexion was significantly lower than baseline during the first step (p<0.001) and over the last 10 steps (p=0.012) against resistance. There were no significant changes in peak knee flexion with resistance (F(2,36)=1.55, p=0.23). At the ankle, there was a significant main effect of resistance on peak dorsiflexion (F(2,36)=6.33, p=0.004). Post

hoc testing showed a significant increase above baseline for the first step against resistance (p=0.01) but not over the last 10 steps against resistance (p=1.00). There were no significant changes in peak toe height with resistance ($F_{(2,38)}=0.83$, p=0.44).
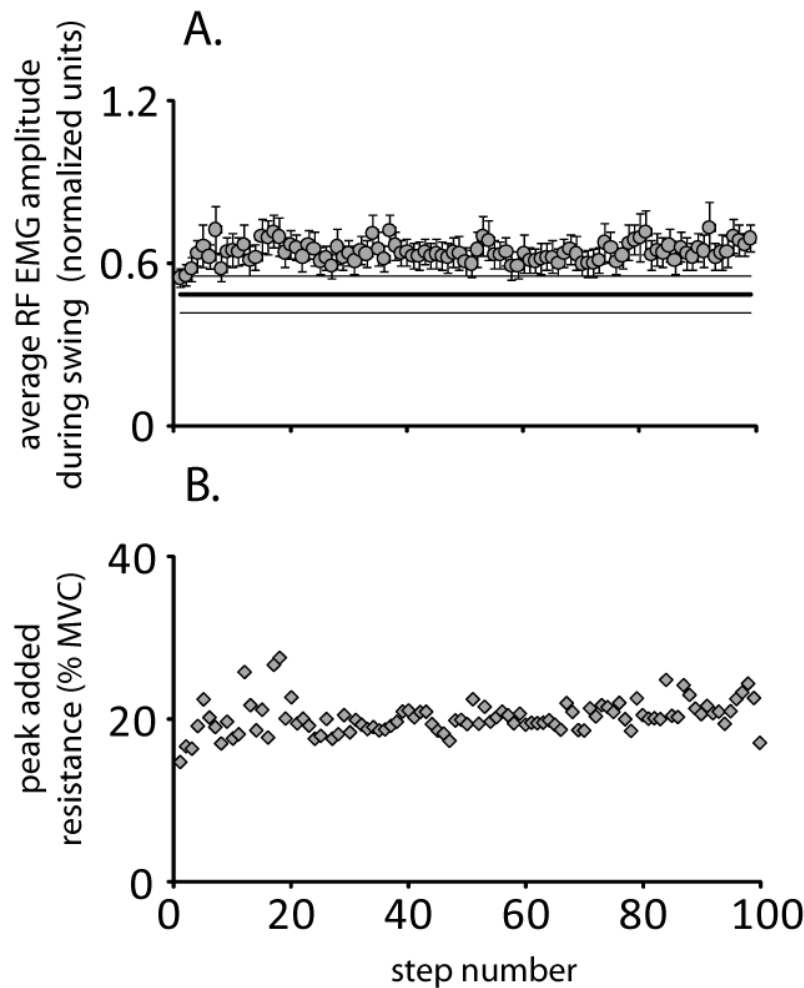
Figure 5 Step by step peak added resistance and average RF EMG amplitude during resisted walking in right leg
A) Average RF EMG amplitude during swing and B) peak added resistance, during each step against resistance of ON2 in the right leg. Error bars represented by +/- standard error of the mean.

Added resistance during the first step was significantly different than resistance over the last 10 steps (t = -9.00, df = 19, p < 0.001; step 1: mean = 10.65, SD = 1.87; last 10

steps: mean = 15.09, SD = 2.58) (Figure 4). Figure 5 shows that peak added resistance rapidly increased and remained steady for the duration of R ON2. Step by step average (+/- standard error of the mean) for RF EMG amplitude during swing is plotted for R ON2 (Figure 5B). It is apparent that the change in RF activity immediately increased with the onset of resistance and maintained a steady level for the duration of R ON2. RF EMG amplitude also appeared to correspond to the changes in added resistance.

After-effects following removal of resistance

Lower limb kinematics during the catch trials of each leg were evaluated compared to baseline walking to determine whether after-effects were present. Figure 6 shows the changes in right lower limb kinematics upon removal of resistance after one step taken with resistance (ROFF1) and after 100 steps taken with resistance (ROFF2). There was an obvious increase in hip flexion, knee flexion, and toe trajectory height in ROFF1 and ROFF2 (Figure 6A). Repeated measures ANOVA revealed main effects of the removal of resistance for hip flexion ($F_{(2,38)}=50.82$, $p<0.001$), knee flexion ($F_{(2,36)}=16.15$, $p<0.001$) and toe trajectory height ($F_{(1,28)}=19.11$, $p<0.001$). Post-hoc testing showed significantly greater hip flexion ($p=0.009$), knee flexion ($p<0.001$) and toe trajectory height ($p<0.001$) compared to baseline in ROFF1. Hip flexion, knee flexion, and toe trajectory height were also significantly greater in ROFF2 compared to baseline (hip: $p<0.001$; knee: $p<0.001$; toe: $p<0.001$). No significant changes were noted in the ankle, so it was not plotted.
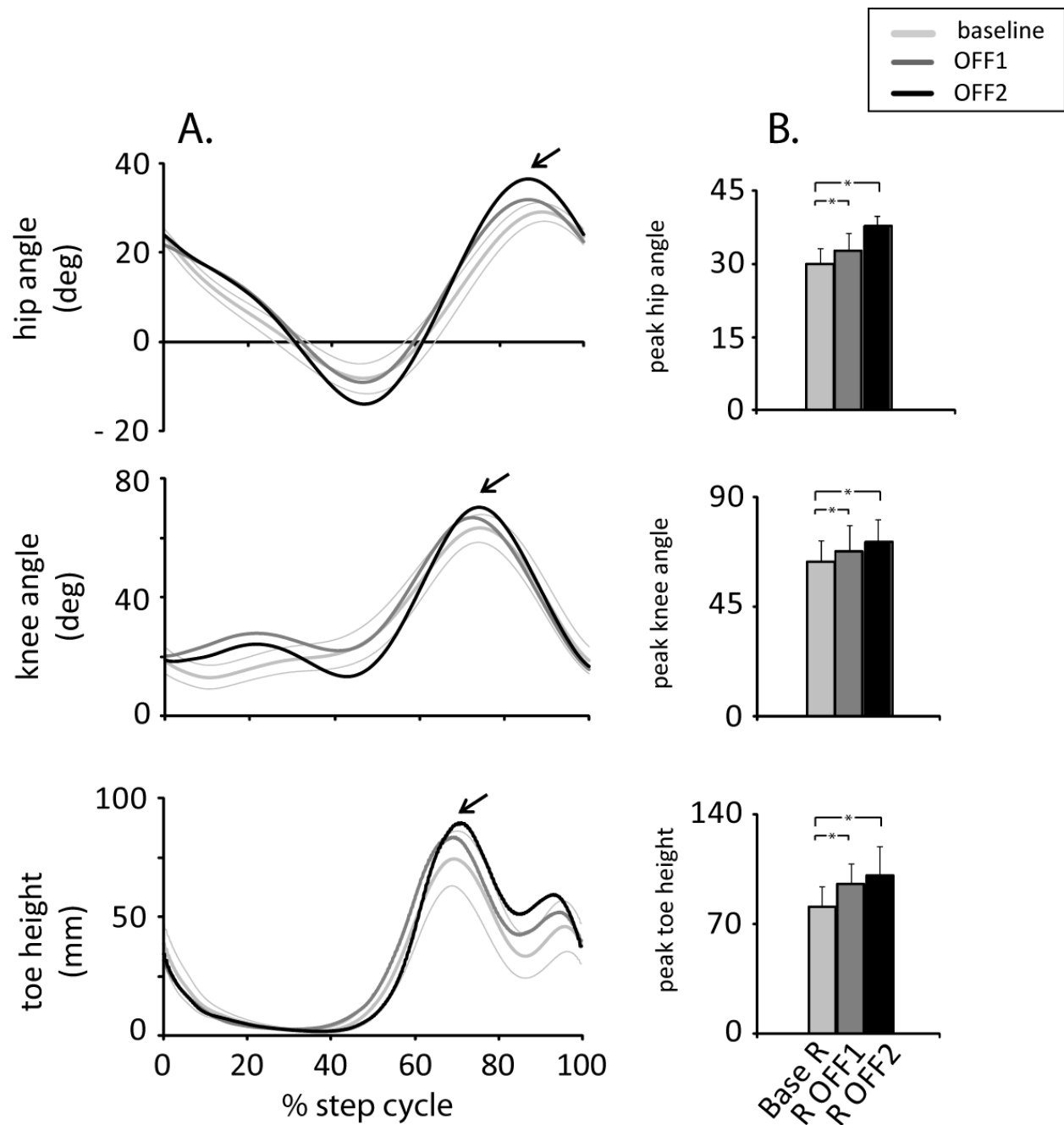
Figure 6 After-effects following removal of resistance in trained (right) leg
A) Average hip, knee angle and toe trajectory during baseline stepping (thick black lines), the step following removal of resistance after 1 step (OFF1-dark gray lines) and after 100 steps with resistance (OFF2-light gray lines) of the right leg. The thin black lines represent +/- SD of baseline across the step cycle. For the angle plots, positive values indicate flexion. All data were normalized in time to 100% of the step cycle. Arrows in the kinematic plots represent the peak flexion angle and toe height used to quantify changes at each joint and the foot. B) Peak hip, knee, and ankle angle and toe height of swing phase. Standard deviation represented by error bars. Asterisks represent statistical significance.

Was there interlimb transfer?

To determine whether there was interlimb transfer in the left leg after previous exposure to resistance in the right leg, changes in after-effect amplitude were compared between the right and left legs. First, it was determined that after-effects in lower limb kinematics were also observed in the left leg as was demonstrated in the right leg (Figure 7). Repeated measures ANOVA revealed main effects of the removal of resistance for hip flexion ($F_{(2,38)}=45.23$, $p<0.001$), knee flexion ($F_{(2,33)}=17.38$, $p<0.001$) and toe trajectory height ($F_{(2,38)}=14.47$, $p<0.001$). Post-hoc testing showed significant differences between LOFF1 and baseline for hip flexion ($p<0.001$), knee flexion ($p<0.001$) and toe trajectory height ($p<0.001$). There was also a significant difference between LOFF2 and baseline for hip flexion ($p<0.001$), knee flexion ($p<0.001$) and toe trajectory height ($p<0.001$).

Second, the size of the after-effects were compared between the legs. The percent changes in lower limb kinematics (with respect to baseline) following the removal of resistance after 1 and 100 steps against resistance (OFF1 and OFF2, respectively) were compared between legs (Figure 8). For hip flexion, the 2 (OFF1, OFF2) by 2 (right leg, left leg) repeated measures ANOVA showed that there was a main effect of time (OFF1 vs. OFF2) ($F_{(1,19)} = 40.05$, $p<0.001$) but no main effect for leg ($F_{(1,19)} = 0.81$, $p=0.78$). There was also a significant interaction effect ($F_{(1,19)} = 8.02$, $p=0.011$). Post-hoc testing showed that OFF2 was significantly higher than OFF1 for both the right
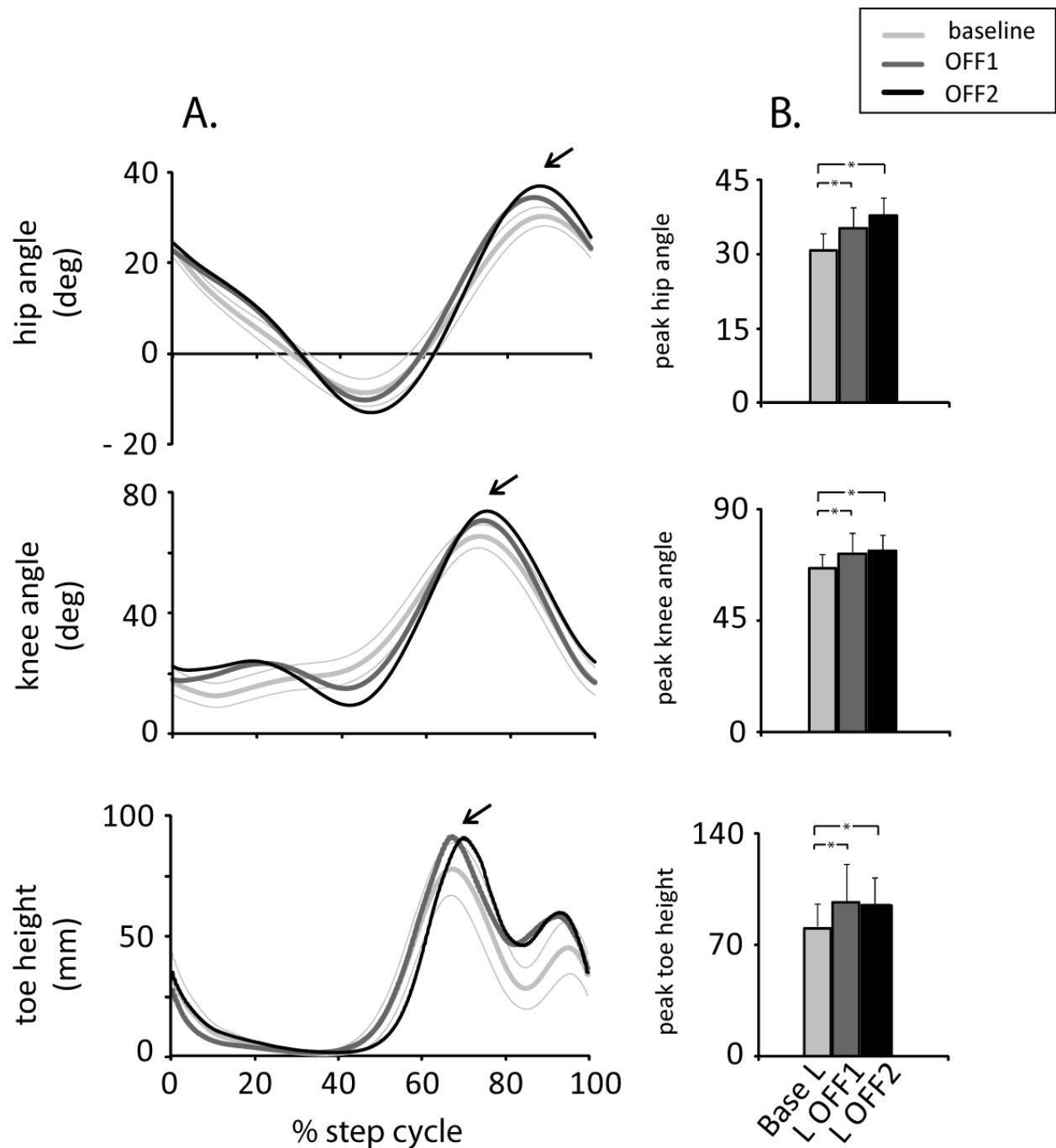
Figure 7 After-effects following removal of resistance in test (left) leg
A) Average hip, knee angle and toe trajectory during baseline stepping (thick black lines), the step following removal of resistance after 1 step (OFF1-dark gray lines) and after 100 steps with resistance (OFF2-light gray lines) of the left leg. The thin black lines represent +/- SD of baseline across the step cycle. For the angle plots, positive values indicate flexion. All data were normalized in time to 100% of the step cycle. Arrows in the kinematic plots represent the peak flexion angle and toe height used to quantify changes at each joint and the foot. B) Peak hip, knee, and ankle angle and toe height of swing phase. Standard deviation represented by error bars. Asterisks represent statistical significance.
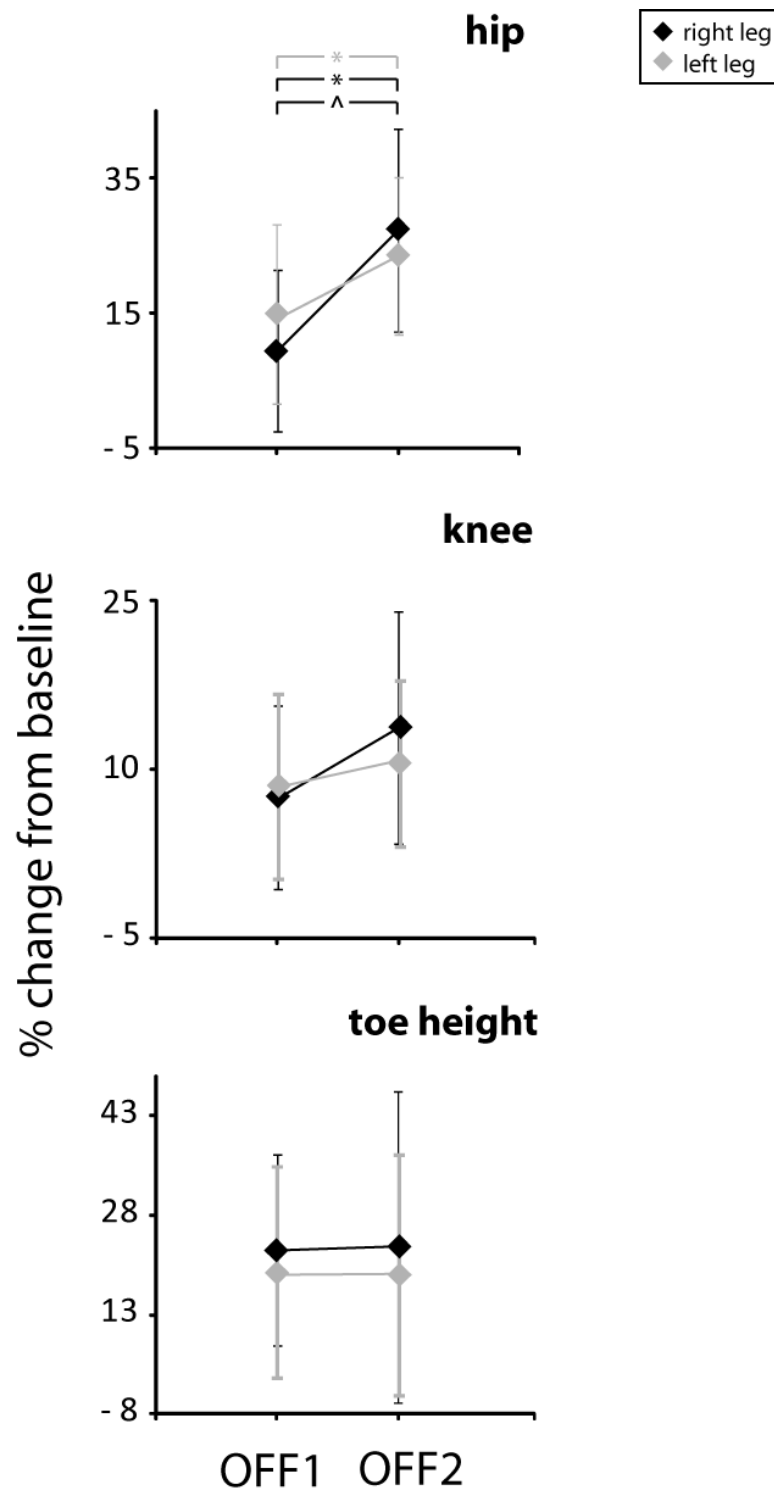
**Figure 8 Change in hip and knee angle and toe height during OFF periods of each leg**
Percent change in hip and knee angle and toe height plotted for OFF1 and OFF2 of each the right (black diamond) and left (gray diamond) legs. Asterisk notation represents statistical significance between OFF1 and OFF2 in each leg. ^ notation represents statistical significance between OFF2R and OFF1L. Standard deviation represented by error bars.

(p=0.00) and left leg (p=0.002). OFF1R vs. OFF1L were not significantly different (p = 0.14) but OFF2R vs. OFF1L were significantly different (p=0.002).

For knee flexion, there was a trend for a main effect of time $(F(1,18) = 3.24, p=0.09)$, no main effect for leg $(F(1,18) = 0.07, p=0.79)$, and no interaction effect $(F(1,18) = 1.82, p=0.19)$. Toe trajectory height also did not have a main effect for time $(F(1,19) = 1.02, p=0.33)$, leg $(F(1,19) = .51, p=0.48)$ or an interaction effect $(F(1,19) = 1.89, p=0.185)$.

Rate of adaptation

A faster adaptation rate in the left leg after previous exposure to resistance in the right leg would indicate the presence of interlimb transfer from the right leg to the left leg. Figure 9 illustrates the step-by-step change in peak hip flexion to steps against resistance in both legs for one subject. The step number in the inset indicates the number of steps required for peak hip flexion to reach within the 95% confidence interval of the last 10 steps against resistance. The average TCA of all subjects (Figure 10) showed a trend towards a faster adaptation rate in the left leg compared to the right however this was not statistically significant $(t = 1.66, df = 19, p=0.114$; right leg : mean = 10.65, SD = 15.03; left leg : mean = 5.40, SD = 5.15). The adaptation rates of each leg were not significantly different from each other.
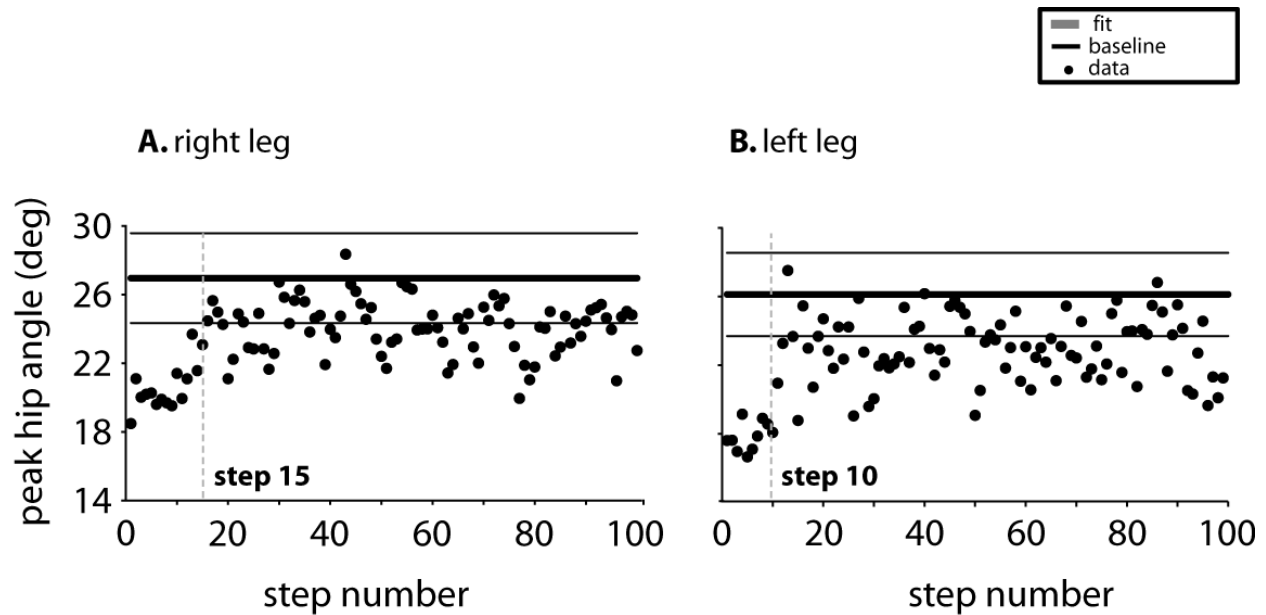
Figure 9 Rate of adaptation to resistance in hip
Peak hip angle for each step taken against resistance in the A) right and B) left leg of a single representative subject. Black thick lines represents average peak of baseline walking for each joint angle. Thin black lines represent +/- standard deviations surrounding baseline. Dotted gray lines indicate the number of steps it took to reach +/-95% confidence interval of the last 10 steps.
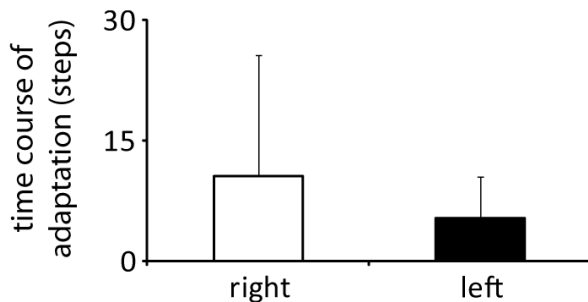
Figure 10 Time course of adaptation during resisted walking
Averaged time course of adaptation-number of steps it took to reach +/-95% confidence interval of last ten steps, in the right and left leg during resisted walking.

Locomotor pattern during washout

In 10 subjects, we tested the possible effects of a washout period after right leg training and prior to the application of resistance during left unipedal walking. No after-effects were present within the first step taken with the left leg. Examination of the first step of

the washout period in left leg indicates no differences (p>0.05) in the lower limb kinematics compared to baseline (Figure 11). Also, it is apparent from Figure 12 that lower limb kinematic patterns remained within baseline values across the duration of the washout period.

A 2 (OFF1, OFF2) by 2 (right leg, left leg) repeated measures ANOVA of lower limb kinematics was performed on the subset of 10 subjects. For hip flexion, there was a main effect of time (OFF1 vs. OFF2) ($F_{(1,9)} = 30.09$, $p<0.001$) but no main effect for leg ($F_{(1,9)} = 0.00$, $p=0.994$) and no interaction effect ($F_{(1,19)} = 3.11$, $p=0.112$).
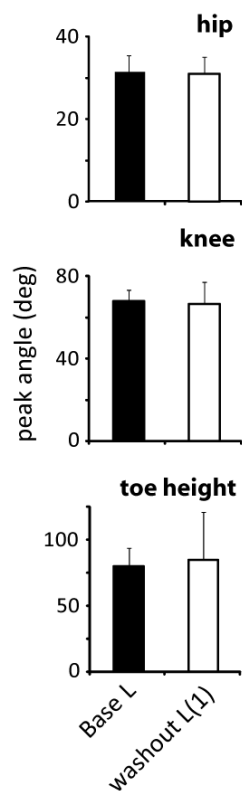
Figure 11 Comparison of first step of washout and baseline of left leg
Peak hip, knee and ankle angle during baseline left leg (Base L) stepping compared to the first step of the washout period of the left leg (washout L(1)).
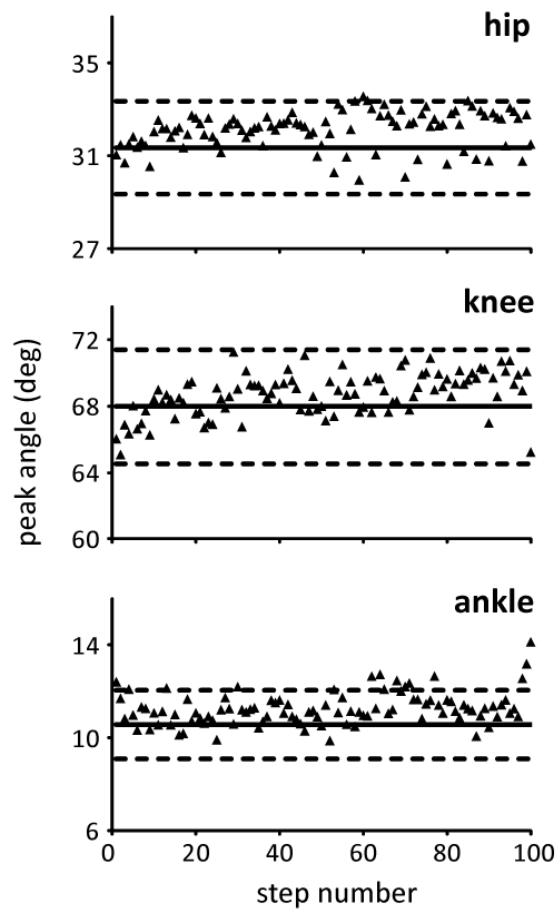
Figure 12 Step-by-step changes in lower limb kinematics during washout
Peak hip, knee and ankle angle across 100 steps taken at the start of left leg unilateral walking before resistance was applied. Average values during baseline walking are depicted as the thick horizontal black lines and +/-SD as the thick dashed lines.

Locomotor-like bursting

Subjects were instructed to keep their stationary leg quiescent during unipedal walking. However, not all individuals were able to accomplish this. To determine if locomotor-like bursting in the stationary leg affected our results, we conducted a secondary analysis where subjects' data were divided into 3 groups according to whether they showed

locomotor-like bursting (n=6), non-locomotor-like bursting (n=12), or no bursting (n=2) (see Methods for definition of the groups). A 2 (OFF1, OFF2) by 2 (right leg, left leg) repeated measures ANOVAs on the percent change in peak hip flexion were performed across the bursting groups. The locomotor-like bursting group showed a main effect of time (OFF1 vs. OFF2) $(F_{(1,5)}=10.24, p=0.024)$ but no main effect for leg $(F_{(1,5)}=0.41, p=0.55)$, and no interaction effect $(F_{(1,5)}=0.013, p=0.92)$. The non-locomotor-like bursting group also showed a main effect of time $(F_{(1,11)}=22.78, p=0.001)$ and no main effect for leg $(F_{(1,11)}=0.603, p=0.45)$, but there was a significant interaction effect $(F_{(1,11)}=7.65, p=0.018)$. Post-hoc testing showed that OFF2 was significantly higher than OFF1 for both the right $(p<0.001)$ and left leg $(p=0.04)$. OFF1R vs. OFF1L were not significantly different $(p=0.13)$, and OFF2R vs. OFF1L were not significantly different $(p=0.05)$.

DISCUSSION

This study examined whether there was interlimb transfer of an acquired motor adaptation to a velocity-dependent resistance applied against hip movements during unipedal walking. Adaptations to resistance were manifested as an immediate increase in RF activity accompanied by changes in peak hip flexion during the swing phase of walking. We found no significant differences in the rate of adaptation to the resistance in the test (left) leg compared to the trained (right) leg. Also, the appearance and magnitude of the after-effects following removal of the resistance were not different across legs. The presence of a washout period or EMG bursting in the stationary leg did not appear to have an effect on the main findings. These results indicate that dynamic motor adaptations in the trained leg did not transfer to the test leg.

Methodological considerations

Unipedal vs. bipedal walking

We tested the training and transfer of locomotor adaptations to resistance using unipedal walking. As previous research has shown, the application of resistance to one leg during bipedal walking may impose differences in kinematic and muscle activity patterns in the non-resisted limb (Savin et al. 2010). It would therefore be difficult to determine whether dynamic adaptations in the second limb exposed to resistance were due to a generalization of a motor program, or a result of the disturbance to that limb

during bipedal walking. Unipedal walking allowed us to isolate training effects to a single limb during walking.

While there were some differences in muscle activity patterns during unipedal walking compared to bipedal walking, lower limb kinematics during unipedal walking were largely the same as those observed during bipedal walking pattern. The most prominent difference in EMG activity between unipedal and bipedal walking is in the BF. The BF demonstrated a marked increase in activity during the stance phase of unipedal walking. During bipedal walking the BF is typically activated during the swing to stance transition, and remains low for the rest of the step cycle. Also, the start of stance in one leg overlaps slightly with the end of stance in the contralateral leg during bipedal walking, providing double support for body weight. Unipedal walking omits the double support phase and all body weight is therefore placed over one leg throughout stance. Greater BF activity during stance likely serves to help support the unipedal stance leg against the full body weight. Despite this difference in EMG activity, hip, knee and ankle joint excursion over the gait cycle of both bipedal and unipedal walking were identical. Furthermore, the response in the RF to resistance was similar to previously observed activity during bipedal walking (Lam et al. 2006). There was an immediate increase in RF activity with the application of resistance that remained significantly above baseline values for the duration of resisted walking. However, the pattern of BF activity with resistance was markedly different in unipedal walking compared to that previously observed during bipedal walking (Lam et al. 2006). Differences in the mechanical demands of unipedal walking, as explained above, likely account for this.

Locomotor-like EMG bursting in the stationary leg

Locomotor-like EMG activity (reciprocal bursting in antagonist muscles) in the stationary leg was observed in 6 subjects. 12 subjects showed bursting in at least 1 muscle of the stationary leg (which we classified as non-locomotor-like activity) and 2 subjects had no EMG bursting in the stationary leg. The results of studies in individuals with complete spinal cord injury suggest that EMG bursting of a stationary leg during unipedal walking is driven by sensory input activating lumbar locomotor circuits (Ferris et al. 2004). In the present study, all subjects were neurologically intact so it is difficult to determine the source of the locomotor-like EMG bursting in the stationary leg. One possibility is that the subjects who showed no bursting may have had exerted more conscious, voluntary control to suppress muscle activity in the stationary leg. The non-locomotor-like activity observed in other subjects could have been due to bracing of the leg in response to minimal vertical downward displacement in the harness. Nevertheless, the amount of bursting did not affect our overall results since we found no systematic difference in the pattern of interlimb transfer of locomotor adaptations between the trained and test leg associated with the presence of bursting activity in the stationary leg.

Temporal component to adaptation

We observed after-effects even after just 1 step against resistance in the right leg (R OFF1), indicating that adaptations developed very rapidly during unipedal walking. This could have been due to the fact that we used a metronome to maintain step cycle

timing. Subjects were instructed to follow the metronome, providing an external source of feedback. The application or removal of the resistance could have changed the temporal aspects of the gait cycle, thus it is possible that attempting to follow the metronome could have enabled a faster adaptation rate.

Feedforward mechanisms

Role of anticipatory motor commands in the control of walking

Results of our study show that after-effects were present with the unexpected removal of resistance during unipedal walking after as little as one step taken with resistance. Hip and knee joint flexion and toe height were all significantly greater than baseline during the swing phase. These data confirm and extend previous research that evaluated the dynamic response to resistance during a motor task. Hip and knee flexor activity during swing increased in response to a 2 kg weight around the lower leg (45-50 strides) (Noble and Prentice 2006) and against Lokomat-applied resistance (within 5 steps) (Lam et al. 2006). Adaptations also occurred in the legs in response to an elastic force field (Blanchette and Bouyer 2009) and at the hip in response to repetitious ankle loading of stance in subjects with incomplete spinal cord injury (iSCI) (Gordon et al. 2009). After-effects were manifested as a further increase in hip and knee flexor activity when the weight was removed (Noble and Prentice 2006), as a high step during the removal of Lokomat-applied resistance (Lam et al. 2006) and a reduction in peak foot velocity and an increase in medial hamstring activity during pre-swing after elastic force

removal (Blanchette and Bouyer 2009). After-effects persisted for 3 minutes upon removal of ankle loading in iSCI (Gordon et al. 2009). Feedforward control was also revealed by the gradual change in BF activation during pre-swing in lokomat resisted walking, a strategy that was thought to help compensate for the swing phase resistance (Lam et al. 2006). In our current experiment, we did not see this pattern of adaptation in BF activity. One possible explanation for this is that the knee joint was not resisted, whereas in previous studies, resistance was applied at the knee as well as at the hip (Lam et al. 2006; Lam et al. 2008). Resistance at the hip appeared to generate variable responses along the kinetic chain. The toe trajectory did not decrease during resistance, as seen in the hip, likely because of the variability in ankle movement, and to ensure foot clearance. However, toe height did increase significantly upon removal of resistance suggesting the formation of feedforward anticipatory programming.

Several lines of research provide evidence that such anticipatory motor commands could be mediated at multiple levels of the CNS. Proprioceptive feedback provides essential input for the formation of feedforward anticipatory control (Pearson 2000). The capacity for anticipatory locomotor adaptations has been observed in spinalized cats (Hodgson et al. 1994) and decerebrated ferrets (Lou and Bloedel 1988) that adapted to the repeated presence of an obstacle on a treadmill and demonstrated after-effects (high step) upon removal of resistance. Further, after-effects with the removal of force were revealed in spinalized rats that adapted to a robotically applied viscous force to the hindlimb during treadmill walking (Heng and de Leon 2007). These studies show that

spinal cord and brainstem structures are capable of producing feedforward commands in quadrupedal animals.

Cortical structures could also be involved in the formation of anticipatory motor commands. The primary motor cortex (M1), located in the pre-frontal cortex, is a structure involved in the cortical, namely volitional, control of movement. It is also thought to be a primary player in predictive movement control (Hwang and Shadmehr 2005). Long-latency reflexes are thought to reveal volitional control via neural pathways to the motor cortex. These reflexes were modified in an arm movement task that involved the anticipation of torque perturbations (Kurtzer et al. 2008). Positron emission tomography (PET) has also been used to demonstrate changes in brain activity associated with motor adaptations. In one study, subjects performed an arm movement task while a PET scan measured the changes in blood flow in response to adaptation to a force field applied via an arm manipulandum (Shadmehr and Holcomb 1997). Results revealed activity in the pre-motor cortex (PMC) during adaptation of the trajectory task and during adaptation to a novel force perturbation 5.5 hours later. Subjects tested for consolidation of the adaptation showed that PMC activation decreased significantly during accurate recall (5.5 hours following task completion) of the original adapted trajectory, while activity in other cortical structures (premotor, posterior parietal and cerbellar cortex) increased. The findings of this study indicate that the PMC is active during the acquisition of an internal model but other brain regions are involved in the consolidation process of that model.

The cerebellum is another supraspinal structure thought to play a significant role in anticipatory movement strategies (Bastian 2006). Indeed, support for this theory has been demonstrated by several studies evaluating motor strategies in patients with cerebellar damage (Bastian 2006). During a split-belt walking task, these patients are capable of feedback related movement but do not demonstrate features of split-belt walking which require feedfoward processing (step length and timing of double support) (Morton and Bastian 2006). Feedforward strategies in patients were also diminished during podokinetic (Earhart et al. 2002) and ball catching (Lang and Bastian 2001) tasks. These studies in adults with cerebellar lesions emphasize the contribution of the cerebellum to internal model formation associated with motor adaptations.

A recent study examined the adaptability to novel force perturbation in developmental abnormalities of the cerebellum. The cerebellum has been established as a site of damage in children with autism (Bauman and Kemper 2005; Fatemi et al. 2002). It therefore follows that impairments in predictive movement strategies could be revealed in subjects with this disorder. However, contrary to this assumption, children with high-functioning autism (HFA) showed no differences in adaptability to a force perturbation in an arm manipulandum task or visuomotor prism goggle task – after-effects were present in both scenarios – compared to children with 'normal' development (Gidley Larson et al. 2008). These results extend previous findings that children with HFA were no different in their ability to adapt to a ball catching task compared to controls (Mostofsky et al. 2004). The authors remark that cerebellar regions devoted to internal model formation are perhaps preserved in children with HFA. However, the delays in other

aspects of motor functioning, commonly observed in autism, may also be a result of damage to other brain regions (e.g. basal ganglia, frontal cortex) implicated in this developmental disorder. Compensations in the cerebellum may also develop in children with HFA and 'normal' motor behaviours could emerge, as opposed to adults that have experienced a cerebellar lesion in which entire regions of the cerebellum are lost (Gidley Larson et al. 2008). This study sheds light on the complexity of cerebellar involvement in internal model formation.

Generalization of motor adaptations

Internal models that develop for a particular movement task are thought to be capable of generalizing to similar, yet novel tasks (Malfait et al. 2002; Mattar and Ostry 2007). Generalizations have been demonstrated to occur across limbs (Savin and Morton 2008; Wang and Sainburg 2004), and this is thought to occur via the 'sharing' or transfer of a stored internal model from one limb to another. Transferring stored motor adaptations reduces time spent acquiring the adaptation in the other limb. By this method, internal models provide a framework by which newly acquired motor adaptations may be transferred across different movement scenarios thereby enhancing efficiency of the motor system. Interlimb transfer of motor adaptations is one example where generalizations could serve to enhance motor adaptations in one limb after previous exposure to an adaptation in the opposite limb.

For walking, there is little evidence that such interlimb transfer of motor adaptations is present. Our results also do not support the existence of interlimb transfer of motor adaptations during walking. The rate of adaptation to resistance in hip trajectory showed a marginal trend towards differences between the legs, however the statistical measures indicate that they were not different and the characteristics of the after-effects were not different between the legs. This is similar to a study that examined after-effects during one-legged hopping over a treadmill to immediate hopping on-the-spot over ground (Anstis 1995). After-effects manifested as forward hopping and were found to occur in the ipsilateral (trained) leg only. The adaptation to forward treadmill hopping on the one leg did not transfer to the contralateral (untrained) leg. Choi and Bastian (2007) also showed that transfer of anticipatory adaptive strategies did not occur between the legs during a split-belt treadmill task that involved one leg moving backwards and the other forwards, simultaneously, or at different speeds (confirming previous findings (Prokop et al. 1995)). It has been argued that each limb has its own central pattern generator and that each is modulated by supraspinal input and interneuronal connections between the legs to promote flexibility in different environments (Choi and Bastian 2007). Together, our results and others suggest that internal models may develop for each leg and there is no transfer of learning between legs during walking tasks.

There is, however, one study that claimed interlimb transfer of a walking task. Van Hedel et al. (2002) showed that there was transfer of 'learning' of an obstacle stepping task over a treadmill. Vision of the oncoming obstacle was blocked and subjects were

provided with an auditory cue that signaled the arrival of the obstacle and provided

feedback about the 'target' foot clearance over the obstacle. Kinematic and lower limb

EMG measures revealed that the adaptation rate in the contralateral test leg was faster

than in the trained leg, indicating that test leg did not have to "re-learn" the target foot

trajectory height over the obstacle. Differences in the nature of the locomotor task could

account for the different findings of the van Hedel (2002) study compared to the hopping

or split-belt studies. It is possible that locomotor tasks that adapt to a specific foot

trajectory (obstacle avoidance) in one leg transfer to the contralateral leg. Also, an

auditory cue for the oncoming obstacle was presented in the obstacle avoidance,

providing a cognitive awareness component that the other studies on interlimb transfer

during walking, as well as the current study, did not include. More cognitive tasks may

facilitate the transfer of motor adaptations.

Leg dominance and interlimb transfer

It was important to consider whether leg dominance could be a factor in interlimb

transfer of the lower limbs. Although leg dominance is not usually a consideration in gait

studies, slight gait asymmetries have been reported in able-bodied individuals (Sadeghi

et al. 2000). However, findings from gait a/symmetry and/or leg dominance studies

remain inconclusive (Sadeghi et al. 2000). In the current study, all subjects were right

leg dominant and the right leg was always the trained leg. Potential differences in

transfer of different directions (right⇔left) were not assessed but nevertheless, we

showed no transfer from dominant to non-dominant leg. Interlimb transfer studies in the

upper limb have examined limb dominance and in particular, handedness. It has long been established that one arm (typically the right) is more dominant (greater strength, dexterity) than the other and that this is reflected cortically (Goble and Brown 2008). The direction of transfer appears to vary depending on the task and whether the dominant or non-dominant arm is trained first (Goble and Brown 2008). Interlimb transfer was demonstrated in both directions during a ball catching task with differently weighted balls (Morton et al. 2001). Frak (2006) showed transfer from the dominant to non-dominant hand during an upper limb reaching-to-grasp task. But transfer from the non-dominant to dominant arm has also been demonstrated during upper limb tasks using force perturbation (Criscimagna-Hemminger et al. 2003; Wang and Sainburg 2004) or visuomotor rotation paradigms (Sainburg and Wang 2002). Thus, the contribution of dominance on interlimb transfer remains open.

It has been postulated that adaptations may be more readily transferable from the dominant limb to the non-dominant, or vice versa, and may also depend on the type of adaptation elicited (Wang and Sainburg 2004). Inter-hemispheric asymmetries in the specialization of specific movement features are thought to underlie this phenomenon (Wang et al. 2010). The *dynamic dominance hypothesis* proposes that, for right hand dominant individuals, the dominant hemisphere specializes in the dynamic properties of a complex movement task (e.g. limb trajectory during reaching) and the non-dominant hemisphere for static, posture-related goals (e.g. target accuracy) (Sainburg and Wang 2002). To demonstrate this theory, right hand dominant subjects were tested in a simple visuomotor interlimb transfer task with a 30 degree visual display shift. Subjects were

randomized into two training groups: those that underwent right (dominant) arm training first and those that underwent left (non-dominant) arm training first. Interlimb transfer of learning occurred in both directions, but careful examination of the features of the movement showed that the transfer effects were manifested differently. Improvements in movement trajectory were better transferred to the dominant arm (i.e. train left side first; test on right) but position accuracy (final position to target) were better transferred to the non-dominant arm (i.e. train right side first, test on left). The authors suggested that if the left arm is trained first, it has access to information about the dynamic movement-related features (e.g. trajectory) from the dominant ipsilateral (left) hemisphere to help complete the task, which will readily transfer to the right dominant arm (Sainburg 2005; Wang et al. 2010). Conversely, transfer of static-related features (e.g. end-point position) to the left non-dominant arm will occur via the non-dominant (right) hemisphere because the initial right arm had access to those features during training. Imaging studes that have demonstrated activation of ipsilateral M1 during a unilateral upper limb movement task provide support for the proposed mechanism of transfer for specific movement features (Chen et al. 1997; Gitelman et al. 1996).

There is other evidence from non-locomotor tasks that leg dominance could play a role in lower limb motor adaptations. Morris et al (2009) tested both directions of transfer of a visuomotor task in the lower limbs. Transfer of ankle motor control was demonstrated to occur from the non-dominant foot (left) to the dominant foot (right). Movement of the feet placed in an ankle potentiometer device was reflected by a cursor in the vertical (dorsi-plantar) and horizontal (e/inversion) displacement on a computer screen.

Subjects aimed towards a target with a cursor that was 30 degrees counter-clockwise to ankle movement with one foot. A decrease in measurement error in both position and direction was demonstrated in the right (test) foot (initial left side training), this did not occur if the test foot was non-dominant (initial right side training). The transfer of trajectory control from left to right limb was consistent with the *dynamic dominance hypothesis*, but the fact that there was also left to right transfer of final position accuracy is inconsistent with this theory. The authors of this study argued that each leg may utilize both dynamic and final position accuracy because the gait cycle (which both legs have to perform equally) require each parameter (Morris et al. 2009). Differences in upper and lower limb hemispheric/corticomotoneuronal control were also suggested as a possible explanation for the discrepancy with the *dynamic dominance hypothesis* (Morris et al. 2009). However, upper limb reaching movements and locomotion have previously been argued to share similar neural correlates (Georgopoulos and Grillner 1989). The coordination of joint movement during a reaching task is considered to have evolved from locomotion (Georgopoulos and Grillner 1989). Likewise, the control of foot trajectory during walking may also be considered as a precision, target task, albeit a dynamic one (Winter 1992).

The question of whether the *dynamic dominance hypothesis* applies during walking and whether it could be used to explain the results of our study remains open. In our study, transfer may have occurred from right to left for final position accuracy, but this measure was not assessed directly. Outcome measures were dynamic (movement trajectory) and subjects were not provided with specific instructions to control certain features of

their lower limb movements during walking. One could argue that the perturbation we used here would have required adaptations in both movement trajectory (e.g. trajectory of the foot during swing) as well as control over the final position (e.g. position of the foot at the end of swing to prepare for weight-bearing) repeatedly with each gait cycle. Perhaps future studies comparing left-right vs. right-left interlimb transfer could shed light on whether these different movement features are also differentially controlled during human walking.

Future directions

Testing the transfer of dynamic motor adaptations in both directions will help to verify whether the *dynamic dominance hypothesis* exists during walking. In addition, some of the methodological issues raised should be addressed. Less resistance (< 10%) to the hip may reduce the adaptation rate in our unipedal walking paradigm. It is possible that the unipedal walking setup introduced a level of novelty to our subjects that contributed to the adaptation rate to resistance. Further investigations aimed at exploring motor outcome measures in this setup may provide insight into the adaptation process of unipedal walking. The rate of adaptation may also be slower if step cycle timing is not restricted via a metronome. Application of resistance to both the hip and knee may induce a slower adaptive response as well and, in addition, generate adaptations in the lower leg that were not observed in this study. Alternatively, interlimb transfer paradigms could be assessed during bipedal walking as a large body of literature exists for this walking pattern.

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