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Walking Adaptation, Training and Assessment in Young Children and Individuals with Incomplete Spinal Cord Injury

by

Kristin Elizabeth Musselman

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Examining Committee

Jaynie Yang, Physical Therapy

Monica Gorassini, Biomedical Engineering

Arthur Prochazka, Physiology

Kelvin Jones, Physical Education and Recreation

Nigel Ashworth, Medicine

Linda Fetters, Biokinesiology and Physical Therapy, University of Southern California

Abstract

This thesis includes four projects that examine motor learning and assess novel approaches for the training and evaluation of walking. In Project 1 we study motor adaptation in children aged 8-36 months using a split-belt treadmill. Split-belt walking, in which one leg moves faster than the other, causes asymmetries in interlimb coordination. Adaptation is manifest as decreases in the asymmetries with practice, and an aftereffect (i.e., asymmetry in the opposite direction) upon the return to normal treadmill walking. Most children showed adaptation in double support time (temporal measure of interlimb coordination), but fewer showed adaptation in the spatial measures of step length and centre of oscillation. Hence, the mechanisms controlling adaptation of temporal coordination may mature before those controlling spatial coordination. In Project 2 we studied interlimb coordination and long-term training in infants aged 3-10 months. We found that most infants expressed the same type of coordination (i.e., alternate or synchronous) when kicking, a non-weight bearing movement, and when weight bearing on the treadmill. We also showed that daily practice of the non-preferred coordination in weight bearing for 1 month changed the preferred coordination for non-weight bearing movements. These findings suggest there is partial sharing of neural substrates for interlimb coordination of different leg movements in infants. In Project 3 we compared 2 methods of walking training – body weight-supported treadmill training (BWSTT) and an over-ground method involving challenging practice of relevant walking skills (called skill training). Four individuals with chronic incomplete spinal cord injury (ISCI) completed 3 months of BWSTT

followed by 3 months of skill training, or vice versa. We found skill training to be as effective as BWSTT at improving walking skill, speed, endurance and confidence. In Project 4 we developed a new measure of walking for ISCI, called the Spinal Cord Injury Functional Ambulation Profile (SCI-FAP). It involves the timed performance of 7 common walking tasks. The SCI-FAP has high inter-rater and test-retest reliability, and discriminative and convergent validity. Collectively the findings of this thesis will contribute to the optimization of walking training programs for adults and children with damage to the central nervous system.

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Chapter 1: Literature Review

Walking is a symmetrical, rhythmic movement that requires precise coordination of the muscles and joints of the legs, pelvis, trunk and arms. The goal of walking is to move the center of gravity through space in an energy-efficient manner (Saunders et al. 1953). In order to walk successfully, we must: 1) step with our legs in an alternate fashion, 2) maintain equilibrium during forward propulsion, and 3) adapt our walking pattern in response to our behavioral goals and the environment (reviewed in Barbeau 2003, van Hedel 2006). Walking results from a combination of biomechanical events under central nervous system (CNS) control. With the swing and stance legs behaving as pendulums and inverted pendulums, respectively, forward propulsion through the passive dynamics of the limbs is possible (reviewed in Kuo and Donelan 2010). However, significant contributions from spinal, supraspinal and afferent sources, and their complex interactions (reviewed in Nielsen 2003, Zehr and Duysens 2004) ensure that all the prerequisites for successful walking are met.

There are few motor behaviors that we perform more often than walking. It is not surprising then, that regaining the ability to walk is a top priority for individuals who have experienced injury or disease to the central nervous system (CNS) (Andersen 2004, Lord et al. 2004, Ditunno et al. 2008). For these individuals, re-learning this skill can be a difficult, lengthy and resource-intensive process. More effective therapies for walking will result if we have a better understanding of how the nervous system controls walking and learns walking movements. We also need valid and reliable measures of walking to accurately gauge walking ability and the effectiveness of training programs. This thesis includes four projects that examine motor learning in the context of walking, and assess novel approaches for the training and evaluation of walking after an incomplete spinal cord injury (ISCI).

In this chapter we review the related work. Much of what we know about the neural control and learning of walking has come from study of non-human vertebrates; however, work involving humans is emphasized and reviewed whenever possible. Sections 1.1 and 1.2 review the literature on short-term and longer-term motor learning, respectively, as it relates to walking. In section 1.3 we discuss what is known about motor learning in young children. Section 1.4 describes walking training for individuals with ISCI, while section 1.5 reviews the requirements of daily walking, as well as the measures used to assess walking ability. The research of this thesis is summarized in section 1.6.

1.1 Short-term Adaptations of Walking Movements

Compared with upper extremity movements, relatively little is known about how humans learn walking behaviors. Without this knowledge, we cannot train walking in an optimal way. Motor learning is broadly defined as the acquisition of a motor skill. Learning is a continuum, from short-term adaptations (reviewed below) to long-term, persistent changes in behavior (reviewed in section 1.3) (reviewed in Davidson and Wolpert 2003). The process of learning involves modifications of neural circuitry that manifest as changes in motor behavior.

Reactive Adaptation of Walking

Unpredictable, sudden changes in walking conditions can result in temporary adaptations of the walking pattern. These adaptations can result from predictive control (discussed below) or reactive control (reviewed in Wolpert and Flanagan 2010). Reactive responses occur immediately upon exposure to the perturbation, and they do not persist once the perturbation is removed. Thus, they may be a direct consequence of sensory feedback or, in some cases, volition. An example of a reactive response is the stumbling corrective reaction - a touch to the foot (Schillings et al. 1996, Lam et al. 2003) or electrical stimulation of the superficial peroneal nerve (Zehr et al. 1997 and 1998) during the swing phase of walking results in increased flexion of the limb. This response to cutaneous input is dependent upon the location of the stimulation, the timing of the stimulation with respect to the gait cycle, and whether or not it impedes stepping behaviour (Eng et al. 1994, Zehr et al. 1997 and 1998, Schillings et al. 2000, Lam et al. 2003). Likewise, timing of the stance to swing transition is altered in a reactive fashion with perturbations to hip position or the load experienced by the leg of spinal and decerebrate cats (reviewed in Pearson 2008) and human infants (Pang and Yang 2000). When velocity-dependent resistance is applied to one leg during walking, there is an immediate increase in the activity of ipsilateral rectus femoris and tibialis anterior muscles during mid-swing (Lam et al. 2006). And when one walks on a split-belt treadmill, coordination within a limb, reflected by measures of stride length and stance time, adapt instantaneously (Reisman et al. 2005). Reactive responses contribute to the preservation of locomotion, but do not reflect learning. Typically, the responses disappear as soon as the disturbance is removed.

Predictive Adaptation of Walking

Predictive adaptation involves modifying a pre-existing motor skill to accommodate a novel environment or movement context. The modified motor program emerges after seconds to minutes of trial-and-error practice (reviewed in Reisman et al. 2010), ensuring that the walking pattern adjusts to perturbations in a timely fashion. One of the first to study predictive adaptation during walking was Lou and Bloedel (1988). While decerebrate ferrets walked over-ground, a bar was repeatedly presented in the forelimb trajectory during the swing phase. Initially the forelimb hit the bar. With practice, the ferrets showed increased elbow flexion to clear the bar, allowing successful locomotion to continue. This response occurred over 5-15 cycles and persisted even after the removal of the bar.

The driving force behind predictive adaptation is error-making (Shadmehr and Mussa-Ivaldi 1994, Kawato 1999). Movement error results when a motor task is changed in some way and the predicted outcome was not met. This error is the catalyst for gradual modifications to the motor program (adaptation). Following adaptation, when we are presented with the original motor task (often called the washout condition), the modified motor program is expressed and movement error results, this time in the opposite direction (aftereffect). Aftereffects are a hallmark of motor adaptation as they suggest that a modification of the motor output has been acquired and stored (Shadmehr and Mussa-Ivaldi 1994, Bastian 2006). This likely coincides with some transient change in underlying neural processes, such as altered synaptic efficacy. Aftereffects persist until the modified program is unlearned (de-adaptation). De-adaptation occurs more quickly when one has previous experience with the perturbation (Davidson and Wolpert 2004, Huang and Shadmehr 2009).

To study predictive adaptation in human adults, novel walking mediums are created by perturbing the forces (Emken and Reinkensmeyer 2005, Noble and Prentice 2006, Lam et al. 2006, Gordon and Ferris 2007, Blanchette and Bouyer 2009) or kinematics (Gordon et al. 1995, Prokop et al. 1995, Weber et al. 1998, Jensen et al. 1998, Earhart et al. 2001, Reisman et al. 2005) of walking. In these situations, the walking pattern adapts to preserve successful locomotion.

Lam and colleagues (2006) used a robotic gait orthosis to apply velocity-dependent resistance to a subject's left hip and knee during the early swing phase. They observed a gradual increase (over 5-7 steps) in ipsilateral biceps femoris and medial hamstrings activity during pre-swing. This adaptation was present during the catch trials and persisted for 30-40 steps during the washout period, hence it is a feedforward or predictive response. Likewise, Blanchette and Bouyer (2009) reported gradual adaptation of, and aftereffects in, peak foot velocity and hamstrings activity in the leg that experienced an elastic force field while subjects walked on a treadmill.

After podokinetic adaptation (i.e., walking adaptation that results from walking on a horizontally rotating disc) subjects were unable to maintain a straight trajectory when blindfolded and asked to either walk straight over-ground (Gordon et al.

1995, Earhart et al. 2001) or step in place (Weber et al. 1998). The stepping trajectory gradually returns towards pre-adaptation values after a number of attempts (Gordon et al. 1995). The aftereffects of podokinetic adaptation, acquired during forwards walking, are seen in backwards walking (Earhart et al. 2001) and hopping (Earhart et al. 2002b), but not in a wheelchair propulsion task (Gordon et al. 2995). The generalization of learning to new movements or situations is called transfer, and it may suggest common elements in the neural control of the movements (Morton and Bastian 2004, Choi and Bastian 2007). Transfer is complete if the aftereffects in two situations are identical.

Bastian and colleagues have used a split-belt treadmill to study predictive adaptations of walking. In able-bodied subjects they found that changes in the coordination of the two legs, as reflected in the measures of double support time and step length (interlimb measures), were under predictive/feedforward control (Reismann et al. 2005). Walking adaptation on such a treadmill is specific to the leg trained (Prokop et al. 1995, Choi and Bastian 2007), the direction of walking (Choi and Bastian 2007), the speed of the slow belt during training (Vasudevan and Bastian 2010), the load-related sensory input received during training (Jensen et al. 1998), as well as the environment, in most cases (Reisman et al. 2009). There was little transfer of aftereffects from the split-belt treadmill to over-ground walking in able-bodied subjects or stroke clients with mild gait asymmetries, but more robust transfer was seen in clients with significant gait asymmetries (Reisman et al. 2009).

Neural control of Predictive Adaptations

The cerebellum is an important contributor to motor tasks, like walking. When walking, the cerebellum receives input about leg movement through the dorsal spinocerebellar pathways (Poppele et al. 2003, Bosco et al. 2005, 2006, reviewed in Bosco and Poppele 2001), as well as information from spinal locomotor circuitry through ventral spinocerebellar pathways (Arshavsky et al. 1978). The cerebellum is therefore in a position to use this sensory information to compare actual movement with the predicted movement (reviewed in Arshavsky et al. 1983, Grillner 1985, Armstrong 1986, Bastian 2006). When there is a mismatch between the two, the cerebellum makes refinements to the motor output through descending connections with motoneurons (Arshavsky et al. 1984, reviewed in Grillner 1985, Armstrong 1986), possibly with the aim of optimizing motor output (i.e., minimizing effort) (Criscimagna-Hemminger et al. 2010).

There is considerable evidence to suggest that the cerebellum plays a significant role in predictive adaptations of eye and upper extremity movements (Baizer et al. 1999, Martin et al. 1996, Imamizu et al. 2000, Xu-Wilson et al. 2009, Criscimagna-Hemminger et al. 2010). Not only is it involved in the short-term process of adaptation, but it also contributes to the storage of the new motor program (Shadmehr and Holcomb 1997, Imamizu et al. 2000, Nitschke et al. 2004). Likewise, the cerebellum is crucial for walking adaptations (Earhart et al. 2002a, Morton and Bastian 2006). Individuals with cerebellar damage can make reactive, but not predictive adaptations to their walking pattern when stepping on a split-belt treadmill (Morton and Bastian 2006). The extent of cerebellar damage appears to affect the ability to learn – those with greater damage show larger deficits in learning (Maschke et al. 2004, Morton and Bastian 2006, Criscimagna-Hemminger et al. 2010).

Strong evidence for the role of the cerebellum in predictive adaptation has come from work in decerebrate cats. When these cats walk on a split-belt treadmill, the firing rates of Purkinje cells in the lateral vermis increase significantly (Yanagihara and Udo 1994). When decerebrate cats are deprived of nitric oxide, which impairs cerebellar long-term depression, adaptation to split-belt treadmill walking is not seen (Yanagihara and Kondo 1996). In humans, the posterior and lateral cerebellum are active during predictive adaptation of arm movements (activity decreases as movement error decreases), as revealed in several imaging studies (functional magnetic resonance imaging (fMRI) - Imamizu et al. 2000, positron emission tomography - Nezafat et al. 2001).

Cerebral structures seem less essential for predictive adaptation. Decerebrate cats can successfully adapt their walking pattern when walking on a split-belt treadmill (Yanagihara et al. 1993), as can individuals with stroke (Reisman et al. 2007). Children with hemisherectomy, however, show an impaired ability to adapt the temporal measure (i.e., double support time), but not spatial measure (i.e., step length) of interlimb coordination (Choi et al. 2009). Since deficits in adaptation are only apparent with extensive damage to the cerebral cortex, it suggests the cerebrum does not play an essential role in motor adaptation.

Work in animals suggests that the spinal cord is capable of simple, short-term adaptation. Hodgson and colleagues (1994) placed a bar in front of the forelimbs of spinal cats stepping on a treadmill. The spinal cats showed an adaptive response (i.e., hyperflexion of the limb) with short-lasting aftereffects. Edgerton and colleagues used an external force field to perturb the locomotion of spinal rats (Timoszyk et al. 2002, de Leon et al. 2002). Temporal and spatial adaptations in stepping were seen almost immediately after application of the force, and upon removal of the perturbation aftereffects were present for about 3 steps.

1.2 Long-term Learning of Walking Following Injury

Longer-term motor learning is characterized by persistent changes in motor ability with underlying modifications in neural circuits (Nudo et al. 1996). It involves adaptive processes, offline learning, and the consolidation and storage of motor memories (reviewed in Reisman et al. 2010). The catalyst for long-term learning is a relatively permanent change in walking conditions, which can be internally-driven (i.e., injury of the individual) or externally-driven (i.e., repetitive exposure to novel walking conditions).

Permanent changes in walking ability have been repeatedly demonstrated in various animal models following injury to peripheral (Carrier et al. 1997, Whelan and Pearson 1997, Bouyer et al. 2001) or central (Eidelberg et al. 1980, Jiang and

Drew 1996, Courtine et al. 2005, Lavrov et al. 2006) nervous structures. Following a neurectomy of one or more nerves supplying hindlimb muscles, intact cats, as well as cats that subsequently undergo decerebration or spinalization, are capable of regaining almost normal stepping patterns 2-8 days post-neurectomy, without any locomotor-specific training (Carrier et al. 1997, Whelan and Pearson 1997, Bouyer et al. 2001). This may suggest that the neural plasticity associated with learning can occur at whichever neural level is available, supraspinal or spinal. Likewise, recovery of stepping ability is possible following a lesion of the spinal cord in cats (Eidelberg et al. 1980, Jiang and Drew 1996), rats (Lavrov et al. 2006), mice (Leblond et al. 2003), turtles (reviewed in Stein 2005), young rabbits (Fayein and Viala 1976) and monkeys (Courtine et al. 2005).

Long-term Learning Following Motor Experience

Motor experience and long-term training (i.e., days to weeks) post-injury to the CNS are crucial for the recovery of any walking ability (Langhorne et al. 2009, van Hedel and Dietz 2010). Locomotor training, often presented in the form of treadmill training, after an injury of the nervous system improves walking ability in animals and humans. Spinalized cats (de Leon et al. 1998) and rats with ISCI (Heng and de Leon 2009) trained to step show better stepping ability than their untrained counterparts. Treadmill training has positive effects on many aspects of walking (i.e., kinematic and motor patterns, efficiency, speed and endurance) in individuals with spinal cord injury (Wernig et al. 2000, Field-Fote and Tepavac 2002, reviewed in Barbeau et al. 2002), stroke (Visintin et al. 1998, Sullivan et al. 2002), cerebral palsy (Schindl et al. 2000) and Parkinson's disease (Miyai et al. 2000, 2002).

Like motor adaptation, long-term learning of walking is also specific to the task trained. Spinal cats trained to step improve their ability to step, but not stand, and *vice versa* (Edgerton et al. 1997). Edgerton and colleagues (1997) also demonstrated that expression of the learned movement is specific to the sensory input experienced during training. In humans with ISCI, several months of training forwards walking on a treadmill did not result in an improved ability to step backwards or step in place (Grasso et al. 2004). Backwards stepping was successful only after 2-3 weeks of backwards walking practice.

Training in varying environments and under variable conditions is beneficial for the learning of upper extremity movements (Shea and Morgan 1979, Catalano and Kleiner 1984, Hanlon 1996). Recent work in spinal mice suggests that variable training may also benefit walking training (Cai et al. 2006). Spinal mice were trained to step on a treadmill with a robotic arm assisting hindlimb movements. Following 6 weeks of training, stepping recovery was greatest in mice whose hindlimb trajectory was not fixed by the robot. The authors proposed that variety in the activation of spinal circuits optimized the effectiveness of training (Cai et al. 2006).

Walking gains made with training will not persist without regular use of the learned skill (individuals with ISCI - Wernig et al. 1998, Wirz et al. 2001, Field-Fote et al. 2005, Hicks et al. 2005). Twelve weeks after the cessation of step training, spinal cats could no longer step on a treadmill (De Leon et al. 1999a). The authors suggested a 'forgetting' of the learned behavior occurred in the spinal cord. Yet, a memory of stepping must have remained stored since after only 1 week of retraining, the cats regained the ability to step. Work involving humans learning a backwards walking task also showed that following a break in training, the relearning process occurred more quickly than the original acquisition (Schneider and Capaday 2003).

Neural Changes Underlying Long-term Motor Learning

Considerable effort has gone into identifying the neural mechanisms underlying long-term locomotor training. Voluntary exercise of the limbs increases the levels of several neurotrophins (i.e., brain-derived neurotrophic factor and neurotrophin 3) in the spinal cord of spinal cord-injured rats (Ying et al. 2003, 2005).

Neurotrophins are a family of molecules that support and promote the survival of neural tissue. Work in spinal cats has found that stepping training reduces glycinergic inhibition (de Leon et al. 1999b) and levels of GAD_{67} (an enzyme important for the synthesis of GABA) in the spinal cord (Tillakaratne et al. 2002), bringing both closer to levels seen in healthy animals. Both glycine and GABA are important neurotransmitters for the generation of stepping movements (Tillakaratne et al. 2002, Nakayama et al. 2004).

Walking training affects several spinal reflex pathways. For example, changes in load-related (Côté et al. 2003) and cutaneous (Côté and Gossard 2004) reflex pathways accompanied improvements in stepping gained by spinal cats through locomotor training. Frigon and Rossignol (2008) studied changes in reflex responses, evoked by tibial nerve stimulation, during locomotion in cats before and after spinalization followed by locomotor training. They found a switch from short latency inhibition to short latency excitation in ankle extensors during stance after injury and training. In healthy humans, activity of the soleus H-reflex was changed with 10 days of backwards walking training (Schneider and Capaday 2003). Depression of the soleus H-reflex was seen in spinal-cord injured humans after single (Trimble et al. 2001) and multiple (Trimble et al. 1998) training sessions on a treadmill, however, walking training had no effect on paired reflex depression of the soleus H-reflex in individuals with ISCI (Phadke et al. 2009). Paired reflex depression – the reduction in size of the second H reflex when 2 stimuli are presented successively - is thought to result from presynaptic mechanisms involved with neurotransmitter release from Ia afferents (Hultborn et al. 1996).

Long-term training also induces changes in higher centres of the nervous system. Physical activity promotes angiogenesis in the motor cortex of rats, but exercise alone does not alter the area of motor maps in the cortex (Kleim et al. 2002). Kleim and colleagues (1996) showed that rats that underwent ‘acrobatic’ locomotor training (i.e., negotiating obstacles) showed a greater number of synapses/neuron and more Fos-positive neurons in layers II and III of the motor cortex than rats trained on an obstacle-free runway or inactive rats. Thus more challenging or complex training may lead to greater neural modifications. Humans with spinal cord injury who participate in treadmill training show increased descending drive to leg muscles (Thomas and Gorassini 2005, Norton and Gorassini 2006), and increased activation of the sensorimotor cortical areas and cerebellum during ankle and toe movements, as measured by fMRI (Winchester et al. 2005).

1.3 Motor Learning in Young Children

Little is known about the neurophysiology of learning motor tasks, like walking, in young children. Yet, like young animals (Smith et al. 1982 – spinal kittens), young children have great potential for walking recovery with training (Prosser 2007, Behrman et al. 2008, Mattern-Baxter et al. 2009, Fox et al. 2010). Simple perturbations to walking have been studied in very young children. Pang and colleagues (2003) gave infants a light tap on the dorsum of one foot during the swing phase of supported walking on a treadmill. An immediate adaptation (i.e., increased hip and knee flexion) was observed in all infants. An aftereffect was present in 45% of the infants tested. The aftereffect was more prevalent in infants who were 9 months of age or older, suggesting that some neural substrate(s) needed for learning was mature in the older infants, but not the younger ones. Similarly, Lam and colleagues (2003) studied infants' ability to adapt to a weight attached to one leg. They reported aftereffects (i.e., high-stepping) in ~1/3 of the infants tested.

Jansen-Osmann and colleagues have studied adaptation of upper extremity movements in response to external forces in children. Children as young as 4 years old show aftereffects, however, the length of time to adapt and subsequently de-adapt increases with decreasing age (Jansen-Osmann et al. 2002, Konczak et al. 2003). Interestingly, children show a heightened ability to transfer the learned skill to a novel environment, when compared with adults (Jansen-Osmann et al. 2002).

Infants as young as 3-4 months can learn new kicking patterns. Intralimb (Chen et al. 2002) and interlimb (Thelen 1994) coordination of the legs can be changed through reinforcement learning with a mobile. This type of learning is likely under more volitional control than the walking adaptations described by Pang et al. (2003) and Lam et al. (2003), and could explain why Chen and colleagues (2002) saw learning at an earlier age in their subjects.

1.4 Training Walking after Spinal Cord Injury

Walking after ISCI

More than half of individuals who sustain an ISCI regain some walking function (Waters 1994a,b), although it is often limited. Their speed and endurance is low compared with able-bodied individuals (Lapointe et al. 2001). They have difficulty adjusting their speed (Pepin et al. 2003), and they use different kinematic strategies for tasks, such as stepping over obstacles (Ladouceur et al. 2003, reviewed in Barbeau et al. 2002) and walking up an incline (Leroux et al. 1999). Individuals with ISCI devote more attention to their walking than able-bodied counterparts (Lajoie et al. 1999), and they place greater reliance on vision for tasks like negotiating obstacles (van Hedel et al. 2005). Some walk with a dropped foot resulting from impaired function of the corticospinal tract (Barthélemy et al. 2010). Given these impairments in walking, it is not surprising that about 75% of individuals with ISCI experience at least one fall per year (Brotherton et al. 2007). Furthermore, their participation in walking is low compared with able-bodied adults. They take significantly fewer steps/day (average of 2 600 steps/day (Saraf et al. 2010) compared with an average of 11 075 steps/day in healthy, young adults (Cavanaugh et al. 2007)) and perform fewer walking skills, such as walking and negotiating doors, obstacles, sloped and uneven surfaces, intersections, and stairs (Musselman and Yang 2007).

Central Pattern Generator for Walking

Walking training for individuals with ISCI has been influenced by work concerning the neural control of locomotion in invertebrates and non-human vertebrates. Walking in many insects and animals is believed to be controlled, in part, by neuronal circuits, called central pattern generators (CPG), that produce the rhythmic muscle contractions needed for walking with little to no sensory or supraspinal input (Brown 1911, reviewed in Pearson 1993, Grillner et al. 1998, Dickinson et al. 2000, Delcomyn 2004). The locomotor CPG is thought to reside in the spinal cord of vertebrates (Langlet et al. 2005, reviewed in Grillner 1981). Researchers studying the CPG in spinal cats discovered that these cats could relearn to step following intensive training on a treadmill with partial body weight support (Smith et al. 1982, Lovely et al. 1986, Barbeau and Rossignol 1987). It is thought that treadmill training activates the locomotor CPG in spinal cats, enabling them to step. This led researchers to question whether the same therapy would be effective in humans with spinal cord injury.

It is not clear whether a locomotor CPG exists in humans. Supporting evidence comes from studies involving humans with spinal cord injury and human infants. There have been numerous reports of individuals with complete spinal cord injuries (i.e. no descending or sensory input) showing stepping-like movements either spontaneously (Holmes 1915, Kuhn and Macht 1948, Nadeau et al. 2010), with electrical stimulation of flexor reflex afferents (Bussel et al. 1996), or with epidural stimulation of the posterior lumbar cord (Dimitrijevic et al. 1998).

Likewise, human infants are capable of stepping from birth if they are supported and moved over a solid surface (André-Thomas and Autgaerden 1966) or held over a treadmill belt (Forssberg 1985, Yang et al. 1998). This behavior is seen in utero as early as 10-14 weeks gestation (De Vries et al. 1984). These stepping movements are thought to be controlled by the spinal cord and/or brainstem since descending inputs from the motor cortices are weak in young children. Maturation of the cerebrum continues after birth (growth of dendrites - Marin-

Padilla 1970, changes in cell density - Amunts et al. 1995, maturation of synapses - Huttenlocher 1979, 1994, and development of myelin - Yakovlev and Lecours 1967, Lebel et al. 2008). Autopsy (Yakovlev and Lecours 1967, Brody et al. 1987) and electrophysiological (Eyre et al. 1991, Khater-Boidin and Duron 1991, Szelenyi et al. 2003) findings suggest the corticospinal tract, an important descending pathway for walking in humans (reviewed in Petersen et al. 2003), is not fully myelinated for some time after birth. Furthermore, anencephalic infants show some stepping movements (Peiper 1961). Thus, taken together the work in individuals with complete spinal cord injuries and human infants support the existence of a CPG for locomotion in humans, however, the evidence is indirect.

Body Weight-Supported Treadmill Training

Walking training after ISCI often includes body weight-supported treadmill training (BWSTT). This training involves walking on a treadmill with a portion of the body weight supported by an overhead-harness system. Unloading the lower extremities during training promotes a more normal gait pattern (Visintin and Barbeau 1989). Load is increased as the gait pattern improves. Therapists provide manual assistance to the client during treadmill stepping to promote normal posture and lower extremity trajectories (Hornby et al. 2005, reviewed in McDonald and Sadowsky 2002). The training is intensive, occurring 3-5 times/week for 2-3 months (Barbeau et al. 1993, Wernig et al. 1995, Gardner et al. 1998, Protas et al. 2001, Dobkin et al. 2003, reviewed in McDonald and Sadowsky 2002). Treadmill walking is thought to activate and strengthen the spinal circuits involved in locomotion by providing the appropriate rhythmic sensory cues (i.e., loading of the legs and extension of the hips) (Calancie et al. 1994, Dietz and Harkema 2004, reviewed in McDonald and Sadowsky 2002). It also reorganizes and strengthens supraspinal circuits involved in walking (Thomas and Gorassini 2005, Winchester et al. 2005, Norton and Gorassini 2006).

BWSTT improves body alignment (Visintin and Barbeau 1989), intralimb coordination (Field-Fote and Tepavac 2002), and electromyographic activity of the legs during stepping (Dietz and Harkema 2004, Gorassini et al. 2009). It increases stride length and single-limb support duration (Visintin and Barbeau 1989), and lowers the oxygen cost of walking (Protas et al. 2001). The effects of treadmill training translate to more functional gains too, as it is effective at improving over-ground walking speed and endurance in individuals with ISCI (Wernig et al. 2000, reviewed in Harkema 2001, Barbeau et al. 2002). The motor benefits of BWSTT are only seen in individuals with incomplete injuries, thus some descending input is needed for successful outcomes (Wernig et al. 1992, Dietz et al. 1994). Improvements in walking ability with treadmill training can be enhanced by combining the therapy with drugs (i.e., noradrenergic agonists) (Fung et al. 1990, Barbeau and Norman 2003), epidural stimulation of the spinal cord (Herman et al. 2002, Carhart et al. 2004) or functional electrical stimulation (Field-Fote 2001). Additional benefits of treadmill training include a reduction in spasticity (Dietz 2001, Gorassini et al. 2009), improvements in cardiovascular function (Ditor et al. 2005), blood glucose regulation (Phillips et al. 2004), and maintenance of bone density (de Bruin et al. 1999) and muscle properties (Stewart et al. 2004).

Few studies compare treadmill training with other therapies for individuals with ISCI (reviewed in Dobkin and Havton 2004). Wernig and colleagues (1995) reported greater walking gains with treadmill training than conventional therapy, whereas others have found no differences in walking-related outcomes between BWSTT and over-ground training (Field-Fote et al. 2005, Dobkin et al. 2006). A recent systematic review concluded that individuals with sub-acute ISCI achieve greater independence in walking after over-ground training compared with BWSTT (Wessels et al. 2010).

Likewise, only half a dozen studies have carried out follow-up investigations after BWSTT (Wernig et al. 1998, Protas et al. 2001, Field-Fote 2001, Behrman et al. 2005, Hicks et al. 2005, Dobkin et al. 2006). The majority report maintenance of walking ability 1-8 months after the completion of treadmill training (Wernig et al. 1998, Behrman et al. 2005, Hicks et al. 2005, Dobkin et al. 2006).

Potential Limitations of BWSTT

Despite the many benefits of BWSTT, there are potential limitations of this approach. First, the equipment is expensive and considerable manpower is needed to administer the therapy (Hornby et al. 2005, Wirz et al. 2005, reviewed in McDonald and Sadowsky 2002). Robotic devices lessen the manpower required (Colombo et al. 2000, Wirz et al. 2005, Winchester et al. 2005, Hornby et al. 2005), but they introduce additional limitations, such as a tendency to encourage passive stepping and the inability to train at high speeds (Hornby et al. 2005, Wirz et al. 2005).

Second, some subjects achieve a plateau in walking ability after several months of BWSTT (Horby et al. 2005, Herman et al. 2002, Carhart et al. 2004). It has been suggested that BWSTT does not prepare individuals with ISCI for community walking (Field-Fote 2001, Herman et al. 2002). Behrman and colleagues (2005, 2006) recommend transitioning from treadmill training to over-ground walking training once clients achieve a normal gait pattern on the treadmill with less than 20% body weight support. Thus, perhaps the extent of walking recovery possible with treadmill training alone is limited.

Third, the speed, amount of body weight support and incline may be varied during BWSTT, but otherwise treadmill walking typically occurs under unchanging conditions. This is not ideal for learning (Catalano and Kleiner 1984, reviewed in section 1.2). Obstacle clearance has been trained on the treadmill (Lam and Dietz 2004, van Hedel et al. 2006), thus there is the potential to incorporate more variety into BWSTT.

Lastly, it is unknown how well walking skills learned on the treadmill transfer to walking in the real world. Reisman and colleagues (2009) reported partial transfer between split-belt walking and over-ground walking. However, the skills gained through BWSTT may not have a large impact on daily walking since BWSTT has been found to be less effective at training independence in walking than over-ground methods (Wessels et al. 2010).

1.5 Functional Walking – Requirements and Measurement

The ultimate goal of walking training after ISCI is to gain the ability to walk in the home and community. Definitions of functional or community ambulation vary in the literature, but all recognize a minimum walking speed and distance (Lerner-Frankiel et al. 1986, Cohen et al. 1987, Robinett and Vondran 1988, Perry et al. 1995). Functional walking also entails the ability to walk on different surfaces (smooth, rough, uneven, sloped); carry objects while walking; walk while negotiating doors, obstacles, narrow spaces and crowded places; and ascend/descend curbs and ≤6 steps (Musselman and Yang 2007). Environmental factors important for community walking include: distance, terrain and temporal characteristics, ambient conditions, external physical load, traffic level, attentional demands, and postural transitions (Patla and Shumway-Cook 1999).

The most commonly used walking measures for ISCI are the 10-meter walk test, 6-minute walk test, and the Walking Index for Spinal Cord Injury II (WISCI II) (Jackson et al. 2008). They all assess walking ability over level ground. Few studies have evaluated functional walking skills after walking training for ISCI (Behrman et al. 2005), most likely because adequate assessments of functional walking are lacking (reviewed in Lord and Rochester 2005 – stroke, Lam et al. 2008 - ISCI).

Some measures assess challenging walking tasks; however, they either include too much subjectivity in the scoring and/or lack assessment of many of the tasks important for functional walking. For example, the Duke Mobility Skills Profile, Dynamic Gait Index and Rivermead Mobility Index (Collen et al. 1991, Shumway-Cook and Woollacott 2007) include few of the tasks commonly encountered in daily walking (Musselman and Yang 2007). Three obstacle courses have been designed to assess walking and balance in the elderly (Means 1996, Rubenstein et al. 1997, Taylor and Gunther 1998, Means and O'Sullivan 2000), and one for use in children (Held et al. 2006), but the majority of the test items assess balance. The course designed by Means (1996) is the most appropriate for functional walking, however, little has been done in the way of validation or reliability testing (Means et al. 1996). Scales evaluating balance and mobility of individuals with acquired brain injuries have been developed (Howe et al. 2006, Williams et al. 2005a&b, Williams et al. 2006), but most items tested are unlikely to be encountered in daily walking (i.e., walking on toes, tandem walk, lateral scooting).

One of the most appropriate measures of functional walking to date is the Modified Emory Functional Ambulation Profile (mEFAP). The mEFAP was developed as a measure of mobility in stroke survivors (Wolf et al. 1999, Baer and Wolf 2001). Four of the five tasks comprising the mEFAP have been identified as walking tasks frequently encountered by able-bodied adults (walking on smooth and carpeted surfaces, negotiating obstacles and steps) (Musselman and Yang 2007). The mEFAP is a timed measure and so produces interval data. It has excellent reliability, concurrent validity and is sensitive to change (Baer and Wolf 2001). The mEFAP lacks assessment of several functional walking tasks, and so it does not provide a complete picture of functional walking ability.

1.6 Overview of Thesis

The above review shows three critical areas in which there is a knowledge gap about the learning of walking and the application of this knowledge to walking training after injury to the CNS. First, little is known about motor adaptation and learning in young children, who may rely more on the spinal cord and brainstem than the cerebrum for learning. Second, with respect to walking training after ISCI, few have compared BWSTT to more functional, over-ground training.

Third, there are no valid and reliable measures of functional walking for individuals with ISCI.

Chapters 2 – 5 report the research of this thesis. We begin by studying learning in healthy, human infants and toddlers (Chapters 2 and 3). Since descending control over limb movements is weak in very young children (i.e., < 1 year old) (Yakovlev and Lecours 1967, Brody et al. 1987, Eyre et al. 1991, Khater-Boidin and Duron 1991, Szelenyi et al. 2003), they provide the only uninjured, human model of spinal and/or brainstem control of walking (reviewed in Yang et al. 2004). In chapter 2 we studied motor adaptation using a split-belt treadmill, which has two belts that operate at different speeds (one for each leg). Such walking adaptation requires the cerebellum (Morton and Bastian 2006), which matures rapidly during the first year of life (reviewed in Wang and Zoghbi 2001). So, it was unknown whether young children were capable of adapting their walking pattern. We found that most infants >8 months of age had the ability to adapt the temporal coordination of their walking. Fewer adapted in spatial coordination, suggesting that the underlying mechanisms controlling spatial and temporal coordination are different.

In Chapter 3 we studied longer-term learning in infants. First, we compared the interlimb coordination shown by infants during non-weight bearing (i.e., kicking) and weight bearing movements. We found that the majority of infants show a preference for the same type of coordination (i.e., alternate or synchronous) when kicking and when weight bearing on the treadmill. Second, we showed that infants can change their preferred interlimb coordination with training, and that the effects of training in weight bearing can transfer to the non-weight bearing condition. Taken together these findings suggest that young children can retain their learning, and that the neural circuits responsible for kicking and stepping may have some shared components.

Current training approaches (e.g., BWSTT) for ISCI are limited (reviewed in section 1.4). In effort to address these limitations, we developed a new training method called skill training. Skill training involves intensive and challenging practice of a variety of relevant walking skills. In Chapter 4 we compared walking outcomes after BWSTT and skill training in a small number of individuals with ISCI. We found greater improvements in walking skill, speed, endurance, and balance confidence with skill training than with BWSTT. In addition, we showed that walking function continues to improve with long-term (i.e., >6 months) training, suggesting that it may be beneficial to extend training beyond the typical 3 months.

Lastly, since adequate assessments of functional walking for ISCI are lacking (reviewed in Lam et al. 2008), we developed and assessed the psychometric properties of a new measure of walking, called the Spinal Cord Injury Functional Ambulation Profile (SCI-FAP) (Chapter 5). We found that the SCI-FAP has excellent inter-rater and test-retest reliability, discriminative validity and convergent validity.

1.7 References

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Chapter 2: Motor Adaptation in Humans in the First Three Years of Life

2.1 Introduction

The ability to modify motor programs to sustained changes in the walking state must be very important for young children, as they learn to walk in varied environments amid enormous changes in body dimensions in the first few years of life. We know that transient sensory disturbances applied during supported stepping on the treadmill in young children result in functionally appropriate responses (Pang et al. 2003, Lam et al. 2003). For example, a touch to the dorsum of the foot during the swing phase causes the foot to be raised higher in the swing phase (i.e., stumbling corrective response). More sustained changes suggest that children have modified their motor program to adapt to the new task. For example, a repeated touch to the foot over consecutive steps causes the high-stepping to persist after the perturbation is removed (called an aftereffect) (Pang et al. 2003). Spinal cats also show this form of adaptation, suggesting the spinal cord alone can support this type of adaptation (Hodgson et al. 1994).

Other forms of adaptation during walking are more complex. For example, the natural symmetry between the left and right legs is perturbed when adults walk on a split-belt treadmill with the belts moving at different speeds (Reisman et al. 2005). They can restore left-right symmetry with continued stepping on the split-belt treadmill for about 10 minutes. When the two belts are returned to the same speed (called tied belt) after split-belt walking, the walking is asymmetric in a direction opposite to that seen initially (aftereffect), indicating the motor program for walking has been altered. Returning to symmetric walking with the belts at the same speed now requires unlearning (called deadaptation). Time-dependent adaptation to split-belt walking has also been described in decerebrate cats with an intact cerebellum (Yanagihara et al. 1993).

The importance of the cerebellum for split-belt adaptation is supported by the absence of this adaptation in individuals with diffuse damage to the cerebellum (Morton and Bastian 2006), and in decerebrate cats with focal inhibition of nitric oxide activity in the vermis (Yanagihara and Kondo 1996). Split-belt walking would be especially interesting to study in young children because the cerebellum is immature at birth, and undergoes rapid maturation through the first year of life (Rorke and Riggs 1969, Altman and Bayer 1997, Lavezzi et al. 2006). We sought to determine when this form of adaptation emerges in young children, and whether there are unique characteristics of adaptation at this young age.

2.2 Methods

Subjects

Healthy, full-term children aged 6 – 36 months were recruited through community parent/infant groups in Edmonton, Alberta. A parent provided written informed consent. All procedures were approved by the local Health Research Ethics Board.

Experimental Procedures

All children attended 1-2 testing sessions. Sessions were 1-1.5 hours in duration. Children were supported under the arms by a researcher over a custom-made split-belt treadmill (model INFSBT-FP, R. Gramlich and S. Graziano, University of Alberta, Edmonton, AB). The researcher rested his/her forearms on a platform to minimize imposing movements on the children. Children were allowed to support as much of their own body weight as possible while avoiding hip and knee collapse during stepping. A piece of plexiglass (15 cm high) between the two belts ensured that each leg stayed on its respective belt. All children were distracted with movies and toys.

Most children attended a familiarization session within a week of the testing, in which they practiced walking on the split-belt treadmill (tied belt, speed 0.25 –

0.4 m/s) for ~10-15 minutes. Practice reduced the variability of stepping in the subsequent testing session.

The sequence of trials for the testing session (Figure 2-1A) consisted of tied-belt walking, followed by split-belt walking, and then tied-belt walking again. The belt speed for both tied-belt trials and the slow belt speed during split-belt walking was 0.25 – 0.35m/s. The belt speed ratio was 2:1 for the majority of the subjects (n=22), and 3:1 for 3 subjects. Each trial was 1-3 min long, depending on the child's tolerance, with sitting breaks of about 1 minute between trials. In adults, breaks in split-belt walking did not change the adaptation (Reisman et al. 2007).

Instrumentation

The motion was videotaped in the sagittal plane from the right side in all children (30 frames/s, Canon Elura 50), and also recorded in 3-D in 6 children with the Optotrak system (Northern Digital, Inc., Waterloo, ON), which was acquired part way through the study. Reflective or infra-red emitting markers (as the case may be for the recording system) were placed at the midline of trunk above the iliac crest, the greater trochanter, the lateral knee joint line, the lateral malleolus and the head of the 5th metatarsal. This was done bilaterally when using infra-red markers, and on the right leg (i.e. camera side) and left medial malleolus when using reflective markers. All children wore black leotards to enhance contrast. The video data was de-interlaced off-line at 60 Hz, and the Optotrak system sampled at 100 Hz. Two force plates, one under each treadmill belt, recorded the vertical forces for each leg.

Video, Optotrak and analog signals were synchronized by a custom-made digital counter that generated a 5V-pulse (1 Hz) and advanced an LED display (resolution 10 ms) in view of the camera. In addition, an output pulse from the Optotrak indicated the timing of the first and last frame from that system. Force-plate signals were low-pass filtered at 30 Hz and A/D converted at 250 Hz (Axoscope, Molecular Devices, Foster City, CA).

Analysis

The analysis was done for children who 1) completed the experiment (i.e., stepped on the treadmill for ≥1 minute during both tied belt conditions and ≥8 minutes during the split-belt condition), and 2) whose stepping was not too variable. Variability was estimated with the coefficient of variation (CV) for double support and step length, for both legs separately (i.e., 4 measures in total). If two of the four CVs were ≥50%, then the child was excluded, because variability could mask adaptation. During split-belt walking, all children showed mostly 1:1 stepping (i.e., left-right alternation for every step). Occasional 2:1 steps were eliminated from the analysis because those steps would not have contributed to adaptation of 1:1 coordination.

Temporal measures of percent time in stance (intralimb measure) and in double support (interlimb measure) were derived from the force plate signals using a customized software program (Matlab, Mathworks). Figure 2-1B shows the force plate signals from which the temporal measures were estimated. The legs that stepped on the fast and slow treadmill belts during the split-belt condition are always referred to as the fast and slow legs, respectively, even during the tied-belt condition. Fast double support is the time from foot contact of the slow leg to lift off of the fast leg, and *vice versa* for slow double support. Foot contact and lift off times are defined by the crossing of a threshold (Figure 2-1B, horizontal dotted line), which is held constant for all trials within a subject. All temporal measures were expressed as a percentage of the total stride time. The peak force exerted during the stance phase by the fast and slow legs for every step was also calculated, and expressed as a percentage of the child's body weight.

Centre of oscillation (CofO), a pure measure of spatial symmetry ((Malone and Bastian 2010, Vasudevan et al. 2009), was obtained from the children recorded with the Optotrak system (n=6). Bilateral kinematic data were available in these children. The CofO is the average limb angle in a stride (see Figure 2-1C). Limb angle is the angle formed with respect to the vertical by a line joining the greater trochanter and lateral malleolus markers.

In many children, bilateral limb angle data were not available, so step and stride length provided another measure containing both spatial and temporal information. Stride length and step length reflect intralimb and interlimb coordination, respectively. Stride length is the distance traveled by the ankle marker in the anterior-posterior direction from foot-contact to toe-off of one leg (modified for treadmill walking, Reisman et al. 2005). Step length is the anterior-posterior distance between the ankle markers of the two legs at foot-contact of the anterior leg (i.e., fast and slow step length is measured at fast and slow foot contact, respectively) (see Figure 2-1D). These measures were obtained off-line using either an automatic tracking system (Peak Motus, Vicon, Los Angeles, CA) in the case of video recordings, or coordinates obtained from the Optotrak system.

For stance time, stride length and CofO, symmetry was the fast leg measure minus the slow leg measure. Symmetry in double support (DS) and step length (SL) were calculated as follows:

$$\text{DS symmetry} = \frac{\text{fast leg DS} - \text{slow leg DS}}{\text{stride time}} \times 100\%$$

$$\text{SL symmetry} = \frac{\text{fast SL} - \text{slow SL}}{\text{fast SL} + \text{slow SL}}$$

To determine if adaptation was present in each child, the symmetries in double support time and step length were estimated from the average of 40 steps from each of: 1) late baseline, 2) early adaptation, 3) late adaptation, and 4) early deadaptation (see Figure 2-1A). Similar calculations were made for CofO when available. The number of steps chosen for analysis ensured a power level of 0.8 for the comparison of the various time periods.

To study the time course of adaptation across subjects, the steps of all children who showed adaptation were combined to produce average plots of double support and step length symmetry for split-belt walking. Double support time and step length data from 10 healthy adults, who participated in the same split-belt walking protocol, are shown for comparison. These adults were also used in Vasudevan et al. (2009). The adults walked for 4 minutes with the belts tied (speed = leg length (m)/s), followed by 15 minutes of split-belt walking (2:1 speed differential), and 15 minutes of tied-belt walking. The average time course plots were fitted with linear, single-exponential and double-exponential functions and the coefficients of determination (r^2) were used to determine which function provided the best fit.

Statistics

Mean values are reported with $\pm$ 1 standard deviation (SD), and the level of significance for statistical tests was 0.05 unless otherwise noted. To determine if a child had an asymmetry during the baseline period, a paired t-test was used to compare double support, step length and CofO for the fast and slow legs. In order to induce adaptation, the split-belt treadmill must produce a significant asymmetry (i.e., error) in the child's walking, defined as a significant difference in the symmetry measures between late baseline and early adaptation periods (one-way independent t-test). Similarily, the presence of adaptation (i.e., an aftereffect) was defined as a significant difference in symmetry between late baseline and early deadaptation (one-way independent t-test).

The mean values for symmetry during the 4 time periods for each child were combined for group analysis. Nonparametric tests were used when the assumption of normality was not met (assessed with Shapiro-Wilk's test). To compare intralimb measures across time periods, a repeated-measures ANOVA was used, with time period as the within-subjects factor. To examine how the interlimb measures of symmetry changed across time periods, children were first divided into 2 groups depending on whether or not they showed adaptation (i.e., significant aftereffect, described above). Children who showed adaptation (adapters), or did not show adaptation (non-adapters) were analyzed separately. Interlimb measures across time periods for each group were compared with a one-way, repeated-measures ANOVA. Age, body weight supported when walking (i.e., average peak force exerted during each time period for each leg), and size of error (i.e., difference in symmetry for the baseline and early adaptation periods) were compared for the adapters and non-adapters with either an independent t-test or the Mann-Whitney U test (when normality assumption not met). The size of the error and the size of the aftereffect (i.e., difference in symmetry values for the baseline and early deadaptation periods) were correlated using Pearson's correlation coefficient (r). Bonferroni was used for all post-hoc analyses at $p<0.008$.

2.3 Results

Thirty-three of the 42 children tested completed all walking conditions of the experiment. Of these 33 children, 8 were excluded because of excessive variability in their walking, leaving 25 children (aged 8.5-35.2 months) for analysis.

Intralimb measures

Consistent changes in stance time and stride length were seen across all subjects. Upon exposure to the split-belt treadmill, asymmetries in both measures occurred immediately. Stance time was shorter in the fast leg compared to the slow leg, while stride length was longer in the fast leg compared to the slow leg. The asymmetries in stance time and stride length were maintained throughout split-belt walking. In early deadaptation there was an immediate return to the baseline values for stance time and stride length (i.e., no aftereffect). Group data for the 2 intralimb measures are shown in Figure 2-2.

Interlimb measure - double support time

Upon exposure to split-belt walking, all but 1 child showed a change in double support time of the 2 legs (i.e., significant error). Following the period of early adaptation, the children showed 1 of 2 outcomes for double support. The first group (n=21, mean age = 15.9 ± 7.2 months) showed changes in double support time throughout the split-belt condition similar to the changes in adults reported by Reisman and colleagues (2005). In these children, the asymmetry in double support time seen in the early adaptation period gradually diminished, approaching baseline values during the late adaptation period. An aftereffect was seen during the early deadaptation period, with an asymmetry in the opposite direction from that seen in early adaptation. An example of a single subject from this group is shown in Figure 2-3A. The second group did not show adaptation with respect to double support time (n=3, mean age = 11.2 ± 2.7 months). Group data is shown in Figure 2-3B. Post-hoc analyses revealed that as a group, the children who showed adaptation 1) reduced the asymmetry in double support time over the course of split-belt walking, and 2) had an aftereffect during the early deadaptation period.

Interlimb measures - step length

Unlike double support time, several children (7/25) did not show any change in their step length with initial exposure to split-belt walking (i.e., no error). Of the remaining 18 children, adaptation of step length was seen in 11 children, all of whom also showed adaptation with respect to time in double support (mean age = 14.6 ± 4.0 months). In these children, the asymmetry in step lengths seen in the early adaptation period gradually returned toward baseline values over the course of the split-belt condition. An aftereffect in step length symmetry was seen during the early deadaptation period in these children. Data from a single subject is shown in Figure 2-3C. Seven children did not show any adaptation in step length (i.e., no aftereffect) (mean age = 17.5 ± 10.2 months). In some of these children the asymmetry in step length seen in the early adaptation period gradually returned toward baseline values during split-belt walking, whereas in others the asymmetry remained unchanged throughout split-belt walking. Group data is shown in Figure 2-3D.

Interlimb measures - centre of oscillation

CofO data was available for 6 children, and most (5/6) showed a significant asymmetry (i.e., error) in CofO in early adaptation. In 2 children this asymmetry was reduced over the course of split-belt walking, but none of the children showed an aftereffect. Data from a single subject is shown in Figure 2-3E, and group data is shown in Figure 2-3F.

Emergence of temporal and spatial adaptation can occur at different times

Only a few children did not show adaptation in double support (3/24), age range 9.4 – 14.3 months (Figure 2-4A). In contrast, more children did not show adaptation in step length (7/18), age range 8.5 – 35.2 months (Figure 2-4B). None of the children showed adaptation in CofO (Figure 2-4C). Hence, emergence of adaptation in temporal (double support) and spatial (CofO) symmetry did not occur at the same time for a child.

Time courses of adaptation

The time courses of adaptation for both double support and step length symmetry are shown in Figure 2-5. The adult data is best fit with a double-exponential curve (r^2 = 0.88 and 0.85 for double support and step length, respectively), whereas the data from the children is best fit with a straight line (r^2 = 0.74 and 0.31 for double support and step length, respectively). Hence, the time courses for adaptation are slower in the children than the adults.

Differences between adapters and non-adapters

For double support time, there was no difference between the adapters and non-adapters with respect to age, size of error, or the amount of body weight supported during the time periods of early adaptation, late adaptation and early deadaptation ($p>0.05$).

For step length, there was a significant difference in the error size between the 2 groups (p=0.004). The adapters experienced significantly less initial error in step length than the non-adapters (error in step length symmetry was 0.10 $\pm$ 0.05 and 0.28 $\pm$ 0.09, respectively). There was a moderately strong, negative correlation between the size of the error and the size of the aftereffect (r = -0.65, p = 0.004) (Figure 2-6). There was no difference between the adapters and non-adapters with respect to age or the amount of body weight supported (p>0.05).

Asymmetry during baseline walking and the effect on split-belt adaptation

Not all children stepped symmetrically during the baseline period. For this reason we compared the step length, CofO and double support times for the left and right sides during baseline stepping. Five of the six children for whom we have CofO data were asymmetric in that measure (mean age = 25.8 $\pm$ 7.2 months) (Figure 2-7A). More children were asymmetric in step length (13/25; mean age = 12.7 $\pm$ 4.9 months) than in double support (7/25; mean age = 13.2 $\pm$ 5.5 months) during baseline stepping (Figure 2-7A). Similar asymmetry has been described for individuals with stroke (Reisman et al. 2007) and children with hemispherectomy (Choi et al. 2009).

Split-belt walking caused either an increase or a decrease in the baseline asymmetry of double support and step length. If the asymmetry was increased, the aftereffect caused the stepping to be more symmetric (an example from a single subject is shown in Figure 2-7B, group data in Figure 2-7C black circles). In contrast, if the baseline asymmetry was reduced with split-belt walking, the children showed a greater asymmetry during early deadaptation, compared with baseline walking (Figure 2-7C, black diamonds).

2.4 Discussion

We show that most children aged 8.5 – 36 months of age adapt to split-belt walking. This adaptation was demonstrated as a reduction in the asymmetries caused by split-belt walking in double support and step length, and the presence of an aftereffect upon the return to tied belt walking. A few children showed adaptation in double support time, but not step length; none showed the reverse. No children showed adaptation in the pure spatial measure – centre of oscillation. In addition, baseline asymmetry was seen more often in step length and CofO, compared to double support, suggesting that the neural mechanisms controlling spatial symmetry are different from that controlling temporal symmetry, in agreement with studies of patient populations (Choi et al. 2009). Furthermore, the time courses of adaptation to both double support and step length were slower in children compared with adults, suggesting that the neural mechanisms for adaptation are either different or not functioning in the same way. In contrast to the gradual emergence of adaptation to interlimb coordination, all children, regardless of age, showed immediate changes in the intralimb parameters similar to those seen in adults (Reisman et al. 2005), indicating early maturation of the neural mechanisms controlling intralimb coordination.

Methodological limitations

Older children tended to support a greater percent of their body weight while stepping than younger children, which may generate greater afferent feedback, and drive adaptation more effectively. Since three of the older children who showed adaptation supported less weight than the young children who did not show adaptation (i.e., <50% and ~55% of their body weight supported, respectively, during early adaptation), we feel this is unlikely to explain the absence of adaptation in some of the younger children.

Young children loose interest much more quickly than adults, resulting in shorter durations of split-belt walking (i.e., correlation between age and number of steps: $r=0.50$, $p=0.009$). The minimum exposure to split-belt walking that produced an aftereffect was 192 steps for double support (subject aged 13.0 months) and 229 steps for step length (subject aged 14.2 months). Thus, the exposure to split-belt walking in the young children was still within the minimum number of steps (i.e.,

>200) necessary for adaptation to develop. The duration of early deadaptation trials is less problematic, as aftereffects can be seen with very few steps (i.e., catch trials of 5-8 steps in pilot data). We were unable, however, to have long enough trials to determine the full time course of deadaptation.

The pure spatial measure of CofO was obtained in the 6 subjects for whom we had bilateral limb angle data. We attempted to extract a similar measure for the remaining 19 subjects by estimating the mid-position of the stride (i.e., horizontal position of the ankle marker from foot-contact to toe-off). While this measure reflected similar information to the CofO, as confirmed from the subjects with both types of measures, the mid-position of the stride was considerably more variable (e.g., coefficient of variation ranged 90-130%). Hence, this surrogate measure was not used.

Split-belt walking did not induce an error in step length in 7 children, whereas only one child showed no error in double support time. Interestingly, children with hemispherectomy sometimes showed the opposite: no error in double support time, but and error in step length (Choi et al. 2009). Since in each of these cases, the children were more asymmetric during baseline walking in the parameter that showed no error (step length for our subjects, double support for the children with hemispherectomy), it may have resulted from a ceiling effect, in that the existing asymmetry was severe enough that the split-belt treadmill could not further exaggerate it (Choi et al. 2009). In our children who did not show an error, however, about the same number showed baseline asymmetries in the two directions (i.e., fast leg step length longer and slow leg step length longer). So, a ceiling effect alone cannot explain the lack of error in all cases.

Neural mechanisms controlling intralimb coordination are mature and distinct from those controlling interlimb coordination

All children showed adult-like changes to intralimb measures of stride length and stance time during split-belt walking with no aftereffect during early deadaptation

(Reisman et al. 2005). Adults with diffuse cerebellar atrophy (Morton & Bastian 2006) and those with cerebral strokes (Reisman et al. 2007) also showed normal changes in these intralimb measures. Although time-dependent changes have not been reported for these intralimb measures in spinal cats, it is clear that spinal cats can adjust their stance and swing phase durations to accommodate split-belt walking (Forssberg et al. 1980). Taken together, the results suggest that neural substrates for intralimb coordination in split-belt walking are contained in parts of the nervous system that mature early, possibly the spinal cord.

Midline structures in the cerebellum may be especially important for split-belt adaptation, since cerebellar patients with gait and postural disturbances (functions controlled by midline cerebellar structures) were more impaired in split-belt adaptation than those with limb ataxia (functions controlled by intermediate and lateral cerebellar structures) (Morton and Bastian 2006). Experiments in decerebrate cats also showed that disruption of nitric oxide activity in the vermis impaired split-belt adaptation (Yanagihara and Kondo 1996). Interestingly, the midline cerebellar structures are earlier to mature than the lateral parts of the cerebellum, as seen from histology (Yakovlev and Lecours 1967, Rorke and Riggs 1969). Perhaps the midline cerebellar structures are not functionally mature in spite of the appearance of mature myelin. Alternatively, split-belt adaptation may also depend on intermediate or lateral regions of the cerebellum which are later to mature.

Time course of adaptation in children is much slower than adults

Adaptation of double support time and step length was seen in many of the children. The time course of adaptation, however, was slower than adults. While the adult adaptation to both double support and step length were best fit with double exponential curves, the data from young children was best fit with a straight line. These data agree well with development of split-belt adaptation in older children, in that the adaptation rate of double support for children 3-5 years old are best fit with double exponential curves (i.e., similar to the adult), while the adaptation rate of step length is best fit with a straight line until adulthood (i.e., >18 years old) (Vasudevan et al. 2009). Hence, there is a continuum in the development of adult-like adaptation rates, and our data show the pattern of adaptation shortly after it emerges.

Mechanisms controlling spatial and temporal symmetry are likely different

Most children showed adaptation in temporal symmetry (double support), but none showed adaptation in spatial symmetry (CofO). In addition, baseline stepping was more often asymmetrical in CofO than double support time. Together these findings suggest that independent neural substrates and/or mechanisms are responsible for coordinating the temporal and spatial coordination of the legs, and that these two substrates mature at different rates in humans. Choi and colleagues (2009) found that the spatial and temporal components of split-belt adaptation were affected differently by damage to the cerebral cortex. Children with hemispherectomy had difficulty adapting double support time and interlimb phasing (temporal measures), yet their ability to adapt step length did not differ from controls (Choi et al. 2009). Individuals with damage to the cerebellum showed some correction of double support asymmetry when walking on the split-belt treadmill, but no improvement in step length symmetry (Morton and Bastian 2006). Furthermore, Malone and Bastian (2010) showed that temporal and spatial coordination of split-belt walking showed differing sensitivities to distraction level while able-bodied adults adapted to split-belt walking. Hence there is converging evidence that spatial and temporal symmetry are independent, and the neural substrates responsible likely different.

Adaptation of step length not seen when initial errors are large

The size of the error used to drive motor adaptation affects learning. For example, healthy adults show greater and more enduring aftereffects when errors in eye or arm movements are introduced gradually, rather than abruptly (Klassen et al. 2005, Kagerer et al. 1997, Michel et al. 2007). The size of the initial error induced by split-belt walking may be another factor influencing the presence of adaptation in children. The asymmetry in step length induced by the split-belt treadmill during early adaptation was significantly greater in the children who did not show adaptation compared to those who did. A similar situation has been reported in patients with severe cerebellar damage, who adapted to a novel reaching task when the asymmetry was presented gradually (i.e., small error), but not when the asymmetry was initially presented at full strength (i.e., large error) (Criscimagna-Hemminger et al. 2010). Like cerebellar patients, children may have greater difficulty learning from large errors. We will explore this in more detail in the future.

Split-belt walking can temporarily correct baseline asymmetries in walking

Some children showed baseline asymmetries in double support or step length that were corrected through split-belt walking. This phenomenon has also been reported in individuals with stroke (Reisman et al. 2007) and children with hemispherectomy (Choi et al. 2009). If split-belt walking worsened the baseline asymmetry, the child's walking became more symmetrical in the early deadaptation period. Thus, split-belt treadmill may prove a valuable therapy for correcting walking asymmetries in individuals with early childhood stroke.

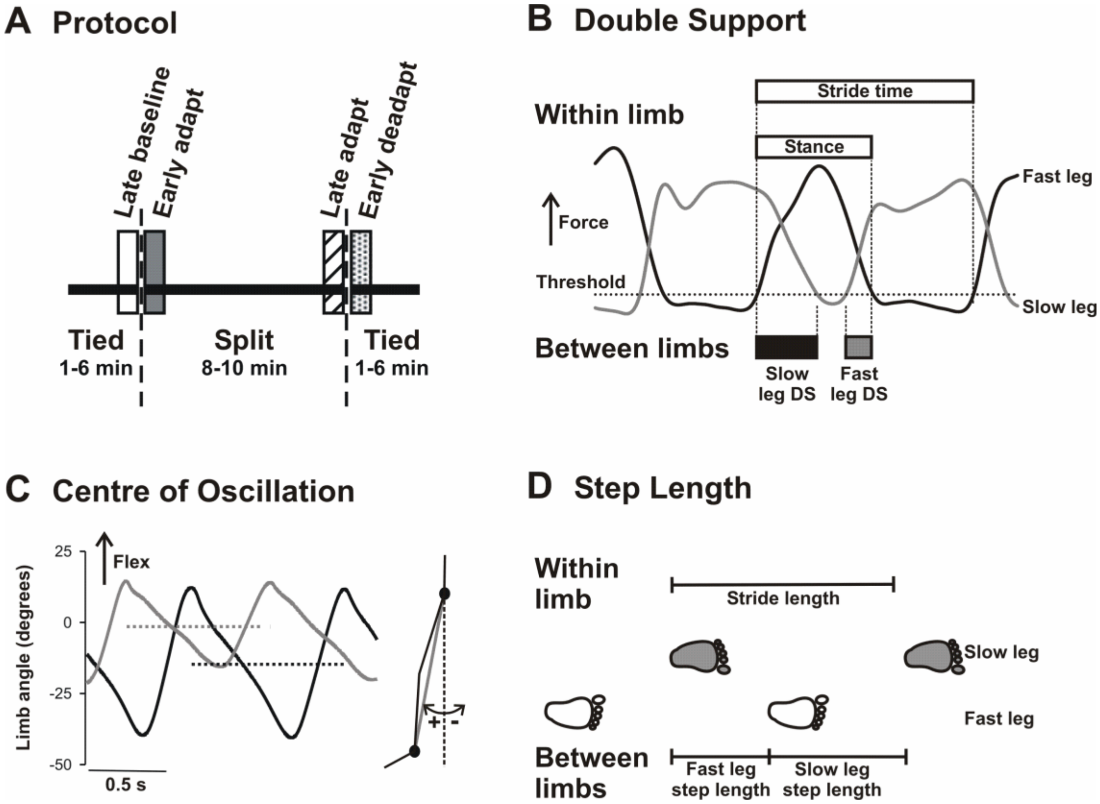


Figure 2-1: Methods. (A) Experimental procedure. Children walked on a split-belt treadmill with the belts at the same speed for 1-6 min (tied), followed by 8-10 min of walking with the belts at different speeds (split), and finally for 1-6 min in the tied condition. Time periods of interest are late baseline (last 40 steps of first tied condition, white bar), early adaptation (first 40 steps of split condition, grey bar), late adaptation (last 40 steps of split condition, striped bar), and early deadaptation (first 40 steps of second tied condition, dotted bar). (B) Temporal measures of walking were derived from the force plates. Force signals for the fast and slow legs are shown in black and grey, respectively. White horizontal bars indicate the duration of 1 stance phase and 1 stride for the fast leg. Interlimb coordination in timing was quantified by double support (DS) times (i.e., time when both feet are in contact with the ground), shown for when the slow leg is trailing (slow DS, black bar), and when the fast leg is trailing (fast DS, grey bar). Dotted horizontal line represents the threshold for foot contact and lift off times. (C) Centre of oscillation is the mean limb angle over a stride. Limb angles of the fast (black line) and slow (grey line) legs are plotted for 1 infant (KMP, 35.2 months) during early adaptation. Horizontal, dotted, black and grey lines represent the average limb angles for the fast and slow legs, respectively. Limb angle is the angle between the vertical and a vector connecting the hip and ankle markers (see stick figure on the right). (D) Step length is illustrated with foot prints for simplicity, although on a treadmill the spatial relationships of foot falls will not be exactly as shown. Step lengths, defined as the distance between the

ankle markers of the two legs in the horizontal direction of the sagittal plane, were measured at the time of foot-contact of the leading limb. The step lengths are named according to the leading leg, by convention.

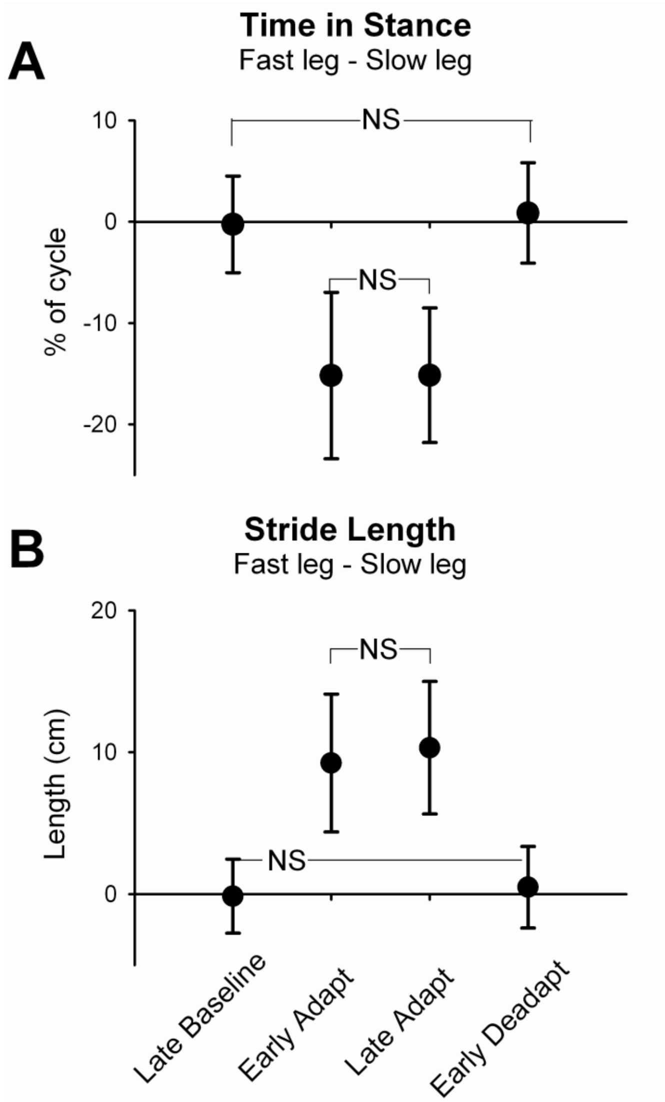
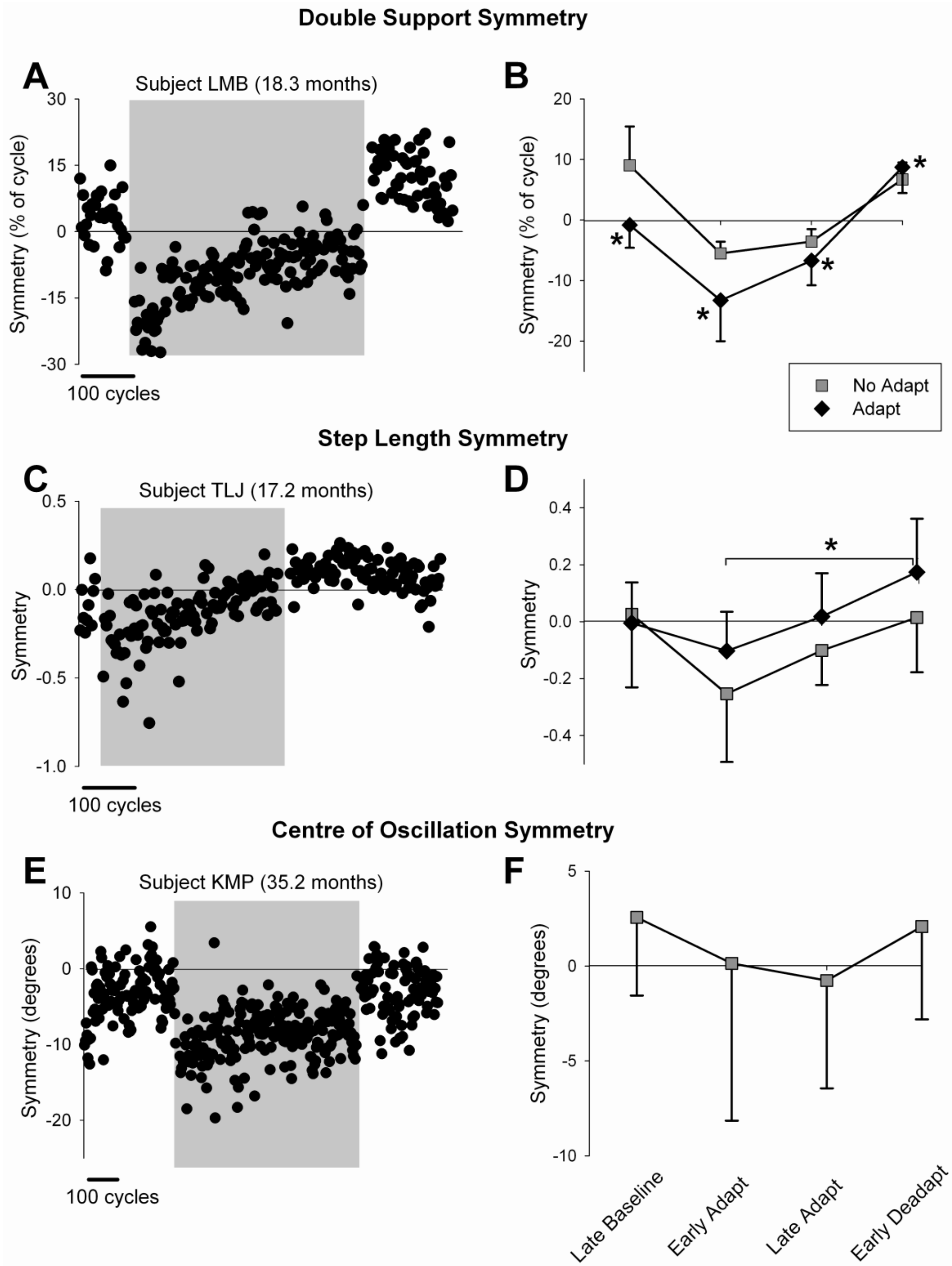


Figure 2-2: Intralimb parameters. Group data (n=25) for time in stance (expressed as % of the step cycle) (A) and stride length (in cm) (B). Black dots represent mean values for each time period with error bars (SD). NS = not statistically significant, all other comparisons significant ($p<0.008$ – Bonferroni).



Double Support Symmetry
A
Subject LMB (18.3 months)
Symmetry (% of cycle)
100 cycles
B
Symmetry (% of cycle)
No Adapt
Adapt
Step Length Symmetry
C
Subject TLJ (17.2 months)
Symmetry
100 cycles
D
Symmetry
Centre of Oscillation Symmetry
E
Subject KMP (35.2 months)
Symmetry (degrees)
100 cycles
F
Symmetry (degrees)
Late Baseline
Early Adapt
Late Adapt
Early Deadapt

Figure 2-3: Symmetry of interlimb measures. (A) and (C) show data from a single subject who showed adaptation in double support and step length, respectively. (E) shows data from a single subject who did not show adaptation in centre of oscillation. Black dots represent the mean of 3 consecutive steps. Grey shading indicates the split-belt condition. (B), (D) and (F) show group data for children who showed adaptation (black diamonds) and those who did not (grey squares) in measures of double support (n=21 and n=3, respectively), step length (n=11 and n=7, respectively) and centre of oscillation (n=0 and n=5, respectively). Mean values $\pm$ 1SD are shown. * = significantly different from other time periods ($p<0.008$). In (D) only 1 comparison was significantly different ($p<0.008$) – early adapt vs. early deadapt in the adapters.

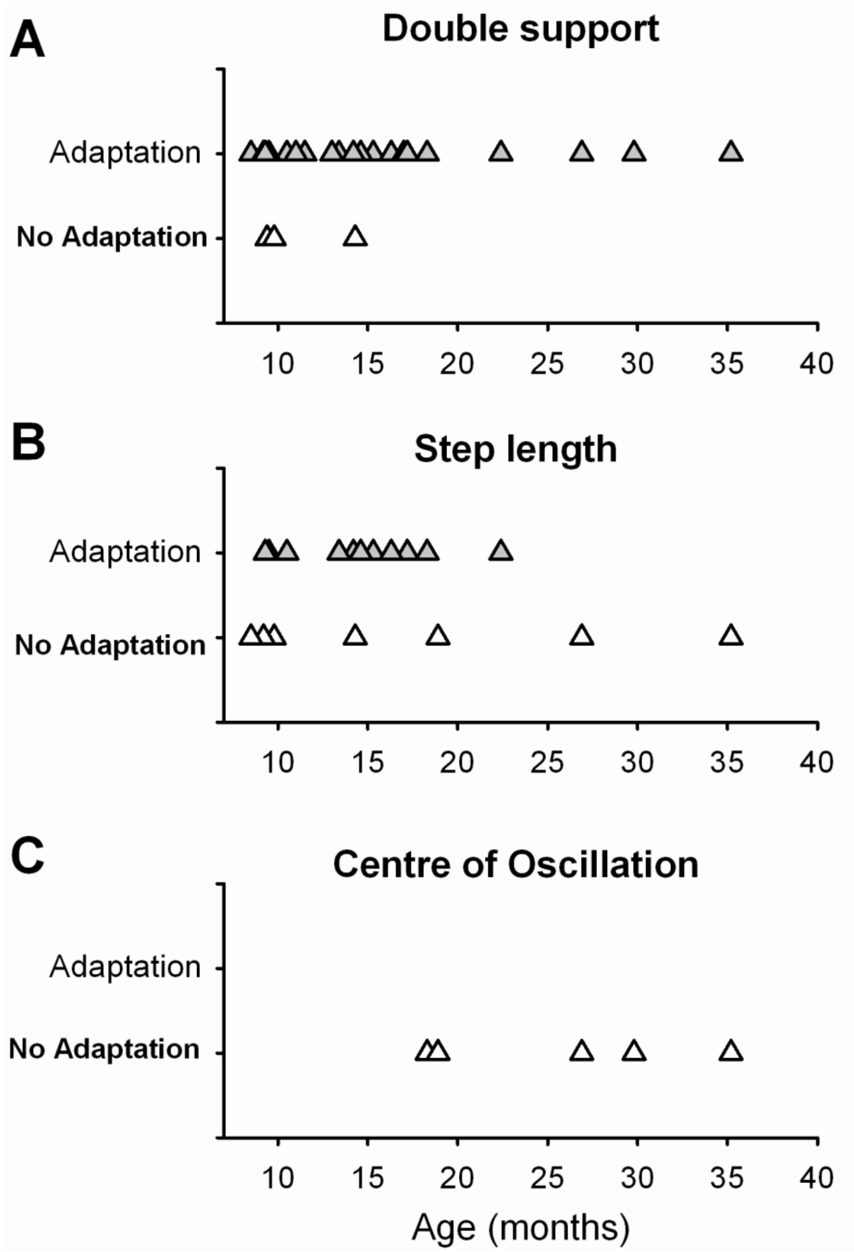


Figure 2-4: Emergence of adaptation. Age at which adaptation for split-belt walking appears. The age (horizontal axes) of those who showed adaptation (filled triangles) and those who did not (open triangles) is shown for double support (top, n=24), step length (middle, n=18) and centre of oscillation (bottom, n=5). Children who did not show an error in a measure upon exposure to split-belt walking are not included in the plot for that measure. Emergence of adaptation in double support time, step length and centre of oscillation does not always occur at the same time.

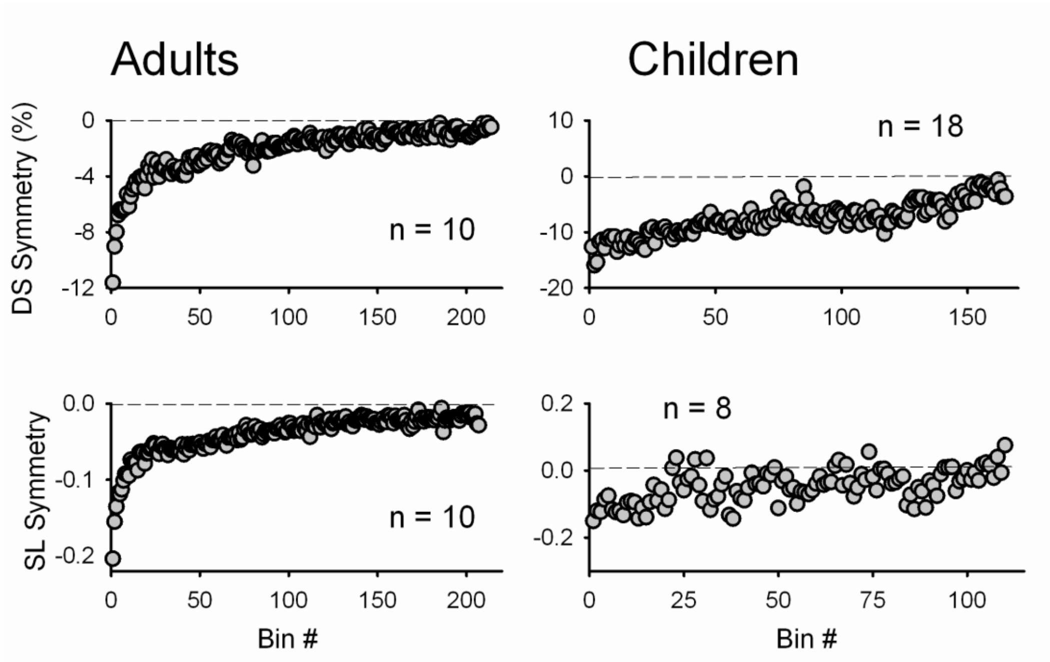


Figure 2-5: Time course of adaptation. Group data showing means across subjects for double support (DS) symmetry (top row) and step length (SL) symmetry (bottom row) for both adults (left) and children (right). 1 dot = average from a number (n) of subjects. Horizontal axes represent consecutive steps, averaged in groups of 3 per bin.

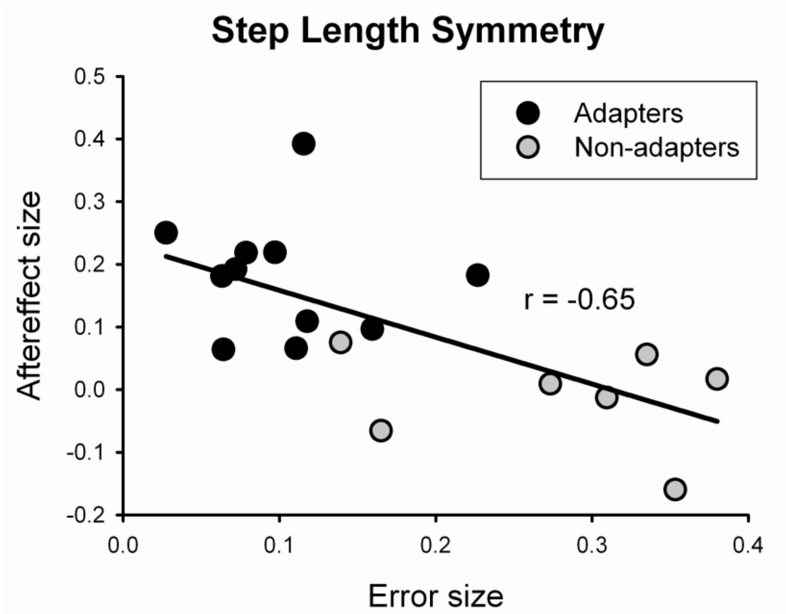


Figure 2-6: Error size. Error size in step length symmetry (difference between mean values for baseline and early adaptation periods) versus the size of the aftereffect (difference between mean values for baseline and early deadaptation periods). Each dot represents 1 child. Black and grey dots represent children who did and did not show adaptation in step length, respectively.

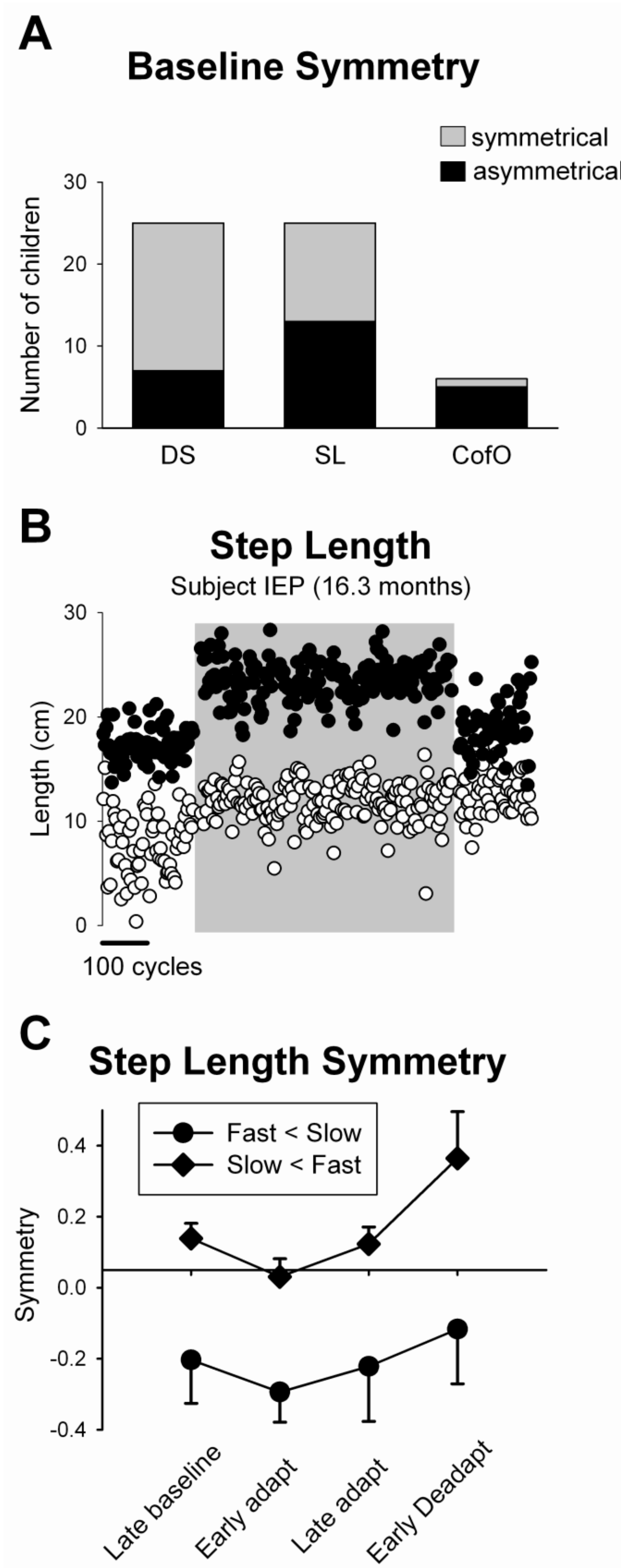

A
Baseline Symmetry
symmetrical
asymmetrical
Number of children
30
20
10
0
DS
SL
CofO
B
Step Length
Subject IEP (16.3 months)
Length (cm)
30
20
10
0
100 cycles
C
Step Length Symmetry
Fast < Slow
Slow < Fast
Symmetry
0.4
0.2
0.0
-0.2
-0.4
Late baseline
Early adapt
Late adapt
Early Deadapt

Figure 2-7: Asymmetries in interlimb measures. (A) Number of children (vertical axis) that showed symmetrical (grey bars) and asymmetrical (black bars) walking with respect to double support (DS), step length (SL) and centre of oscillation (CofO). (B) Step length data from a single subject who showed an asymmetry during the baseline period (fast step length < slow step length). White and black dots represent the fast and slow legs (mean of 3 steps), respectively. Grey shading indicates the split-belt condition. (C) Mean ± 1SD step length symmetry for children who 1) showed asymmetries in step length at baseline, 2) who showed an error in step length symmetry during early adaptation, and 3) who showed adaptation (total of 5 children). Two children had fast < slow asymmetry (black circles) and 3 children had slow < fast asymmetry (black diamonds).

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Chapter 3: Interlimb Coordination in Rhythmic Leg Movements: Spontaneous and Training-Induced Manifestations in Human Infants

3.1 Introduction

Animals exhibit a variety of rhythmic movements that share some underlying neural circuitry. These circuits are reconfigured by sensory input and/or neuromodulators to control different movements (reviewed in Stein 2005, Dickinson 2006). In many cases, the sharing of circuitry is reflected in shared features of the movements, such as similarities in the kinematics and muscle activations (reviewed in Stein 2005). Moreover, movement forms that share circuitry show smooth transitions from one form to another without breaks or discontinuities (Robertson et al. 1985, Mortin et al. 1985, Carter and Smith 1986, Earhart and Stein 2000). The degree of sharing in circuitry has been examined in human adults by inducing an adaptation in one form of movement, such as forward walking on a split-belt treadmill (Reisman et al. 2005), and determining if the adaptation is expressed in another form of rhythmic movement, backward walking on the split-belt treadmill (Choi and Bastian 2007). Interestingly, there was no transfer of the learning from forward to backward walking, suggesting that there was no sharing of the circuitry involved in the adaptation. Transfer of learning was only found when the direction of the leg movement was the same (i.e., forward walking leg in hybrid walking to regular forward walking). Bastian and colleagues concluded that there may be little sharing of circuitry between forward and backward walking (Figure 6 in Choi and Bastian 2007).

Human infants exhibit a variety of rhythmic leg movements including stepping (Andre-Thomas and Autgarden 1966), kicking (Thelen et al. 1981) and swimming (McGraw 1939). Few attempts have been made to determine if the behaviors are similar (Thelen et al.1981). Coordination between the legs in these movements has been reported to be either mostly alternate or synchronous (Thelen et al. 1983, Piek and Carman 1994, Pang and Yang 2001, Musselman and Yang 2007a,b).

This chapter is published in the *Journal of Neurophysiology*.
Musselman KE, Yang JF. Interlimb coordination in rhythmic leg movements: spontaneous and training-induced manifestations in human infants. *J Neurophysiol* 100: 2225-2234, 2008. doi: 10.1152/jn.90532.2008.

Here, alternate and synchronous coordination are relative terms to indicate movements that are closer to being alternate versus synchronous, as has been described for mammalian locomotion (English and Lennard 1982). By using this natural tendency of infants to exhibit predominantly one of the two opposite patterns for interlimb coordination, we determined if weight bearing and non-weight bearing movements might share circuitry for interlimb coordination.

If interlimb coordination in weight bearing and non-weight bearing movements share coordinating circuitry, then the two activities should show the same interlimb coordination (i.e., either synchronous or alternate). Moreover, if we induce a change in interlimb coordination in one situation (i.e., weight bearing movements) using exercise over a period of a few weeks, there should be a change in interlimb coordination in the other movements that received no practice (i.e., non-weight bearing). Finally, in infants who exhibit both synchronous and alternate movements, the transition between the two forms of coordination should occur smoothly, with steps that assume intermediate values between the two forms of coordination (Stein et al. 1986, Earhart and Stein 2000). These results have been reported in preliminary form (Musselman and Yang 2007b).

3.2 Methods

Subjects

Infants in good health were recruited through community parent/infant groups in Edmonton. Babies ~6 months of age were preferentially recruited because infants this age play in supine or prone positions (Piper et al. 1992), which facilitates recording. Moreover, for the training part of the study, infants aged ~6 months are unlikely to impose other forms of practice (i.e., crawling or cruising) on their own (Piper et al. 1992), which could confound the study. A parent provided written informed consent at the time of testing. Study procedures were approved by the Health Research Ethics Board of the University of Alberta and Capital Health, Edmonton.

Experimental Procedures

All infants attended a one-hour testing session. Prior to testing, parents were asked questions concerning their infant's play habits, so that we could determine if there was a relationship between the play habits and the interlimb coordination expressed in the experiment.

<u>Non-weight bearing</u>: Non-weight bearing activity was elicited first, followed by weight bearing activity on a moving treadmill belt. The parents and a researcher played with the infant to induce excitement and as a result, rhythmic movements of the legs (Thelen 1985). One to two trials of each behavior were attempted. Trials were 0.5 – 3 minutes long with 1 – 2 minute rests between trials. Kicking occurred in at least one of 4 ways: 1) lying supine, 2) lying prone, 3) sitting on the edge of a small bench, upper body supported by a researcher and the legs hanging over the edge of the bench, or 4) air-stepping. Air-stepping was elicited by holding the infant under the arms in an upright position with the feet suspended.

<u>Weight bearing</u>: To elicit rhythmic leg movements in weight bearing, the infants were held under the arms by a researcher over a custom-made split-belt treadmill (model INFSBT-FP, R Gramlich and S Graziano, University of Alberta, Edmonton, AB). The researcher's forearms were supported on a platform to minimize imposing movements on the infant. The infants were allowed to support as much of their weight as possible without the legs collapsing into flexion. The two treadmill belts were always set at the same speed, usually between 0.1 - 0.4 m/s.

<u>Training</u>: Nineteen parents agreed to practice one type of interlimb coordination in weight bearing with their infants at home for 4 weeks (Practice Group). An infant was selected for the Practice Group if he/she showed mostly one type of interlimb coordination at the first testing session. Parents practiced the coordination type that their infant did not show at the first visit. Practice was prescribed for a minimum of 5 minutes, 2 times daily, for 1 month, based on

previous experience (Yang et al. 1998). Parents were shown how to induce the desired movement at the first testing session. To induce alternate coordination, the parent supported the infant under the arms and leaned the infant forward. If there was no spontaneous stepping, another adult moved the infants' legs in a stepping motion. This assistance was withdrawn once the infant initiated stepping. To induce synchronous coordination, the parent bounced the infant up and down in standing to generate jumping movements. Jumping was also practiced in the jolly jumper if the parent preferred that method. Parents were asked to avoid play of the opposite coordination type (i.e., not to use the jolly jumper if the infant was practicing alternate coordination). Weekly phone contact with the parents verified the frequency of practice. Following the practice period, infants attended a second testing session. At this session the parent demonstrated how he/she had been practicing with his/her infant. Practice was deemed successful if the infant actively performed the practiced movement, as seen from electromyography (EMG) during the parent's demonstration. Infants who did not actively perform the desired movement were excluded.

<u>Control Group</u>: Four additional infants were seen a second time. These infants maintained their usual play patterns between the first and second testing sessions and served as controls. The control group was included to determine whether changes in interlimb coordination occur in a 4-week period due to growth and maturation. Testing at the second session was identical in procedure to the first session for infants in the Practice and Control groups.

Instrumentation

Knee movements were measured with twin-axis electrogoniometers bilaterally (Penny and Giles, Biometrics Ltd., Blackwood Gwent, UK). The goniometer arms were aligned with the long axes of the femur and tibia. Two infants were observed to kick mainly from the hips, so the goniometers were instead placed over their hip joints bilaterally (goniometer arms aligned with the midline of the trunk and long axis of the femur).

Surface EMGs were recorded from the quadriceps and hamstrings bilaterally. Recordings from the gastrocnemius-soleus and tibialis anterior were obtained from a few infants only, since preliminary data showed that these muscles were not consistently involved in kicking. Disposable, silver-silver chloride electrodes, 1 cm recording diameter (Kendall, Chicopee, MA) were placed 1 cm apart (centre-to-centre) on the above-mentioned muscles. The signals were amplified and bandpass filtered at 10 to 1000 Hz (AMT-8 Bortec Biomedical, Calgary, Canada).

Movements were videotaped in the sagittal plane, either from the left or right side of the infant (30 frames/second, Canon Elura 50). The leg facing the camera was the reference leg. White adhesive markers were placed on the reference leg at the midline of the trunk above the iliac crest, greater trochanter, lateral knee joint line, lateral malleolus and head of the fifth metatarsal. Markers were also applied to the contralateral leg over the medial knee joint line, medial malleolus and medial aspect of the great toe. The infants wore black leotards to enhance the contrast with the markers.

The video and analog signals were synchronized by a timer that advanced an LED counter visible to the camera and a TTL pulse recorded with the analog signals, at a rate of 1 Hz. The goniometer signals and the full-wave rectified EMGs were amplified, low-pass filtered at 30 Hz, and converted from analog to digital form at 250 Hz (Axoscope, Axon Instruments Inc., Foster City, CA). All raw signals were also recorded on video tape with a pulse-code-modulated encoder (A.R. Vetter, Redersburg, PA) for back-up.

Analysis

The video footage was reviewed off-line. Sequences of at least 2 sequential cycles in both legs were identified. A cycle was defined as the onset of knee or hip flexion to the subsequent onset of knee or hip flexion based on the goniometer signals (change in joint angle $\geq$20 degrees and no pauses $\geq$1 second). The fully extended knee and neutral position of the hip were defined as 0°. Positive angles represent flexion. An infant's data were included if he/she performed $\geq$15 non-weight bearing cycles and $\geq$15 weight bearing cycles. A customized software program (Matlab, MathWorks, Inc., Natick, MA) was used to quantify the phase lag between the movements of the 2 legs. Phase lag was defined as the delay in time from the onset of the cycle in the reference leg to the onset of the cycle in the contralateral leg, expressed as a percentage of the cycle in the reference leg.

Some infants showed transitions between alternate and synchronous coordination in weight bearing and non-weight bearing. A transition was defined as a change in phase lag of at least 20%, in which the phase lag changed from synchronous (phase lag 75% - 25%) to alternate (phase lag of 25% -75%) coordination or vice versa. A smooth transition was defined as one without pauses in limb movement $\geq$0.03s.

Statistics

The distribution of phase lags for all the cycles was first plotted as a histogram. Using circular statistics (Batschelet 1981), the phase lag was then represented as an angle in a circle. For simplicity, the angles were also represented from 0-100% as is commonly done for rhythmic movements (Gosgnach et al. 2006). The mean vector angle (henceforth referred to as mean phase lag) and mean vector length were calculated for each type of rhythmic movement for each infant. The mean vector length ($0\leq r\leq 1$) is a measure of dispersion with $r = 0$ indicating a random distribution (Batschelet 1981). Whether the phase lag distribution differed significantly from random was determined with Rayleigh's test (Batschelet 1981). A non-random distribution indicates that one type of interlimb coordination was more frequently performed. Distributions that appeared bimodal from inspection of the phase lag histogram were further analyzed to determine if they were bimodal, using the Dip Intensity test (Giacomelli et al. 1971).

Kuiper's test was used to identify significantly different phase lag distributions between the two types of leg movements for individual infants and for group data (Batschelet 1981). Kuiper's test compares the cumulative distributions of two-samples. It is adapted for circular statistics from Kolmogorov and Smirnov's test (Batschelet 1981). The sign test (Moore and McCabe 1999) was used to assess the statistical significance of the total number of infants with similar distributions of phase lag. An independent t-test was used to compare the mean ages of the infants with similar and different distributions. For those infants who engaged in practice, we also compared the phase lag distribution between the first and second sessions for each form of movement. Significance was set at $p<0.01$ for all statistical tests. Mean values are reported with ± 1 standard deviation (SD).

To examine the group data for all movements, the distribution of phase lags from each infant was first normalized to the total number of cycles recorded from the infant, and expressed as a percentage (i.e., histograms in Figure 3-1). Average histograms were then calculated across subjects.

3.3 Results

Subjects

Forty-six of the 68 infants tested met the inclusion criteria for analysis (age range 3.2 – 9.7 months, mean±1 SD = 6.2 ± 1.4 months, 23 males and 23 females). Ten out of 19 infants (mean age 5.9 ± 0.5 months, 6 males and 4 females) practiced successfully and completed a second testing session. Three infants participated successfully as controls (mean age 5.6 ± 1.0 months, 2 males and 1 female).

Most infants showed one type of interlimb coordination

Of the 92 individual phase lag distributions (2 per infant), 69 (75%) were non-random, and the vast majority of distributions (98%) for individual subjects were unimodal. Examples of alternate and synchronous coordination for individual infants are shown in Figure 3-1A and 3-1B, respectively. Of those infants who showed non-random distributions for both weight bearing and non-weight bearing movements, 41% showed the alternate form (similar to Figure 3-1A) and 51% showed the synchronous form (similar to Figure 3-1B). Although there is a visible difference in the spread of the distribution between the subjects shown in Figure 3-1A (alternate) versus 3-1B (synchronous), this was not a consistent finding between the two forms of coordination.

To determine if kicking position affected the interlimb coordination expressed, we studied 9 infants who kicked in different positions (i.e., supine, prone, sitting or air-stepping). The distributions of interlimb coordination were similar between kicking in different positions ($p>0.01$).

Group data is shown in Figure 3-2. Distributions of phase lag for all the cycles recorded are shown for non-weight bearing and weight bearing (Figure 3-2A). While there was a continuum across all phase lags, greater proportions of cycles are clustered around 50% and 0% or 100%. The distribution of the mean phase lag (i.e., vector angle) for all the infants, during weight bearing and non-weight bearing movements (Figure 3-2B) showed the same pattern ($p>0.01$).

Younger infants (<5 months old) tended to show alternate coordination, whereas older infants showed both alternate and synchronous, as reflected by the mean phase lag for non-weight bearing (Figure 3-3A – vertical dashed line separates infants less than and greater than 5 months old). Moreover, the vector length increased moderately with age (Figure 3-3B). Weight bearing activity also showed similar trends, but vector length showed no strong relation with age (not shown).

Comparison of interlimb coordination in weight bearing and non-weight bearing movements

Most infants (38/46 or 83%) showed the same interlimb coordination when weight bearing on the treadmill and when kicking ($p>0.01$, Kuiper's test comparing weight bearing and non-weight bearing distributions of phase lag for each infant). The sign test indicated that the proportion of infants showing similar distributions could not be due to chance. Interestingly, the average age of the infants who had different distributions was significantly greater than the infants found to have similar distributions (7.6 $\pm$ 1.6 months and 5.9 $\pm$ 1.2 months, respectively, independent t-test comparing group means, $p<0.01$).

The mean phase lags expressed when kicking and when weight bearing on the treadmill are plotted against each other for all infants except the 6 who showed random distributions of phase lag in weight bearing and non-weight bearing (Figure 3-4). The majority of infants showed similar mean phase lags in non-weight bearing and weight bearing movements (i.e., fall near the unity line).

Play habits

Sixteen of the 18 infants who showed synchronous coordination in weight bearing and non-weight bearing activities used the jolly jumper at least 5-7 times/week. In contrast, only 1 of the 17 infants who showed alternate coordination jumped in a jolly jumper 5-7 times/week.

Practice of an interlimb coordination pattern

Five infants practiced alternate coordination and 5 practiced synchronous coordination. Eight of the 10 infants showed a significant change in coordination of the weight bearing task at the second visit ($p<0.01$, Kuiper's test). This finding indicated that the practice successfully altered their interlimb coordination during weight bearing. Of the two infants who did not show a change, one practiced alternate coordination and the other synchronous coordination. One of these infants showed the trained pattern in weight bearing (just below statistical significance), and a significant change in the non-weight bearing distribution. Hence, only one baby failed to show any change in interlimb coordination as a result of practice.

Data from the 9 infants that altered their interlimb coordination are shown in Figure 3-5. Figure 3-5A shows the interlimb coordination during weight bearing and non-weight bearing activities for the infants that practiced synchronous coordination. Prior to training, they expressed predominantly alternate coordination. After 4 weeks of practice, all 5 showed synchronous coordination in weight bearing. Three of the 5 also showed a change in the non-weight bearing activity (2 statistically significant, 1 showed a trend, Kuiper's test comparing first and second testing sessions for each infant separately). Figure 3-5B shows the coordination for the infants that practiced alternate coordination. Before training, these babies showed synchronous coordination. After training, all babies switched to alternate coordination during weight bearing, although some infants showed cycles of synchronous coordination as well. Interestingly, none of these babies changed their interlimb coordination in non-weight bearing. The 3 infants in the Control Group showed no significant change in interlimb coordination of weight bearing and non-weight bearing tasks over a 4 week period ($p>0.01$, Kuiper's test, each infant tested separately). Infants who participated in the practice part of the study also showed more bimodal distributions of phase lag at the second visit. Prior to training, 1 of 16 distributions was significantly bimodal, while after practice, 4 of 16 were significantly bimodal ($p<0.01$, Dip Intensity Test).

Infants made smooth transitions between alternate and synchronous coordination

Seven of the 10 infants in the Practice Group showed transitions between the two types of coordination, whereas only 26% (12/46) of infants showed such transitions at the first testing session. Transitions were observed during weight bearing and non-weight bearing activities, but they were more commonly seen during weight bearing movements. Figure 3-6 shows data from two infants during transitions on the treadmill (one infant showed an alternate to synchronous transition and the other infant a synchronous to alternate transition). Not only did the phase lag change with the transition, but the cycle and extension durations often changed as well. Typically, cycle and extension durations were shorter during synchronous compared to alternate movement (Musselman and Yang 2007a).

Figure 3-7 shows the interlimb coordination and the cycle and extension durations of the reference leg for 6 infants who performed an alternate to synchronous transition (8 sequences), and 4 infants who showed the synchronous to alternate transition (7 sequences). Three infants showed both types of transition and therefore counted in both groups of infants. In some cases the interlimb coordination changed instantaneously (i.e., 1 cycle), while other transitions were more gradual. Similarly, the cycle duration of the reference leg changed over 1-3 cycles. Changes in extension duration mirrored changes in cycle length. In contrast, changes in flexion duration of the reference leg were independent of cycle duration and showed no consistent pattern across the transition. If the reference limb showed an instantaneous change in cycle and extension durations, then the opposite limb typically showed a more gradual change (not shown), and vice versa.

3.4 Discussion

The primary new findings are that the majority of infants expressed the same interlimb coordination in weight bearing and non-weight bearing activities. Moreover, practice of one type of coordination in weight bearing over four weeks induced a change in the coordination expressed during weight bearing, and in addition, translated to a change in non-weight bearing activity in some infants who practiced synchronous coordination. Finally, infants with both synchronous and alternate coordination in their repertoire showed smooth transitions between the two forms of coordination. Together, these findings suggest that there is partial sharing of circuitry for interlimb coordination of rhythmic leg movements in weight bearing and non-weight bearing in young infants. Furthermore, there must be close interaction between the circuitry for synchronous and alternate coordination to allow the seamless transition of movement between the two modes.

Expression of interlimb coordination

As a group, infants showed a full range of phase lags for interlimb coordination in both weight bearing and non-weight bearing movements (Figure 3-2A), indicating that the phase relationship between the legs can assume any value from completely synchronous to completely alternate. Two phase lags were more commonly adopted, however; phase lags around 0% or 100% (synchronous) and around 50% (alternate) (Figure 3-2). The same pattern is seen in rhythmic limbed movements of other neonatal and adult vertebrates under a variety of movement conditions (e.g., intact turtles walking and swimming – Walker 1979, intact cats stepping – English 1979, neonatal rats swimming – Bekoff and Trainer 1979, Cazalets et al. 1990, chicks hatching and stepping - Bekoff et al. 1987). Since the two types of interlimb coordination are seen in spinal preparations (Field and Stein 1997, Fayein and Viala 1976, Stelzner et al. 1975, Guiliani and Smith 1985, Grillner and Rossignol 1978, Bradley and Smith 1988b), and at least alternate coordination has been reported in human adults with clinically complete spinal cord injuries (Dimitrejevic et al. 1998, Gerasimenko et al. 2002), the coordination likely reflects the two primary forms of left-right commissural circuitry in the spinal cord, mutually excitatory or inhibitory (reviewed in Kiehn 2006).

Age-related trends in expression of interlimb coordination

The younger infants (<5 months old) in our group showed alternate coordination, in agreement with other reports (Touwen 1976, Thelen et al. 1983). They occasionally, however, exhibited synchronous coordination also, just as has been shown in other young mammals (Bradley and Smith 1988a, Howland et al. 1995, Fayein and Viala 1976, Bekoff and Trainer 1979). Hence, while synchronous coordination is not as commonly expressed in the very young human, the neural substrates for the activity are operational.

After 5 months of age, alternate and synchronous forms of coordination were equally likely in our subjects, although individual infants tended to show only one type. These results are somewhat different from those of Thelen et al. (1983), who suggested that infants show a decline in alternate kicking between 4 to 8 weeks of age, and an increase in synchronous kicks over the first 6 months of age. The difference in results could be attributed to the small number of subjects examined in the earlier study (8 infants).

Lack of experience may be the main reason why infants younger than 5 months did not show much synchronous coordination. Both alternate and synchronous forms of coordination were seen in a small number of infants (3/46) in the initial portion of this study (i.e., phase lag distribution was bimodal). In contrast, a much higher proportion of infants exhibited a bimodal distribution of phase lag after they practiced the opposite form of coordination. Since the practice was only for 4 weeks, age is unlikely to be the major reason for the change. This is further supported by the fact that none of the infants in the Control Group changed their interlimb coordination. Hence, exposure to different forms of interlimb coordination likely caused this greater diversity in the movement form, and may be the main reason why older infants more commonly showed both forms of coordination.

Possibility of shared circuitry for interlimb coordination of rhythmic movements

Recent findings in the rodent have identified many classes of commissural interneurons in the spinal cord that control interlimb coordination of the legs in locomotor movements (Kremer and Lev-Tov 1997, Butt and Kiehn 2003, reviewed in Kiehn and Butt 2003). The considerable complexity in classes of commissural interneurons identified in the rodent spinal cord suggests the possibility that different types of rhythmic leg movements in mammals use different crossing fibers. Furthermore, recent results in human adults suggest that the circuitry involved in forward and backward walking, including that associated with interlimb coordination, may be quite different because there was no transfer or interference between the adaptation to forward and backward walking on a split-belt treadmill (Choi and Bastian 2007).

Our evidence, however, is consistent with partial sharing of circuitry for interlimb coordination in the movements for two reasons. First, the vast majority of our infants showed the same type of interlimb coordination in weight bearing and non-weight bearing movements. Second, and more importantly, when an infant practiced the coordination pattern that was not performed at the first visit, this resulted in the expression of the same coordination pattern in the unpracticed movement (i.e., non-weight bearing) in some cases. Surprisingly, this transfer of learning was only seen in infants who practiced synchronous coordination. One possible explanation for this difference between the groups is a discrepancy in practice time. Although the practice duration we specified was the same for both groups, anecdotal evidence (comments from parents) suggested the infants who practiced synchronous coordination practiced more than the prescribed time (an average of 20 minutes/day rather than the prescribed 10 minutes/day) because they spent extended periods of time in the jolly jumper. It is impossible to restrict patterns of coordination in our case, as has been done in other animals (Viala et al. 1986). Hence, the effective duration of practice may have been different between our groups, and in retrospect should have been documented.

A plausible explanation for our results is as follows. Circuitry coordinating the movements of each leg interacts with mutually excitatory or inhibitory interconnections. With repeated practice of alternate coordination, the mutually inhibitory circuits were presumably activated by descending and/or peripheral input. Hence, in the second visit, this alternate coordination was expressed when the descending and/or peripheral input were present (i.e., during weight bearing), but not when they were absent (i.e., non-weight bearing). In contrast, perhaps because of the greater amount of time spent in practice by the group that trained in synchronous coordination, the mutually excitatory neural circuits between the legs may have been sufficiently reinforced that they could be expressed even when the descending and/or peripheral input was not present (i.e., non-weight bearing). The conclusions arrived at by Choi and Bastian (2007) are very different from ours. Of course, there are many differences between the studies, including the time course of learning and the similarities of the two tasks compared. We suggest, however, that the adaptation induced by short-term exposure to the split-belt environment could also have been upstream from the circuits in the spinal cord (i.e., descending and/or peripheral input). These circuits are clearly different for forward and backward walking, and may indeed reside in the cerebellum (Morton and Bastian 2006). Changes to upstream circuits would allow the spinal circuits used to remain the same. These ideas may be testable with animal models in the future.

Transition between alternate and synchronous movements

Transitions between alternate and synchronous forms of coordination were more common in the infants in the Practice Group (Figures 3-6 and 3-7). Transitions were characterized by a change in phase lag between the limbs of ~50%, and often a concurrent change in the cycle duration of ~30-50% (synchronous shorter than alternate), very similar to the trot-gallop transition in intact and reduced preparations of quadrupeds (Shik et al. 1966, Grillner 1973, Miller et al. 1975, English and Lennard 1982). The transitions typically occurred with just one or two intermediate cycles, in which the phase lag and cycle durations assumed intermediate values (Figure 3-7). Typically, when abrupt transitions occurred in one leg, the transition in the other limb was more gradual, reminiscent of that seen in quadrupedal coordination (English and Lennard 1982). Such smooth transitions suggest that the circuitry for coordinating synchronous and alternate coordination interact to bring about the transition, and perhaps are both operative during the transition period.

Conclusions

The results are consistent with the idea that there is some sharing of circuitry for interlimb coordination between weight bearing and non-weight bearing leg movements in young infants. The sharing is unlikely to be complete, because a small proportion of infants exhibited different interlimb coordination during weight bearing and non-weight bearing, and the transfer of learning in the Practice Group was not complete. Finally, the expression of interlimb coordination is clearly malleable through experience.

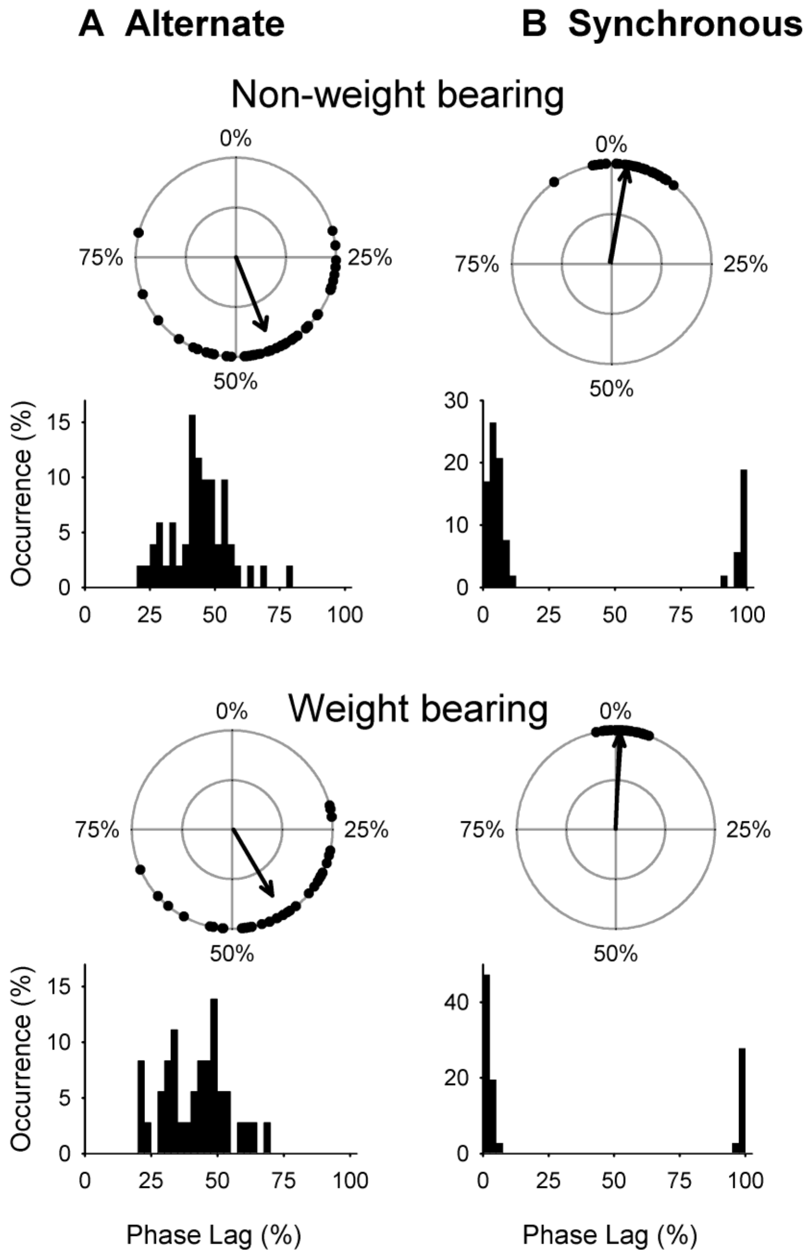

Figure 3-1: Phase lag distributions for single infants showing the beginning of a cycle in one leg as a function of the cycle in the other leg (cycle from 0-100%). Each distribution is presented as a histogram and a polar plot. The black arrow in the polar plot represents the mean vector (maximum length=1, represented by the outer circle). Each filled dot on the perimeter represents one cycle. (A) Example of an infant who showed alternate coordination in both weight bearing and non-weight bearing. (B) Another infant who expressed synchronous coordination in both activities. Bin size in the histograms is 2.5%.

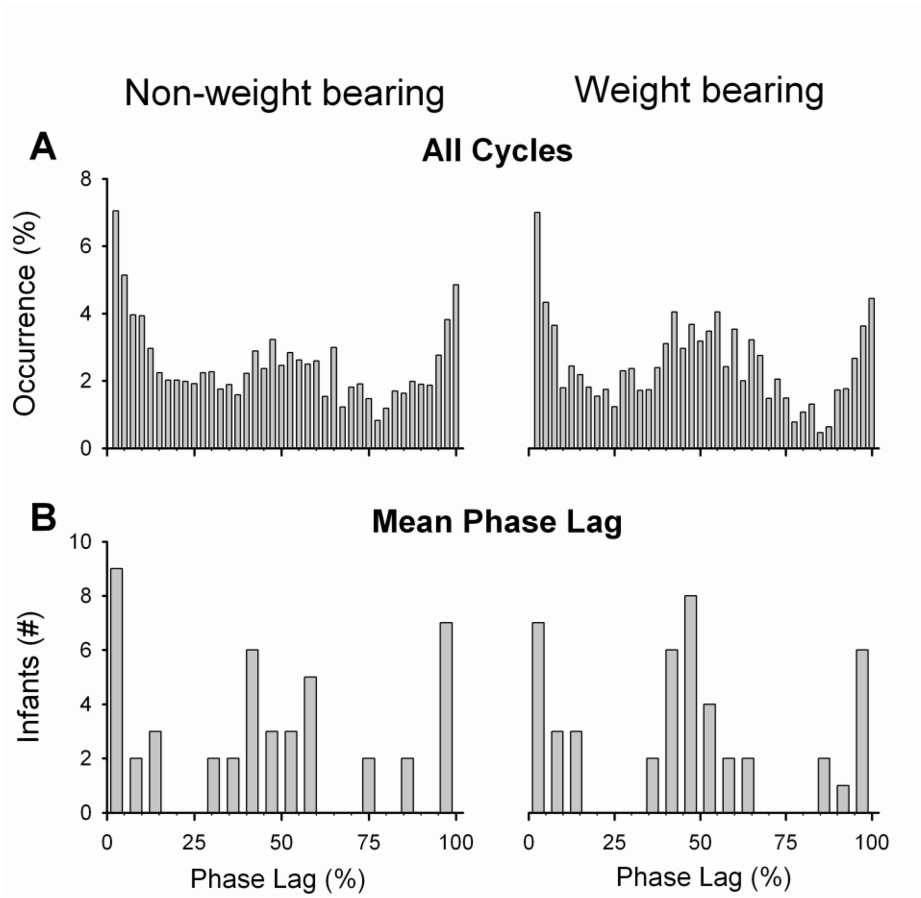

Figure 3-2: Group data showing the distribution of phase lags. (A) Distribution for all cycles of non-weight bearing (left) and weight bearing (right) movements from all 46 infants. The number of cycles per infant varied from 15-119 for non-weight bearing and 15-87 for weight bearing. The distribution of phase lag from each infant was normalized to the number of cycles recorded from the infant, so all infants are represented equally. Bin size is 2.5%. (B) Distribution of the mean phase lag (i.e., the angle of the vector shown in Figure 3-1) for all infants. Bin size for phase lag is 5%.

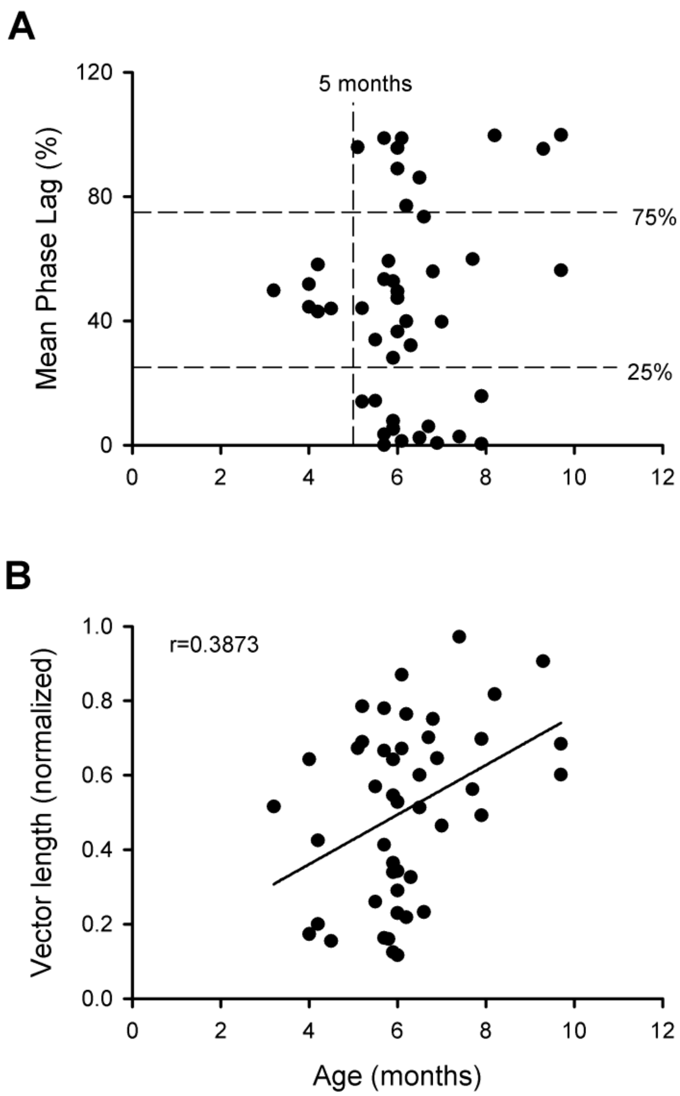

Figure 3-3: The effect of age on interlimb coordination. (A) The mean phase lag for kicking is shown as a function of age. Infants under 5 months of age (left of vertical dashed line) tended to show alternate coordination (i.e., ~50%), whereas older infants showed either alternate or synchronous coordination. Divisions between our definitions of alternate and synchronous forms of coordination are shown in the horizontal, dashed lines. (B) The length of the mean vector increased moderately with age.

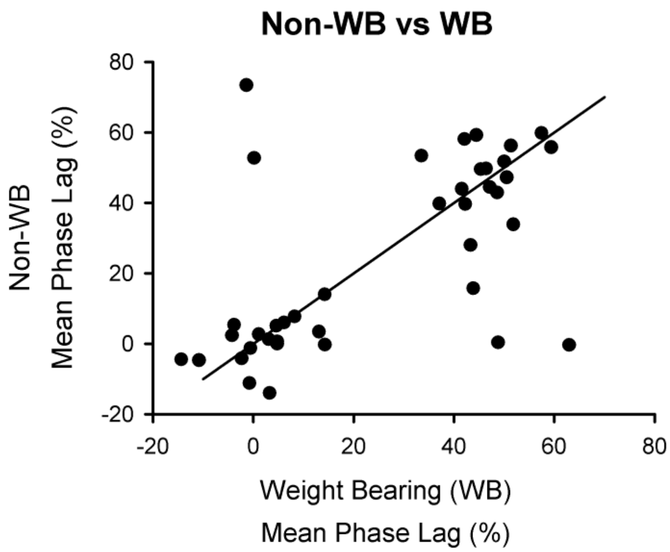

Figure 3-4: Mean phase lag in non-weight bearing is plotted as a function of the mean phase lag in weight bearing for each infant. With a few exceptions, most data points fall near the unity line. Each circle is from one infant. Phase lags greater than 75% were reflected about 0 (i.e., subtracting the phase lag by 100%).

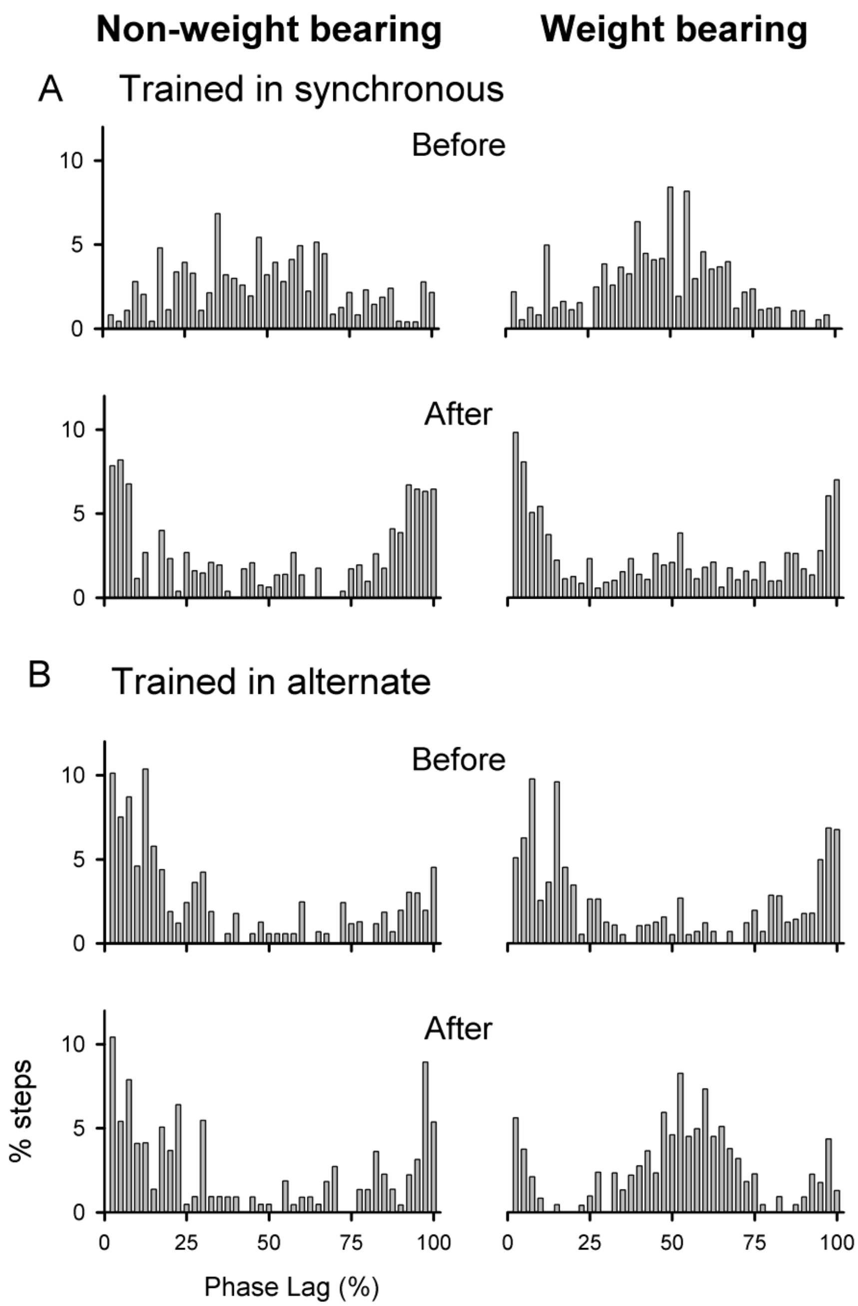

Figure 3-5: Phase lag distribution for the infants that practiced the interlimb coordination they did not express at the first visit. (A) Data from 5 infants who practiced synchronous coordination. These infants showed more alternate coordination prior to training (Before). After 4 weeks of practice (After), they showed a conversion to synchronous coordination both in weight bearing and non-weight bearing. (B) Data from 4 infants who practiced alternate coordination. These infants showed mostly synchronous coordination prior to training. After practice, alternate coordination was seen in weight bearing, but not in non-weight bearing.

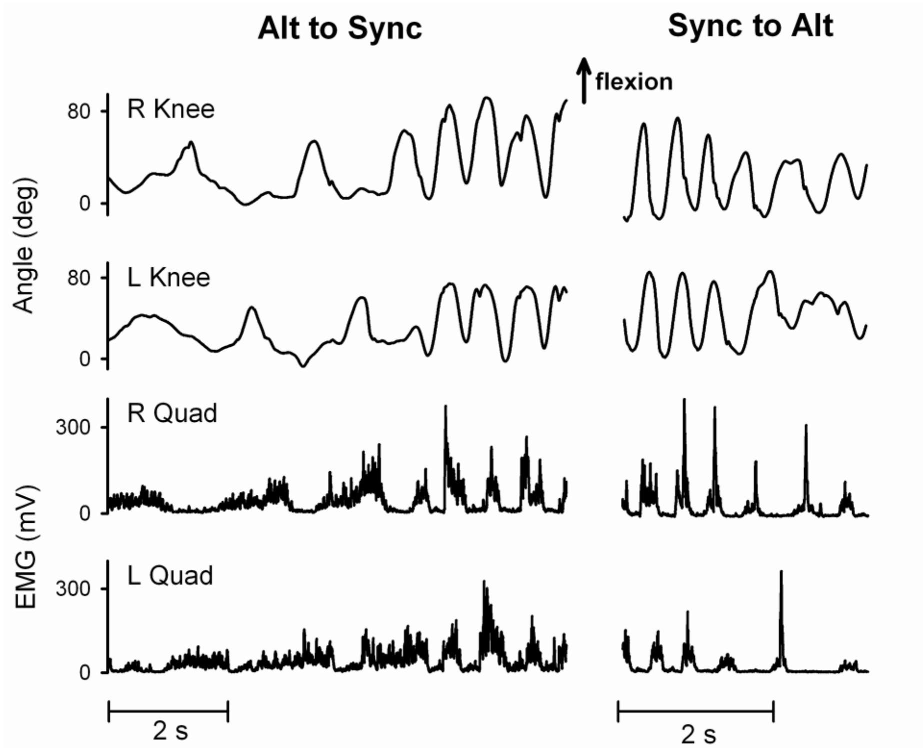

Figure 3-6: Single subject data from 2 infants showing transitions between alternate and synchronous coordination on the treadmill. One infant showed a transition from alternate to synchronous coordination (left) and the second infant showed a transition from synchronous to alternate (right) coordination. Electrogoniometer data from the right and left knee (top two traces) and rectified EMG from the quadriceps muscles on each side are shown. Transitions occurred smoothly with just one or two intermediate steps. Alt: alternate; Sync: synchronous.

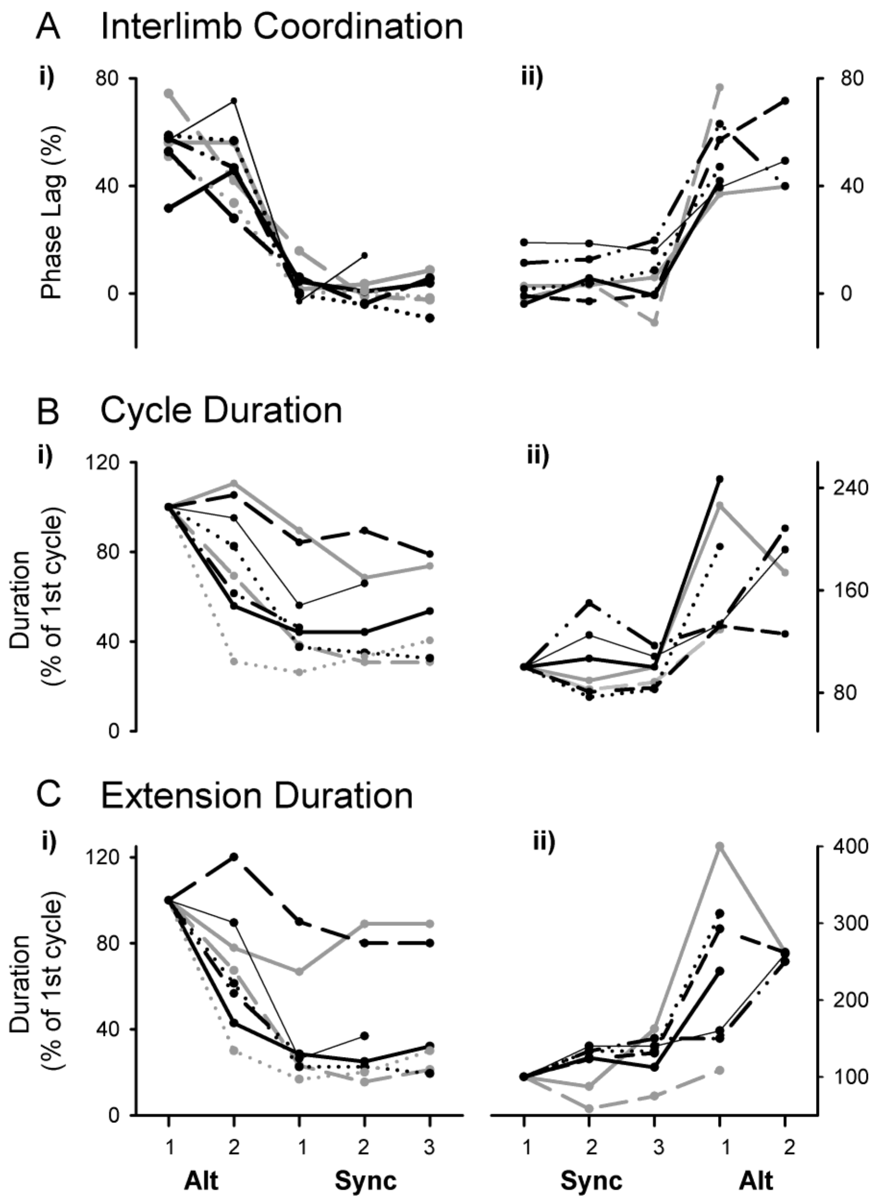

Figure 3-7: Changes in cycle parameters during transitions from alternate to synchronous (left, subplots i) and synchronous to alternate (right, subplots ii). Coordination between the left and right legs (A), cycle duration of the reference leg (B) and extension duration of the reference leg (C) are plotted for 8 and 7 transitions on the left and right, respectively. Each line type refers to a single transition. For the plots in A, phase lags greater than 75% were reflected about 0% by subtracting the phase by 100%. Cycle and extension durations are expressed as a percentage of the duration of the first cycle.

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Chapter 4: Training of Walking Skills Over-ground and on the Treadmill: Case Series on Individuals with Incomplete Spinal Cord Injury

4.1 Introduction

There has been considerable interest in body weight-supported treadmill training (BWSTT) after incomplete spinal cord injury (ISCI) (Wernig et al. 1995). The ultimate goal of gait retraining after ISCI is successful ambulation in the home and community. Walking in the real world encompasses a variety of walking skills, such as negotiating doors, uneven surfaces, slopes, curbs and obstacles (Musselman and Yang 2007). Few studies have investigated whether BWSTT is effective practice for this diverse set of walking skills. The only study that considered functional walking status suggests that BWSTT does not transform individuals with a chronic, ASIA C ISCI into community walkers (Field-Fote 2001).

Greater improvements in walking ability are seen when the training closely resembles the functional task of walking (i.e., task-specific) (Salbach et al. 2004). BWSTT is a very constrained task of repetitive stepping with little variation. Work in animals suggests that repetitive training of one specific task results in improved performance of that task, but at the expense of related, untrained tasks (Edgerton et al. 1997, Girgis et al. 2007). Thus, it is unclear how specific walking training should be. Perhaps a highly constrained task is not optimal for community walking (Musselman and Yang 2007). Intensive training of a variety of relevant walking skills may better prepare individuals for community walking.

A small number of studies have combined BWSTT with over-ground training for individuals with ISCI, either concurrently (Wernig et al. 1995, Protas et al. 2001, Behrman et al. 2005, Dobkin et al. 2006) or as a training progression (Behrman and Harkema 2000). None of the over-ground training has been based on

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comprehensive, empirical information of what is required for community living. Here, we report the results from a case series involving four individuals with ISCI, who participated in alternating blocks of BWSTT and over- ground training of walking skills (henceforth called skill training). The tasks practiced in skill training were known to be important for community ambulation (Musselman and Yang 2007). The tasks were varied daily to approximate the situation in daily life. The training was intensive ~1 hour/day, min 3x/week, over 3 months. The tasks were challenging (i.e., rated as difficult by the patients and could induce falls). Our aim was to determine the effectiveness of skill training, and to compare its effectiveness with the method of BWSTT, in a small group of individuals.

4.2 Methods

Patient History and Review of Systems

Volunteers were recruited through the Edmonton branch of the Canadian Paraplegic Association and rehabilitation clinics in Edmonton, AB. To be included, the patients must have been 1) ≥10 months post-injury, and 2) able to walk 5 meters over-ground with or without walking devices and/or physical assistance. Patients were asked not to begin a new exercise/rehabilitation program, or to change medications during the study. The study was approved by the Health Research Ethics Board, University of Alberta and Capital Health Edmonton. Informed written consent was obtained from the patients.

Patient characteristics are shown in Table 4-1. Medical histories were noteworthy only for ISCI, with the exception of Patient 3 who also had a mild brain injury. Initial walking ability varied amongst the patients, as indicated by a range of 6-12 on the Walking Index for Spinal Cord Injury II (WISCI II). The WISCI II is a 21-point ordinal scale that rates an individual's ability to walk 10 m based on the braces, devices and assistance needed (Ditunno and Ditunno 2001). The WISCI II has concurrent validity and good reliability in the spinal cord-injured population (Ditunno et al. 2000).

Prior to training, Patient 2 could walk at least 100 meters independently with devices and was a home ambulator (i.e., he walked at home and used a wheelchair in the community). In contrast, Patients 1, 3 and 4 were able to walk short distances only and used a wheelchair for mobility in all environments. The patients were considered good candidates for skill training because they could all walk short distances over-ground. Moreover, all 4 patients were community-dwelling, but did limited or no walking in the community. Skill training might enhance their participation and independence in community walking.

Two additional patients were recruited, but dropped out after the first phase (BWSTT) of training for reasons unrelated to the training. One patient left because of severe pain, which was present prior to the training, and was not made worst or better by the training. The other fell at home and suffered a dislocated shoulder. This individual was a community ambulator prior to training.

Intervention

All patients completed ≥9 months of training. They received 3 months of BWSTT and were then allocated using a random permuted blocks method into 1 of 2 groups. The allocation to treatment was not concealed from the experimenters. Patients 1 and 2 received 3 months of skill training followed by 3 months of BWSTT, whereas Patients 3 and 4 received the training in the reverse order. Patient 4 was involved in an additional 2 blocks of training, also presented in an alternating order. There were no breaks between the blocks. The single case, alternating treatment design allowed each patient to act as his/her own control. We randomly allocated patients into treatment groups in order to offset any carryover effects (Franklin et al. 1996).

Training Programs

Skill training and BWSTT lasted ~1 hour/day (including rest breaks), with a target frequency of 5 days/week for 3 months. The programs were administered by a physical therapist, with the assistance of a volunteer, as needed. Braces were worn during both types of training to increase comparability. Rest breaks were taken as needed.

Skill Training: The researchers and 2 physical therapists developed the aim and principles of skill training. The aim was to engage patients in challenging walking tasks. Skill training was based on 3 principles. First, tasks practiced were those known to be important for daily walking (Musselman and Yang 2007). Second, a variety of environments and conditions were used to approximate the situation in daily life. Third, the tasks practiced were sufficiently challenging to induce errors, since learning is augmented in situations where errors are induced rather than suppressed (Patton et al. 2006, Reisman et al. 2007). The tasks practiced in skill training were grouped into 5 categories, with the frequency of training specified a priori (Table 4-2). The proportion of time spent training each of the categories was determined by the therapist and varied day to day. Walking aids were permitted during skill training.

Three measures were used to gauge how challenging the training was. First, patients rated how difficult they found each training task on a visual analog scale, from 0 (very easy) to 10 (extremely difficult, would fall without assistance). Our target was a difficulty rating of ≥ 7. This target was based on the therapist observation that a rating of 7 was associated with a need for significant concentration and/or resulted in a loss of balance that the patient could self-correct. Secondly, the therapist recorded the number of near falls (i.e., unable to recover balance and fall prevented by therapist) experienced in each session. Our target was ≥ 1 near fall per training session. Thirdly, the Borg Rating of Perceived Exertion (RPE) (Borg and Linderholm 1967) was used to gauge the perceived cardiovascular load (target: Borg RPE of 13/20 (somewhat hard) or higher), since endurance was one of the categories of tasks in the training (see Table 4-2). During training, if the difficulty ratings were above or below the target level, the therapist would adjust the task accordingly (e.g., change walking aid or size of obstacle).

Parameters for each skill training session were documented with a standardized table. Table 4-3 summarizes this information for each patient. Four main categories of tasks were targeted (panel 2 in Table 4-3). Skill training varied somewhat between patients because of the individual's abilities. For example, Patients 1 and 4 did not practice crossing traffic intersections since their walking speeds were not sufficiently high to attempt the task safely.

To further verify that the skill training administered by the therapist was meeting the expectations of the study, a researcher videotaped a full training week for Patients 1, 3 and 4. An independent reviewer identified from the videotape: 1) the number of times/week each of the skill training categories were practiced, 2) the number of different environments within which training occurred each day, and 3) which of the important walking skills (Musselman and Yang 2007) were targeted in that training week. The independent review indicated that the criteria of skill training were met with respect to the target frequency for training categories and environments. The majority of relevant walking tasks (Musselman and Yang 2007) were practiced during the week, but walking in a crowded environment and walking on a slippery surface were consistently missed.

BWSTT: A standard treadmill equipped with an over-head counterweight system (custom made) was used. Training criteria were determined as follows: 1) training speed was the maximum speed tolerated by the patient, and was always greater than a patient's over-ground walking speed, 2) amount of body weight support was the lowest possible without a patient's knee(s) and hip(s) collapsing into flexion during stance, and 3) the body weight support and speed selected must allow a bout duration of at least 3 minutes. Manual assistance was provided to the lower extremities and/or trunk as required. Patients were permitted to hold side rails for stability while walking. The rails were positioned at about chest height to prevent weight bearing through the arms.

BWSTT was progressed when one of the following criteria was met: 1) a Borg RPE <13, or 2) the ability to walk for >10 minutes with minimal physical assistance. Progressions involved increasing the speed and/or decreasing body weight support. If the speed reached 1.0m/s, body weight support was reduced rather than increasing the speed further. Otherwise, the therapists and patients decided whether to increase speed or decrease body weight support. For Patient 2, who required no body weight support, progressions involved increasing speed and duration of walking, and adding arm swing. Borg RPE was monitored during each BWSTT session. The parameters of BWSTT are summarized in Table 4-4 for each patient. There was a trend towards longer walking times for skill training than BWSTT (compare Tables 4-3 and 4-4).

Patient 2 completed his second block of BWSTT in his own home since he lived 150 km from Edmonton, and he did not require body weight support. The therapist visited his home prior to this second bout of BWSTT to set up the training program, and she maintained daily phone/email contact with him to ensure training quality and recommend progressions. Patient 2 recorded the training parameters and Borg RPE for each training day.

Outcomes

Testing of clinical measures was done prior to the beginning of training, monthly during training and at the end of training. Follow-up assessments were 3 months post-training, and for Patient 2, an additional assessment at 6 months post-training. A therapist blind to group allocation assessed all the patients. This was possible because the assessing therapist worked at a different institution, and carried out all assessments in the evenings. The assessor and patients were instructed regarding the blinding. There were no breaches to the blinding. Patients used the same walking aids in all assessments except the mEFAP (see below), which accounts for changes in walking aids. The clinical measures were assessed in the following order:

1) The Berg Balance Scale measures static and dynamic standing balance (Berg et al. 1989). Its measurement properties have been established in individuals with ISCI (Ditunno et al. 2007). Both BWSTT and skill training could affect balance. The best possible score is 56, with a score less than 45 being associated with a risk of falls in the elderly (Berg et al. 1992). The minimum clinically important difference (MCID) is 6 points in individuals with stroke (Stevenson 2001), but it is not known for the ISCI population.

2) The Modified Emory Functional Ambulation Profile (mEFAP) evaluates walking ability based on timed performance of 5 walking tasks (walking 5 meters on a smooth floor and on carpet, the timed up-and-go test, negotiating obstacles and stair-climbing) (Wolf et al. 1999, Baer and Wolf 2001). The total score reflects the total time (in s) to complete the tasks. Ambulation aids and physical assistance are accounted for by a multiplication factor. The reliability and validity of this scale has been established (Wolf et al. 1999). An option for forearm crutches was added to the scoring of the mEFAP (multiplication factor = 7) since this is a common aid used by individuals with ISCI. This was the most objective measure of walking skill available that suited the abilities of our patients. The MCID for this measure is not known.

3) The 6-minute walk test measures walking endurance (Guyatt et al. 1985). The score is the total distance (m) traveled in 6 minutes. The test is valid and reliable for individuals with ISCI (van Hedel et al. 2005). This measure was used because endurance was one of the aims of our training. The MCID was estimated to be 54 m for individuals with chronic obstructive lung disease (Redelmeier et al. 1997), and is unknown for those with SCI.

4) The 10-meter walk test was used to measure comfortable and fast walking speeds. For fast walking speed, patients were instructed to walk as fast as they could without losing their balance. The 10-meter walk test is valid and reliable for individuals with ISCI (van Hedel et al. 2005). The MCID was estimated to be 0.05-0.06 m/s for a group of community-dwelling individuals with ISCI (Musselman 2007).

5) The Activities-specific Balance Confidence (ABC) Scale requires patients to rate their confidence (from 0%=no confidence to 100%=complete confidence) in their ability to maintain balance during 16 functional activities (Powell and Myers 1995). The ABC scale was shown to have acceptable psychometric properties in individuals with stroke (Botner et al. 2005). It provided a measure of the patient's opinion, independent of the objective measures of performance. The MCID is not known, but a score of 67% was a threshold that separated fallers from non-fallers among community-dwelling seniors (Lajoie and Gallagher 2004).

4.3 Results

Figure 4-1A shows mEFAP scores during training and follow-up for each patient. The change scores are shown above or below the trace for each phase of training (i.e., score at end of phase – score at beginning of phase). Patients 1 and 3 showed improvement during skill training and BWSTT, while there was a tendency for Patients 2 and 4 to show greater improvement with skill training than with BWSTT. Retention of gains was estimated by [(follow-up score – score at beginning of training)/ (score at end of training – score at beginning of training)] x 100%. Gains on the mEFAP were maintained post-training with the exception of Patient 4 (retention of gains 3 months post-training: median (IQ) = 99.5% (51%)).

Changes in comfortable (Figure 4-1B) and fast (not shown) walking speeds were very similar. The change scores are shown above or below the trace for each phase of training for comparison with the known MCID ($\geq$0.05 m/s) for persons with ISCI (Musselman 2007). Patient 4 showed the smallest overall change and the least retention of gains on follow-up. The other 3 patients showed improvements >MCID during the skill training phase. Patients 1 and 3 also showed gains >MCID for one of the BWSTT phases. Retention of gains on follow-up was good except for Patient 4 (median (IQ) = 92% (83%)).

Qualitatively, changes in the 6-minute walk test (not shown) were similar to those seen for comfortable walking speed (Figure 4-1B). The improvement in score from beginning to end of all training was 75 m, 47 m, 85 m and 8 m for Patients 1 through 4, respectively. Two exceeded the MCID reported for individuals with COPD (change of 54 m (Redelmeier et al. 1997)). Retention of gains was good for Patients 1, 2 and 3 (median (IQ) = 103% (98%)).

Results from the Berg Balance Scale varied among patients, but for the most part, minor gains were made. Total improvements over the entire training period were 9, 0, 10 and 5 for Patients 1 through 4, respectively. Results from the ABC scale also varied among the patients. Interestingly, increases in balance confidence were consistently seen during skill training (median (IQ) = 11% (9%)), but much less frequently during BWSTT (median (IQ) = -2% (14%)). In all cases, however, the scores on the ABC scale remained below 67%, scores which suggest a risk of falling in seniors (Lajoie and Gallagher 2004).

Functional walking status: Training led to changes in functional walking status in 2 patients. Patient 2 was walking for short distances (i.e., <100m) in the community post-training. Patient 1 was walking within the home (including going up and down stairs) after training, but continued to use her wheelchair in the community. Functional walking status did not change for Patients 3 and 4, although Patient 3 walked daily within her home for exercise.

Group Data: The median value (and range) of the change in clinical scores is shown in Figure 4-2. In Figure 4-2A, the data were collapsed across each block of training regardless of the type of training. The scores shown are change-scores (i.e., change-score = score at end of training – score at beginning of training). For most patients, greater improvements were made in the latter blocks of training (i.e., months 4-9 of training). In Figure 4-2B, the data were collapsed across each type of training regardless of when it occurred. With the exception of the Berg Balance Scale, all measures tended to show greater gains with skill training than with either block of BWSTT.

4.4 Discussion

We show that an intensive program to retrain walking skills over-ground may be as effective as BWSTT in this small group of patients. Clinically important changes were seen in walking speed for all patients over the whole duration of the training, and also during the skill training portion alone for 3 of the 4 patients. The same 3 patients also showed good retention of gains 3 months after training terminated.

Effectiveness of skill training and BWSTT

Overall, the findings suggest that skill training resulted in gains in walking speed, endurance, balance confidence and performance of several walking skills (i.e., mEFAP) in our patients (Figure 4-2B). Patient 2 showed considerably greater gains on all outcome measures, except the Berg Balance Scale, during skill training compared with BWSTT. Since Patient 2 completed the second block of BWSTT in his home, we cannot rule out the possibility that this training was different to the training others received in the laboratory. This is unlikely, however, as he also showed minimal improvement during the first block of BWSTT. To determine whether his results biased the findings in favor of skill training, the analysis was redone without his data. The median and range of scores changed very little for the ABC Scale and Berg Balance Scale (Figure 4-2B, black dots show median). The median scores on the mEFAP, 6-minute walk test, and 10-meter walk test, however, were generally more similar across training methods once Patient 2's data were removed. For example, the change in score from TT_1 is more similar to ST for the mEFAP when data from Patient 2 is removed (i.e., dots closer together than median lines in Figure 4-2B), and change scores for TT_2 are more similar to ST for the 6-minute and 10-meter walk tests.

Skill training and BWSTT, as implemented in this study, are quite different. The only similarities are that both require a training frequency of 3-5 times/week and a moderate cardiovascular load (i.e., Borg RPE≥13/20). BWSTT involved repetitive practice of forward stepping movements, typically with little variation except changes in speed and amount of weight-support. BWSTT, as reported by others, has not always been confined to stereotypical stepping on the treadmill. For example, some have included over-ground training as soon as possible (reviewed in Behrman et al. 2006). In all forms of BWSTT, however, patients wear a harness that supports some of their body weight and provides trunk stability, likely reducing balance demands in comparison to over-ground training. While the amount of weight-support is reduced as the patient progresses, the demands on balance are likely still less than walking over-ground in our subjects, as the handrails were available for stability if needed. In contrast, skill training requires full weight-bearing and challenges balance well beyond walking on level ground. It encompasses practice of >10 walking tasks frequently encountered in daily life (Musselman and Yang 2007), such as negotiating obstacles, doors, stairs, curbs and crowded environments, in varying situations and environments. We speculate that the incorporation of varied walking situations facilitates the patient's ability to adapt, which is necessary for community and household walking (Musselman and Yang 2007). The degree of challenge (i.e., near falls) and the use of tasks similar to those in daily life may have contributed to the increase in patient confidence and skill. Hence, we suggest, as others have, that BWSTT may not be sufficient for training balance and adaptability during walking (van Hedel 2006). Perhaps skill training should be considered a progression of BWSTT for walking retraining, since BWSTT can be implemented when walking ability is low.

It was difficult to equate the intensity of the two forms of training because they are very different in nature. The patients judged the 2 forms of training to be equally intensive (Borg RPEs in Tables 4-3 and 4-4). There was, however, a trend for the sessions during skill training to be longer than during BWSTT (Tables 4-3 and 4-4). Thus, we cannot discount the possibility that the longer session durations of skill training contributed to the outcomes reported here. In retrospect, other measures of dosage would have been useful to include, such as step count or distance covered.

There are surprisingly few reports comparing walking outcomes with BWSTT and over-ground training. In acute ISCI, no differences in a number of walking-related outcome measures (i.e., Functional Independence Measure for Locomotion, walking speed, 6-minute walk test, Berg Balance Scale, WISCI II) were reported between individuals who trained using BWSTT and those who trained over-ground (Dobkin et al. 2006). The study, however, remained under-powered statistically, in spite of the impressive recruitment of 117 subjects. Similarly, BWSTT and over-ground training (both with electrical stimulation) were found to be equally effective at improving walking speed, step length and step symmetry in individuals with chronic ISCI (Field-Fote et al. 2005), but it too was statistically under-powered. In our case-report, when training was begun early (i.e., Patients 1 and 3 both ~1 year post-injury) gains in walking were seen regardless of the type of training. In contrast, Patients 2 and 4 (4.4 and 23 years post-injury, respectively) tended to show more improvement with skill training (Figure 4-1). The possibility that skill training may be especially effective for individuals who were injured some time ago would be valuable to explore with a large number of patients in the future.

Long-term training results in ongoing improvement in walking ability

Patients continued to show improvement with long-term training (i.e., $\geq$6 months). For example, improvements were seen in mEFAP scores and walking speed for at least 6 months of training in Patient 2, and up to 9 months or more for the other patients (Figure 4-1). These results are consistent with those of Hicks and colleagues (2005). They reported that about half of their subjects with SCI showed improved ability to walk over-ground, as measured with a modified version of a scale by Wernig et al. (1998), throughout 12 months of BWSTT (Hicks et al. 2005). Hence, there are benefits to extending the length of walking retraining for ISCI beyond the typical 3 months. Indeed, both Patients 2 and 4 required ≥3 months to show initial improvements. Hence, for some individuals with ISCI, ≥3 months of training are needed to bring about meaningful change.

Practice and minimum ability needed for retention of gains

The 3 patients who showed good retention of gains after training continued to walk at home. Hence, regular walking is necessary to retain function (Wernig et al. 1998, Wirz et al. 2001, Field-Fote et al. 2005, Hicks et al. 2005). Skill training may have facilitated retention of walking ability as it allowed practice of relevant walking skills in an appropriate environment. Perhaps this type of practice provided our patients with the confidence to perform these skills on their own (as seen in the ABC scale Figure 4-2B). Patient 4 was the exception. Not only did Patient 4 report no walking post-training, he also had the lowest walking speed at the end of training (0.15 m/s). Hence, there may be a minimum walking speed, below which walking is not realistic in the home.

Limitations of the study

Two difficulties were identified in the implementation of skill training. First, individuals differed in their willingness to take risks (Table 4-3, # near falls). Ways to increase the patient's confidence to take risks during training should be sought. Second, two tasks, walking in a crowded environment and on a slippery surface, were frequently omitted. Both are difficult to simulate in a clinical environment. Innovative ways to incorporate these in the future would be useful.

There was surprisingly little change in the Berg Balance Scale with either form of training (Figure 4-2). At the beginning of training, scores on the Berg Balance

Scale were low (11 for Patient 1, 8 for Patients 2 and 3, and 22 for Patient 4), thus there may have been a floor effect. The Berg Balance Scale does not permit the use of walking aids, which all of our patients required for standing and walking activities. Also, perhaps the Berg Balance Score does not reflect the dynamic balance needed for walking.

This is a small scale, single case series. Hence we cannot generalize beyond our group of patients. The case series describes a systematic, over-ground training program that could be used for study with a larger cohort of patients. Such future studies would benefit from a better measure of the skills need for community walking. We used the mEFAP, which includes some skilled walking tasks, but does not consider other walking tasks known to be commonly performed in everyday life, such as negotiating ramps, curbs, doors, uneven surfaces, and walking while carrying objects (Musselman and Yang 2007). Unfortunately, this is also true of other gait-related scales for the ISCI population (Lam et al. 2008). There is a great need for better walking scales to evaluate skillful aspects of walking.

The promising results of this case series suggest that skill training may be an effective method for individuals with ISCI who have some pre-existing ability to walk. Future studies could modify skill training to include individuals who do not have adequate strength, endurance, postural control and/or balance to stand upright and step. For example, others have described systems to support body weight while walking over-ground that could be used for training (Miller et al. 2002, Field-Fote et al. 2005, Patton et al. 2008). Such a system would permit variable, over-ground practice of many of the walking tasks needed for daily life (Musselman and Yang 2007). Likewise, some skilled tasks, such as obstacle clearance, have been executed on a treadmill with body weight support (Lam and Dietz 2004, van Hedel et al. 2006). It may be feasible to practice other important walking tasks on the treadmill, such as negotiating different walking surfaces and carrying objects while walking. Either approach would enable individuals with limited walking ability to participate in variable practice of relevant walking skills.

Patient	1	2	3	4
Age (yrs)	42	61	24	47
Gender	F	M	F	M
Injury Level	T2	L1	T10	C5
Years post-Injury	1.0	4.4	0.9	23.0
Mechanism of Injury	Surgery	Fall	Car Accident	Hockey
Medications	Baclofen Diovan	Tegretol	Baclofen	None
ISCSCI	C	C	C	C
WISCI II	9	12	6	9
Walking Aid	2WW	2 FC	4WW/1 PA	St.W
Braces	2 AFO	2 AFO	2 AFO	2 AFO
Comfortable Speed (m/s)	0.07	0.61	0.18	0.11
6-Minute Walk (m)	25	191	50	39
Living Situation	House, family	House, family	House, family	House, family
Employed?	No	No	No	Yes

Table 4-1: Characteristics of Patients: M = male, F = female. **Injury level** = neurological level of injury as defined by ISCSCI. **ISCSCI** = International Standards for Neurological Classification of Spinal Cord Injury (Maynard et al. 1997). **WISCI II** = Walking Index for Spinal Cord Injury II, 4WW = 4-wheeled walker, 2WW = 2-wheeled walker, St.W = standard walker, FC = forearm crutches, 1PA = assistance of 1 person required. AFO = ankle-foot orthosis. Values for comfortable walking speed and 6-minute walk represent scores at the beginning of training on the 10-meter walk and 6-minute walk tests, respectively.

Skill Training Category	Examples of Tasks	Training Frequency
1. Walking balance	▪ Walking on different surfaces/in different directions/in windy conditions ▪ Walking and reaching	5 times/wk
2. Skilled walking tasks	▪ Negotiating obstacles, stairs, curbs, sloped surfaces, crowded environments, narrow spaces, doors	5 times/wk
3. Walking with secondary task	▪ Walking and looking/reaching/talking/ carrying an object/pushing an object	5 times/wk
4. Endurance	▪ Walking long distances (i.e., $\geq$100m) indoors/outdoors	2-3 times/wk
5. Speed	▪ Walking short distances (i.e., $\leq$25m) at fast pace indoors/outdoors ▪ Crossing intersections	2-3 times/wk

Table 4-2: Skill Training Categories: The five categories of skill training (left column), examples of tasks practiced in each category (middle column), and the target training frequency of each category.

Patient	1	2	3	4_i	4_{ii}
# Sessions/wk	4.5±0.7	4.1±0.6	3.2±1.1	3.0±1.0	2.9±0.8
Session time (min)	33±8	44±7	31±8	39±12	32±7
% Time: Balance	19±10	24±8	24±13	26±11	29±10
Skilled Walk	24±10	28±10	20±9	25±12	27±14
2° Task	19±13	25±9	30±13	25±13	21±11
Endurance & Speed	38±12	23±9	26±15	25±19	23±15
Difficulty: Balance	5.7±1.2	8.9±1.0	7.3±2.6	6.9±1.4	8.6±1.3
Skilled Walk	5.4±1.0	9.1±0.9	7.1±2.1	7.0±1.8	8.4±1.0
2° Task	5.1±1.2	8.6±0.9	8.1±2.2	6.6±1.5	7.5±2.0
Borg RPE	14.9±1.0	17.6±2.6	13.0±2.5	13.0±0.9	12.5±2.3
# Near Falls	1.7±1.2	2.8±1.5	7.4±3.2	2.1±1.8	1.4±1.1
# Surfaces	2.6±1.3	3.5±1.6	2.6±1.2	2.4±1.3	3.1±1.3
Curbs (%)	10.7	63.5	20.9	11.1	15.0
Stairs (%)	73.2	53.8	62.8	47.2	50.0
Slopes (%)	19.6	69.2	32.6	30.6	37.5
Doors (%)	23.2	75.0	39.5	44.4	22.5
Crowded Place (%)	5.4	15.4	16.7	11.1	5.0
Narrow Space (%)	12.5	71.2	16.7	33.3	22.5
Carrying (%)	41.1	73.1	61.9	52.8	32.5
Obstacles (%)	26.8	57.7	25.6	50.0	60.0
Intersections (%)	0	13.5	4.7	0	0

Table 4-3: Description of skill training by patient: Patient 4_i and 4_{ii} refer to the first and second blocks of skill training, respectively, for Patient 4. The number of sessions/week, session duration excluding rests, percent time spent on each category, difficulty ratings, Borg RPE, number of near falls, and number of surfaces encountered/session are expressed as mean$\pm$1 standard deviation. Difficulty ratings were measured at the midpoint of the training category. Encounters with the remaining tasks (i.e., curb, stairs, slope/ramp) are expressed as a percentage:
(number of training days encountered/total number of training days) x 100%. **Balance** refers to the training category walking balance, **Skilled walk** to skilled walking and **2^o task** to secondary tasks.

	BWSTT Time (min)	Days/ wk	BWS (% BW)	Speed (m/s)	Borg RPE
1_i	31±8	3.9±0.9	41±3	0.64±0.09	15.0±1.2
1_{ii}	25±4	4.0±1.2	24±6	0.85±0.07	14.0±0.6
2_i	23±5	3.8±1.1	0	0.99±0.08	18.3±0.7
2_{ii}	37±6	4.3±1.0	0	1.26±0.25	19.9±0.2
3_i	22±5	3.1±1.0	30±7	0.77±0.17	12.2±1.2
3_{ii}	25±7	3.0±1.0	18±4	1.08±0.08	12.4±1.4
4_i	37±7	3.5±0.8	36±8	0.5±0	14.5±1.5
4_{ii}	29±4	2.9±0.9	30±0	0.72±0.23	15.0±0.0
4_{iii}	25±6	3.0±0.6	22±12	0.5±0	13.3±0.6

Table 4-4: Description of BWSTT: BWSTT parameters for all patients. Patients 1, 2 and 3 received 2 training blocks of BWSTT (subscript i and ii), and Patient 4 received 3 blocks of BWSTT (subscript i, ii, and iii). The left-most column indicates the patient and the block of training ($patient_{block}$). **Time** = average duration of 1 session excluding rests. **Days/wk** = average number of sessions attended/week. **BWS** = body weight support expressed as a percentage of the patient's body weight. **Speed** = treadmill speed. **Borg RPE** = Borg scale for rate of perceived exertion. Values are expressed as mean±1 standard deviation.

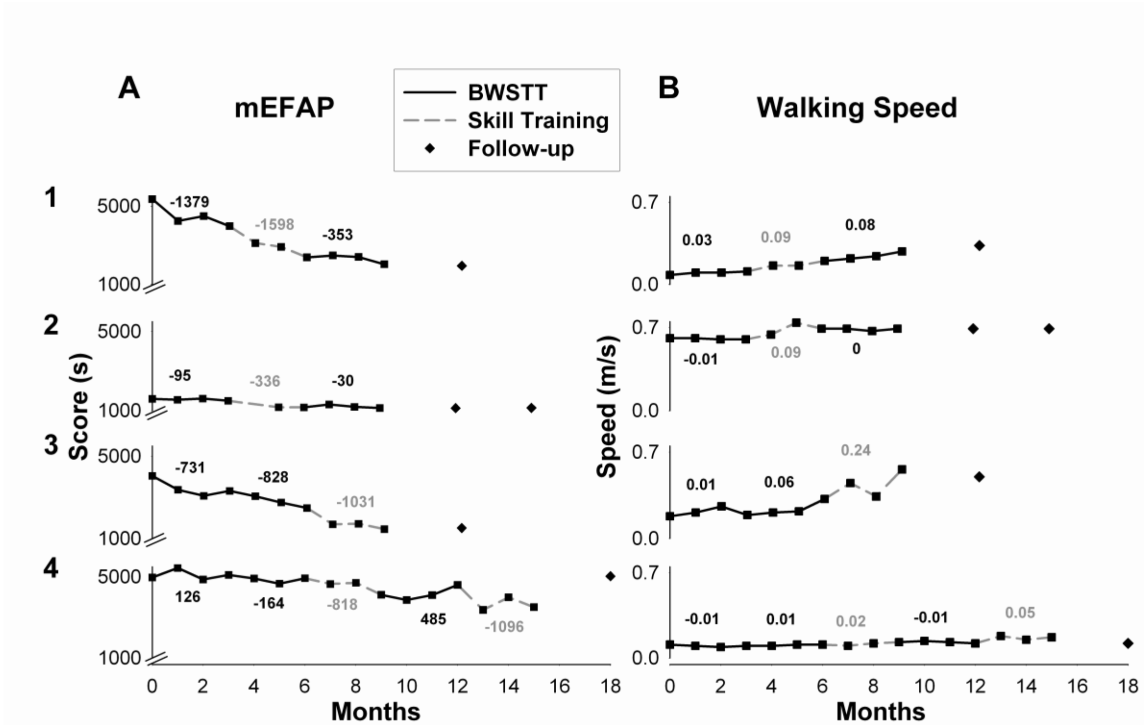

Figure 4-1: Modified Emory Functional Ambulation Profile (mEFAP) score (A) and comfortable walking speed (B) for all patients over the course of training and follow-up. Each plot shows the data from 1 patient. Score in seconds (A) and meters/second (B) are plotted for each month of training during BWSTT (black, solid lines) and skill training (dashed, grey lines), and for follow-up (black diamonds). A decrease in score on the mEFAP indicates an improvement since the mEFAP is a timed measure. There is no mEFAP score for Patient 2 at month 4 due to an equipment problem. Numbers above/below the traces in A and B indicate the change in mEFAP score and walking speed, respectively, from the beginning to the end of each training type (black: BWSTT, grey: skill training). A change in walking speed ≥0.05 m/s is clinically important (Musselman 2007).

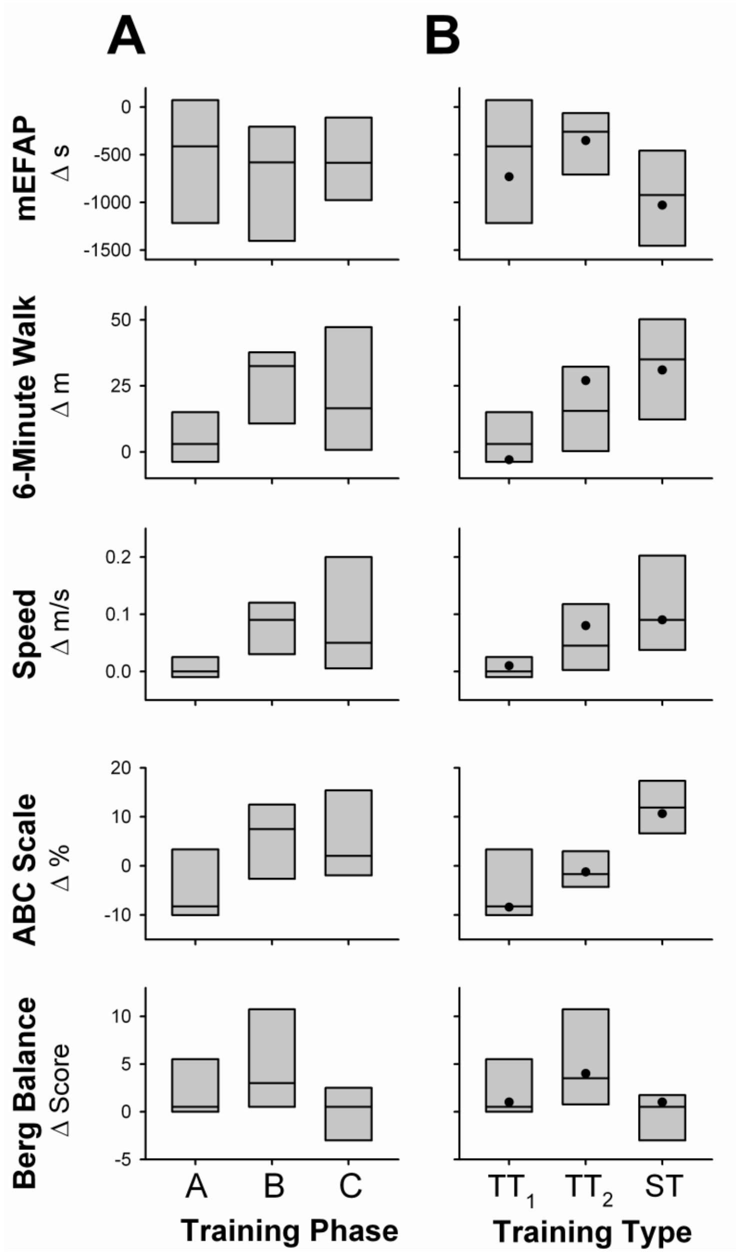

Figure 4-2: Boxplots show the improvement in score from the beginning to the end of each training block for all patients. Median and range are expressed as a change in score in the original measurement units. The five outcome measures shown are the mEFAP, 6-minute walk test, comfortable walking speed, Activities-specific Balance Confidence (ABC) Scale, and Berg Balance Scale. A decrease in score on the mEFAP indicates an improvement since the mEFAP is a timed measure. (A) Scores were collapsed for each block of training, regardless of the method of training. This shows the effect of the length of training. (B) Scores were collapsed for each type of training, regardless of when they occurred. TT_1 = first block of BWSTT, TT_2 = second block of BWSTT, ST = skill training. The black dots are the medians recalculated with the scores from Patient 2 removed (see Discussion).

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Chapter 5: The Spinal Cord Injury Functional Ambulation Profile: a New Measure of Walking Ability

5.1 Introduction

Regaining the ability to walk is important for individuals who have experienced an injury to the central nervous system (Andersen 2004, Lord et al. 2004). More than half of individuals who sustain an incomplete spinal cord injury (ISCI) regain some walking ability (Waters et al. 1994a,b). Objective and comprehensive measures of walking are extremely important for quantifying the effect of gait interventions.

Currently, the 10-meter walk test and the Walking Index for Spinal Cord Injury II (WISCI II) are considered the most useful measures of walking for individuals with ISCI (Jackson et al. 2008). While these measures provide valuable information concerning walking speed and general walking function, respectively, they assess walking over smooth, level ground only. Measures of more challenging walking tasks have been developed, such as the Dynamic Gait Index (Shumway-Cook and Woollacott 2007), Rivermead Mobility Index (Collen et al. 1991), and several obstacle courses (Means 1996, Rubenstein et al. 1997, Taylor and Gunther 1998, Means and O'Sullivan 2000). These measures, however, lack assessment of many of the tasks frequently encountered in daily walking (Musselman and Yang 2007), and most include subjectivity in the scoring.

Functional walking involves the ability to walk on different surfaces (smooth, rough, uneven, sloped), carry objects, negotiate doors and obstacles, and ascend/descend curbs and stairs (Musselman and Yang 2007). The most objective measure of functional walking is the Modified Emory Functional Ambulation Profile (mEFAP), which is a timed measure that quantifies mobility in stroke survivors (Wolf et al. 1999, Baer and Wolf 2001). Four tasks comprising the mEFAP have been identified as walking tasks frequently encountered by able-bodied adults (walking on smooth and carpeted surfaces, negotiating obstacles

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and steps) (Musselman and Yang 2007). The fifth task, the Timed Up and Go, is generally regarded as a critical transition task needed for walking (Shumway-Cook and Woollacott 2007). The scoring accounts for the devices, braces and physical assistance needed to complete each task. It has excellent reliability, concurrent validity and is sensitive to change (Baer and Wolf 2001), but it lacks several frequently encountered walking tasks (Musselman and Yang 2007). To fill this gap, we modified the mEFAP, based on our earlier study (Musselman and Yang 2007), to create the Spinal Cord Injury Functional Ambulation Profile (SCI-FAP) (Appendix); a measure of functional walking that assesses function at the Activity level according to the International Classification of Functioning (Üstün et al. 2003).

The objectives of the present study were to 1) develop a measure of functional walking for ISCI (the SCI-FAP), 2) assess the inter-rater and test-retest reliability of the SCI-FAP in individuals with ISCI, 3) evaluate the discriminative validity of the SCI-FAP by comparing performance on the measure between individuals with ISCI and age- and gender-matched, able-bodied adults, and 4) assess the SCI-FAP's convergent validity by comparing, within the ISCI-group, the results obtained on the SCI-FAP, the 10-meter walk test, the 6-minute walk test and the WISCI II.

5.2 Methods

SCI-FAP Development

A small focus group developed the first version of the SCI-FAP, based on the mEFAP and 5 additional tasks known to be commonly encountered in daily walking (Lerner-Frankiel et al. 1986, Lord et al. 2004, Musselman and Yang 2007). The devices, braces and physical assistance categories used in the mEFAP were retained, with slight modifications (e.g. forearm crutches were added). This first version was tested on two individuals with ISCI. Based on their feedback and that of therapists who work with patients with ISCI, a second version was developed containing 9 tasks (5 from mEFAP and 4 new ones – walking while carrying a bag, negotiating a ramp, stepping up and down 1 step, and walking through a door).

The second version of the SCI-FAP was sent to 10 recognized experts in the area of spinal cord injury rehabilitation. Feedback was received from 6 of these experts. Overall they were positive about the new measure, stating it included important walking skills, thus supporting content validity. The grading of devices/braces and assistance level was identified as a problem. There was no rationale for the ordering of devices/braces. Moreover, selecting an assistance level was subjective. As a result, we simplified the rating of devices/assistance (see Appendix, henceforth abbreviated to 'assistance'), and had 12 physical therapists rank the assistance from greatest to least independence. Eleven therapists ranked the levels in the order shown in the Appendix.

The final revision was made after the data were obtained. Two tasks (walking on smooth floor and on a ramp) were removed to reduce redundancy (see below). Thus, the current version of the SCI-FAP includes 7 tasks (Appendix).

Scoring of the SCI-FAP

Scoring of the SCI-FAP is based on the time it takes a participant to complete each task at a comfortable walking pace, and a multiplication factor to quantify the assistance needed for each task (Appendix, **Assistance**). The largest assistance level is given when a participant is 'unable to complete' a task. This includes situations where participants cannot attempt the task, and situations where they complete part of the task, but are unable to finish.

Maximum times for each task, set at 50 times the mean from able-bodied participants, have been established to allow scoring of individuals who cannot complete a task (Appendix). Fifty was chosen because the 2 lowest-functioning participants with ISCI who could complete all tasks took 10-50 times longer than the able-bodied participants. Participants who complete a task, but take longer than the maximum time, are assigned the maximum time for that task, multiplied by the factor that reflects the assistance used. Participants who do not attempt or complete a task are assigned the maximum time for that task, multiplied by a factor of 6 (i.e. 'unable to complete').

To avoid the problem of one or more tasks dominating the scores because they take longer to complete or are more difficult, we normalized the scores by the mean able-bodied time for each task (Appendix). Thus, the score for each task is:

$$\text{task score} = \frac{\text{time X factor}}{\text{mean able-bodied time}} \quad [1]$$

Since the SCI-FAP is a timed measure, a low score reflects better function. The highest total score on the SCI-FAP is 2100, composed of 300 for each task (i.e., normalized score of 50 x 6).

Participants

Participants with ISCI were recruited from the University of Alberta (UA) and the University of British Columbia (UBC). To be included, they: 1) had to be at least 6 months post-injury, 2) were able to walk at least 5 meters with or without physical assistance of another person and/or walking aids, 3) were free of any disease, injury or condition other than their ISCI that affected walking ability, 4) were not receiving rehabilitation services that included walking practice, 5) did not change medications that affect walking ability during the study, and 6) were able to follow spoken commands in English.

Able-bodied participants, greater than 18 years of age, were recruited at UA. To be included, able-bodied individuals must have: 1) had $\leq$1 fall in the previous month (to exclude individuals with undiagnosed pathology in equilibrium), 2) been free of any disease, injury, condition or medication that affected walking ability, and 3) been able to follow spoken commands in English. Written informed consent was obtained from all participants prior to participation in the study. Ethical approval was received from the Capital Health and UA Health Research Ethics Board and the UBC Clinical Research Ethics Board.

Study Design

Participants with ISCI: Most participants with ISCI were tested at UA. These individuals attended 2 testing sessions. At Session #1, participants completed the SCI-FAP, 10-meter walk test, 6-minute walk test and WISCI II. At Session #2, only the SCI-FAP was completed. The SCI-FAP tasks were performed in the same order on both days and across participants so that the testing conditions were consistent for the evaluation of test-retest reliability. The order was: carpet, floor, up & go, obstacles, stairs, carry, step, ramp, and door. The 6-minute walk test, a measure of walking endurance (Guyatt et al. 1985), was performed on a 25-meter walkway. The score is the total distance (in meters) traveled in 6 minutes. The 10-meter walk test, a measure of comfortable walking speed, was performed over a 15-meter walkway, with the middle 10 meters timed. The WISCI II is a 21-point ordinal scale that rates an individual's ability to walk 10 meters based on the braces, devices and assistance needed (Ditunno and Ditunno 2001). Self-selected and maximal WISCI II ratings were assessed (Kim et al. 2007). The 10-meter walk test, 6-minute walk test and WISCI II are valid and reliable measures for individuals with ISCI (Ditunno et al. 2000, van Hedel et al. 2005).

The SCI-FAP was assessed first, followed by the remaining 3 tests in a random order. The SCI-FAP was administered first to ensure the same testing conditions in Sessions #1 and #2. The sessions were spaced 1-2 weeks apart to reduce the chance of practice effects, and were scheduled at the same time of day for each participant. Three raters (authors KM, JY, KB) scored each participant simultaneously on the SCI-FAP at Session #1. Each rater used a silent stopwatch and recorded the time to 1/10 of a second. All raters were trained as physical therapists, with two currently licensed (KM and KB). One rater, designated the lead rater (KM), provided verbal instructions to all participants. Only the lead rater scored the 6-minute walk test, 10-meter walk test and WISCI II, and attended Session #2.

For 5 participants with ISCI, the SCI-FAP was scored by a total of 5 raters (the 3 raters mentioned above, plus 2 additional physical therapists) at Session #1. This determined the inter-rater reliability beyond the original 3 raters, who were very familiar with the measure as they were involved in its development. The 2 additional therapists, unfamiliar with the SCI-FAP, spent ~15 minutes reviewing the instructions and scoring with the lead rater prior to testing.

Some participants with ISCI were tested at UBC. These participants attended 1 testing session where they completed the 6-minute walk test, 10-meter walk test, SCI-FAP, and WISCI II, in that order. One rater scored their performance on all measures. The SCI-FAP tasks were administered in the same order outlined above for the UA site. All equipment used for the SCI-FAP was identical in dimension to the equipment used at UA. The 6-minute walk test was tested on 1 of 2 circular loops that were 41.1 m and 51.8 m in circumference. The assessment of comfortable walking speed (i.e. 10-meter walk test) was the same as that described above. The data from these individuals contributed to the assessment of validity (i.e. discriminative and convergent).

<u>Able-bodied participants</u>: Data were collected from able-bodied adults in order to establish normative scores for the SCI-FAP and to assess its discriminative validity. Able-bodied adults attended 1 testing session at UA to complete the SCI-FAP. The lead rater administered the test to 23 of the able-bodied participants. A physical therapy student trained in administering the SCI-FAP assessed the remaining 37 subjects. The student was trained by one of the authors, and pilot data were collected to ensure the scoring was comparable.

Analysis

Mean values are reported with $\pm$ 1 standard deviation (SD). Significance was set at 0.05 for all statistical tests.

Able-bodied data: To determine whether performance on the SCI-FAP changed with age, SCI-FAP scores (total and task scores) were compared for 5 decades (20-29 years, 30-39 years, 40-49 years, 50-59 years, and 60-69 years). A one-way ANOVA with the Bonferroni correction for post-hoc analyses were used for this analysis.

Homogeneity: An exploratory factor analysis was performed to assess the dimensionality of the SCI-FAP. Inter-task correlations and task-total correlations (i.e., correlation of task A with total score minus task A) were performed using Pearson's correlation coefficient (r). Nine SCI-FAP tasks were included in these analyses. For the remaining analyses described below, two tasks (floor and ramp) were removed from the total SCI-FAP score based on the inter-task correlations (see Results). Cronbach's alpha was used to assess internal consistency. A moderately high α (i.e., $0.95 > \alpha \geq 0.7$) was desired, as this indicates good internal consistency without much redundancy (Streiner and Norman 2003). SCI-FAP scores used from the UA participants were those measured by the lead rater at Session #1.

Inter-rater reliability: SCI-FAP scores from the 3 original raters at Session #1 were used to assess inter-rater reliability (i.e. data from UA only). A two-way random effects intraclass correlation coefficient (ICC) for absolute agreement was used (Streiner and Norman 2003, Shrout and Fleiss 1979). ICC values were calculated for the total SCI-FAP score, as well as individual task scores, to determine if all tasks had similar reliability. For the 5 participants whose SCI-FAP performance was assessed by 5 raters, inter-rater reliability was also calculated using the total scores of the lead rater and the 2 additional raters.

Test-retest reliability: SCI-FAP scores assigned by the lead rater at Sessions #1 and #2 were used to assess test-retest reliability (i.e. data from UA only). Two participants did not return for Session #2, so a total of 22 subjects were included in this analysis. A one-way random effects ICC for absolute agreement was used (Streiner and Norman 2003, Shrout and Fleiss 1979). ICCs were calculated for the total SCI-FAP score and each task score.

Discriminative validity: Each participant with ISCI was age-matched (± 5 years) and gender-matched to an able-bodied subject. Total SCI-FAP scores, as well as scores on each task, were compared between the 2 groups using a one-tailed, independent t-test. For participants with ISCI tested at UA, SCI-FAP scores measured by the lead rater at Session #1 were used.

Convergent validity: Performance on the SCI-FAP (i.e., total score) was correlated with performance on the 10-meter walk test and 6-minute walk test using Pearson's correlation coefficient (r) for all participants with ISCI. SCI-FAP scores were correlated with self-selected and maximal WISCI II scores using Jaspen's coefficient of multiserial correlation (M), which is appropriate when correlating ordinal and interval scales (Freeman 1965). For UA participants, SCI-FAP scores measured by the lead rater at Session #1 were used.

5.3 Results

Participants

Thirty-two individuals with ISCI participated (24 males, age = 47.6 ± 14.2 years, age range = 20-81 years). Eight were tested at UBC. All participants were community-dwelling, but varied greatly with respect to injury and walking ability (Table 5-1). Sixty able-bodied adults participated (34 males, age = 42.9 ± 16.0 years, age range = 23-88 years). The age categories and number of participants (in brackets) were: 20-29 years (16), 30-39 years (13), 40-49 years (9), 50-59 years (12), 60-69 years (6), 70-79 years (3), and 80-89 years (1).

SCI-FAP performance by able-bodied participants

All able-bodied participants completed the SCI-FAP without assistance. SCI-FAP tasks (mean time) were: floor (4.4 ± 0.6s); carpet (4.4 ± 0.6s); up & go (9.1 ± 1.2s); obstacles (11.4 ± 1.3s); stairs (6.2 ± 0.8s); carry (4.4 ± 0.5s); step (3.7 ± 0.5s); ramp (6.2 ± 1.0s); door (5.0 ± 0.7s). These mean times are used to normalize the task scores (see equation [1]). There was no difference in the total SCI-FAP score or task scores across ages (i.e., 20-69 years), with the exception of the up & go task (p=0.031). For this task, participants in their 20's scored significantly lower (i.e. performed the task faster) than participants in their 50's.

SCI-FAP performance by participants with ISCI

Twenty-nine of the 32 participants with ISCI were able to complete all SCI-FAP tasks. Participants 27, 30 and 31 did not complete all tasks – see Table 5-1. The tasks (number of participants that did not complete) were as follows: obstacles (2), stairs (3), carry (1), step (3), ramp (3), and door (3). Fifteen participants hit ≥1 obstacle at either the first or second session, resulting in a penalty of 1 factor (see Obstacles in Appendix). Two participants (#6 & #30) exceeded the maximum time on some tasks (including step, carpet, up & go). The SCI-FAP took 15-45 minutes to complete.

Homogeneity and redundancy of the SCI-FAP tasks

The factor analysis revealed all 9 tasks loaded strongly onto a single factor (right column Table 5-2; accounted for 86.4% of the variance). Inter-task correlations ranged from 0.63–0.99 (p<0.001, Table 5-2). Very high inter-task correlations (i.e., r = 0.99) were found for 3 groups of tasks: 1) the floor, carpet and carry, 2) the up & go and obstacles, and 3) the stairs, ramp and door (Table 5-2). The task-total correlations ranged from 0.82–0.95 (p<0.001, Table 5-2). Two tasks with very high correlations were removed. First, the floor task in the first grouping was removed because walking on a smooth surface is a component of other SCI-FAP tasks. Since the task-total correlations for carpet and carry tasks were <0.90, these tasks were retained. Second, in the third grouping of stairs, ramp and door tasks, we chose to remove the ramp task, because it may be difficult to reproduce exactly in a clinical setting (as identified by one of our experts). It was surprising that the stairs and door tasks were correlated so highly. Both require use of the upper extremities, but otherwise they appear to be very different in nature, and so were retained. No changes were made to the second grouping, because the up & go and obstacles tasks are very different. The revised SCI-FAP, comprised of 7 tasks (Appendix), has high internal consistency (Cronbach's $\alpha = 0.95$).

Reliability of the SCI-FAP

Inter-rater and test-retest reliability were both high (Table 5-3). Inter-rater reliability for the total SCI-FAP, the normalized total time, and the total assistance scores were all 1.000. ICC values for the 7 tasks individually were all ≥ 0.975. The tasks with the lowest inter-rater reliability were the obstacles and stairs. This resulted from an occasional discrepancy in whether or not an obstacle was hit or in the number of rails used (stairs). The ICC values for inter-rater reliability were very similar for the original 3 raters (ICC = 1.000) and the lead rater with the 2 therapists unfamiliar with the SCI-FAP (ICC = 0.998). Test-retest reliability of the SCI-FAP was slightly lower than inter-rater reliability (ICC = 0.983, Table 5-3). ICC values for the tasks range from 0.959 to 0.992.

Discriminative Validity of the SCI-FAP

Participants with ISCI scored significantly higher on the SCI-FAP (total score $p=0.002$, and task scores $0.001<p<0.01$) compared to their able-bodies counterparts. The mean total score of the SCI-FAP was 7.2 ± 0.8 (range = 5.8–9.6) for able-bodied participants and 271.3 ± 451.0 (range = 8.5–1900.0) for the ISCI group. Figure 5-1A shows the mean scores for each task for the ISCI group. There is a lot of variability amongst the participants with ISCI. Five participants achieved total scores on the SCI-FAP similar to those of able-bodied individuals, while the 3 participants who could not complete all SCI-FAP tasks scored >1000.

Relationship between time and assistance scores

The assistance score helped reduce the ceiling effect of the time score. Figure 5-1B shows that many higher functioning participants with similar time scores had varying assistance scores, indicating that the assistance score made an important contribution to differentiating walking ability among the higher functioning individuals.

Convergent Validity of the SCI-FAP

Total scores on the SCI-FAP were moderately correlated with the results from the 10-meter walk test (r=-0.59, p=0.001), the 6-minute walk test (r=-0.59, p=0.001), the self-selected WISCI II (M=-0.68, p=0.001), and the maximal WISCI II (M=-0.70, p=0.001) (Figure 5-2). The individual SCI-FAP tasks also showed moderately strong correlations with the other 4 walking measures (Table 5-4).

5.4 Discussion

Our findings suggest that SCI-FAP is a valid and reliable measure of functional walking for the ISCI population. It has high internal consistency, inter-rater reliability and test-retest reliability. Experts in the ISCI rehabilitation field confirmed its content validity, and discriminative and convergent validity are demonstrated.

SCI-FAP as a measure of functional walking ability

Few SCI-specific measures of walking exist (Lam et al. 2008, van Hedel et al. 2009). In addition to the WISCI II, there is the Spinal Cord Injury Functional Ambulation Inventory, which focuses on the quality of gait (Field-Fote et al. 2001). The Spinal Cord Independence Measure assesses indoor and outdoor mobility (Catz et al. 1997). As the SCIM tasks can be performed with a wheelchair, it is not strictly a measure of walking function.

The tasks included in SCI-FAP were based on our knowledge of what constitutes functional walking (Lerner-Frankiel et al. 1986, Lord et al. 2004, Musselman and Yang 2007). All important tasks that can be reasonably assessed in a clinical setting were included. Moreover, many of the SCI-FAP tasks (obstacles, carry, door) are tasks that individuals with ISCI encounter at a significantly lower frequency than able-bodied counterparts (Musselman and Yang 2007), suggesting they are a challenge for this population.

The SCI-FAP was intended to measure one construct only (i.e. functional walking). The results from the factor analysis, assessment of internal consistency and inter-task correlations suggest this is the case (Schmitt 1996). Redundancy was reduced by the removal of the floor and ramp tasks. Some other tasks may be improved in the future to further minimize redundancy. For example, the carry task did not challenge our participants, resulting in very similar results to the carpet task (Figure 5-1A). A weighted bag held in the hand or on the forearm may be more challenging, as is done in the Community Balance and Mobility Scale (Howe et al. 2006). The obstacles task was highly correlated with the up and go task. Removing the 180^{o} turn (which is present in both tasks) from one of the tasks might help reduce the similarity in the future.

The step task showed the lowest correlations with the other tasks (Table 5-2). Moreover, it had the highest mean score (Figure 5-1A), suggesting it was the most challenging for individuals with ISCI. The step task likely requires greater limb strength and balance than the other tasks.

Scores on the SCI-FAP were moderately correlated with scores on the 6-minute and 10-meter walk tests, and WISCI II. Moderately strong correlations suggest the SCI-FAP was measuring the same construct as the other tests, but was also contributing new information (Streiner and Norman 2003). While all three tests are a function of over-ground walking speed, SCI-FAP adds the unique aspect of other daily walking tasks.

The SCI-FAP may be most appropriate for individuals with moderate walking function

We have shown that the SCI-FAP is an appropriate measure for individuals with some walking function; however, even clients who cannot walk can be scored on the SCI-FAP. The SCI-FAP, however, has a ceiling effect. It will not discriminate between individuals who walk at normal speeds without devices or physical assistance. There is little difference in SCI-FAP scores for our highest-functioning participants. This is not surprising since the SCI-FAP is meant to reflect common walking tasks rather than challenge walking balance or skill beyond daily requirements. Measures like the 6-minute walk test, where individuals can walk at fast rather than comfortable speeds, may be more appropriate for tracking change over time in these very high-functioning individuals. The assistance ratings, however, reduce the ceiling effect. Without these ratings in the total SCI-FAP score, all participants who walked at normal walking speeds would experience a ceiling effect (Figure 5-1B).

We made an effort to minimize the floor effect of the SCI-FAP by setting high maximum times for the tasks. However, a participant who cannot walk at all would score the maximum score of 2100, as would a participant who could walk very short distances, but never long enough to complete a task. Thus, the SCI-FAP may be most appropriate for clients with moderate walking function, i.e., those who walk slower than their able-bodied counterparts or need walking aids to complete the tasks.

Considerations when using the SCI-FAP

First, the SCI-FAP does not distinguish between different levels of manual assistance. This was done to remove subjectivity from the scoring of the SCI-FAP, a potential limitation that was identified by our experts. Furthermore, whether an individual requires supervision or moderate assistance to walk, he/she ultimately needs another person to complete the task. Therapists can make note of the amount of assistance provided in the 'Comments' section (Appendix).

Second, the SCI-FAP does not consider the use of braces, such as an ankle-foot orthosis. This differs from the WISCI II (Ditunno and Ditunno 2001) and mEFAP (Baer and Wolf 2001). A rating for braces was removed from the SCI-FAP because none of our participants completed any tasks with braces only (i.e., no other device or assistance). Likewise, a WISCI II rating of 18 – 'ambulates with no devices, with braces and no physical assistance' – is rarely encountered (Morganti et al. 2005). If someone completes a SCI-FAP task with braces only, he/she should be rated as 'independent'.

Third, timing begins with participants in a stationary position, as opposed to already walking as is done for the 10-meter walk test. As a result, the recorded time includes acceleration effects. This better reflects functional walking, which consists of many starts and stops. Indeed, most SCI-FAP tasks involve periods of acceleration and deceleration throughout the task (e.g., pause to lift a foot over the obstacle or open a door).

Fourth, SCI-FAP score consists of 2 components – time and assistance rating. The sums of the normalized times and assistance ratings from each task can be reported separately to create a total score for both time and assistance. Both total time and assistance scores showed high inter-rater and test-retest reliability (Table 5-3), and moderately strong correlations with other measures of walking (Table 5-4).

Lastly, while we chose equipment for the SCI-FAP that is generally available (e.g., standard therapy stairs, a step height that approximates the standard curb height), it may still be difficult to reproduce in some centres. The SCI-FAP tasks, however, can be treated as independent tests. Each task has been shown to have acceptable inter-rater reliability, test-retest reliability, and discriminative and convergent validity. Clinicians and researchers can choose to include whichever tasks are feasible in their setting. In the Appendix we specify the dimensions of the equipment we used. These dimensions should be adhered to if one chooses to score the SCI-FAP as we have in the present study (Appendix). The mean able-bodied times would have to be re-evaluated if the dimensions of the equipment are different from those reported here.

Limitations

We tested the SCI-FAP on only a few individuals with very low walking function. We required our participants to be able to walk $\geq$5 meters to ensure that all participants would likely be able to complete at least 1 SCI-FAP task (i.e. carpet task); as well as attempt the WISCI II, 10-meter and 6-minute walk tests. In the future it would be beneficial to try the SCI-FAP in more individuals with very low walking ability.

Two procedural differences in the testing at the two sites may have influenced the results. The 6-minute walk test was performed on a 25-m walkway at UA, and a circular loop at UBC. A loop is preferable for this test since it eliminates the need to make 180º turns, which can take a significant amount of time in lower-functioning individuals. Furthermore, the 6-minute walk test was performed first at UBC, whereas at the SCI-FAP was performed first at UA. Both these differences could have biased the 6-minute walk distance to be higher at UBC than at UA. Thus, we matched the subjects tested at the two sites according to their SCI-FAP scores ($\pm$10), and compared their 6 minute walk distances. No differences were found (p=0.685; n=4).

Future directions

The SCI-FAP may be a useful measure for the acute and sub-acute ISCI populations as well, and should be tested in the future. Its sensitivity to change and the minimal clinically important difference will also need to be assessed.

Participant	Sex	Age (yrs)	Injury level	Years post-injury	AISA score	WISCI II score
1	M	55	C5	32.8	D	9
2	M	36	C3	3.7	D	19
3	F	45	T2	1.9	C	9
4	M	44	C3	3.9	C	9
5	M	81	T4	5.7	D	20
6	M	48	C5	24.6	C	9
7	M	57	T12	31.0	D	13
8	M	37	L1	3.2	C	12
9	M	46	C6	9.3	C	19
10	M	70	C5	1.3	C	13
11	M	51	C6	1.0	D	20
12	M	63	C4	20.2	D	19
13	M	59	C3	7.4	D	13
14	M	60	C5	2.2	D	20
15	M	53	C5	7.0	D	16
16	F	26	L1	7.1	C	9
17	M	43	T12	17.6	D	20
18	M	33	C4	1.5	C	20
19	M	42	C3	2.1	D	20
20	F	50	T6	2.0	D	13
21	F	50	C6	3.8	C	13
22	M	43	L1	0.8	C	9
23	M	25	T6	1.8	C	9
24	F	20	C6	1.2	C	9
25	F	53	T3	2.2	C	12
26	M	63	C5	2.0	D	16
27	M	59	C4	4.8	D	8
28	F	27	T10	12.8	D	16
29	M	57	C4	1.9	D	13
30	F	52	C4	2.0	C	8
31	M	60	T10	4.0	D	8
32	M	43	T11	1.8	D	13

Table 5-1: Characteristics of participants with ISCI. Participants 25-32 were tested at the University of British Columbia site. Injury level = neurological level of injury as defined by the *International Standards for Neurological Functional Classification of Spinal Cord Injury* (Maynard et al. 1997), ASIA score = American Spinal Injury Association Score, WISCI II = self-selected scores on the Walking Index for Spinal Cord Injury II.

	Floor	Carpet	Up&Go	Obstacles	Stairs	Carry	Step	Ramp	Task-Total	Factor Load
Floor									0.90	0.94
Carpet	0.99								0.89	0.94
Up&Go	0.90	0.90							0.93	0.95
Obstacles	0.92	0.92	**0.99**						0.95	0.97
Stairs	0.78	0.78	0.85	0.88					0.95	0.94
Carry	0.99	0.99	0.84	0.87	0.73				0.83	0.90
Step	0.70	0.69	0.78	0.77	0.83	0.63			0.82	0.84
Ramp	0.80	0.79	0.86	0.89	0.99	0.74	0.83		0.95	0.94
Door	0.79	0.78	0.85	0.88	0.99	0.74	0.80	0.99	0.94	0.93

Table 5-2: Inter-task and task-total correlations of the SCI-FAP tasks. Pearson correlation coefficients (r) are shown, all $p<0.001$. Factor loads for each task are reported on the right. Three groupings of tasks were correlated highly with one another: 1) floor, carpet and carry (shaded grey), 2) up & go and obstacles (in bold text), 3) stairs, ramp and door (underlined).

SCI-FAP	Inter-rater	Test-retest
Total Score	1.000	0.983
Carpet	1.000	0.972
Up & Go	1.000	0.978
Obstacles	0.996	0.977
Stairs	0.994	0.964
Carry	1.000	0.992
Step	1.000	0.959
Door	0.999	0.982
Total Time	1.000	0.952
Total Assistance	1.000	0.998

Table 5-3: Inter-rater and test-retest reliability. Intraclass correlation coefficient (ICC) values (all $p<0.001$) are shown for each task score and total scores. Total score refers to total SCI-FAP score (equation 1). Total time and total assistance refer to the sum of the normalized times and assistance ratings, respectively, for the SCI-FAP. Inter-rater ICC was calculated from the measures of the 3 original raters.

SCI-FAP	6MW	10MW	Self-WISCI II	Max-WISCI II
Total Score	-0.59	-0.59	-0.68	-0.70
Carpet	-0.53	-0.53	-0.58	-0.61
Up & Go	-0.58	-0.58	-0.63	-0.65
Obstacles	-0.55	-0.55	-0.62	-0.63
Stairs	-0.51	-0.51	-0.66	-0.66
Carry	-0.47	-0.47	-0.54	-0.57
Step	-0.64	-0.63	-0.64	-0.69
Door	-0.50	-0.49	-0.67	-0.67
Total Time	-0.63	-0.62	-0.67	-0.71
Total Assistance	-0.80	-0.78	-0.82	-0.86

Table 5-4: Correlations between SCI-FAP scores and 4 other measures of walking function (6MW = 6-minute walk test, 10MW = 10-meter walk test). Total score refers to SCI-FAP score calculated with equation [1]. Total time and total assistance refer to the sum of the normalized times and assistance ratings, respectively, for the SCI-FAP. $p<0.007$ for all correlations.

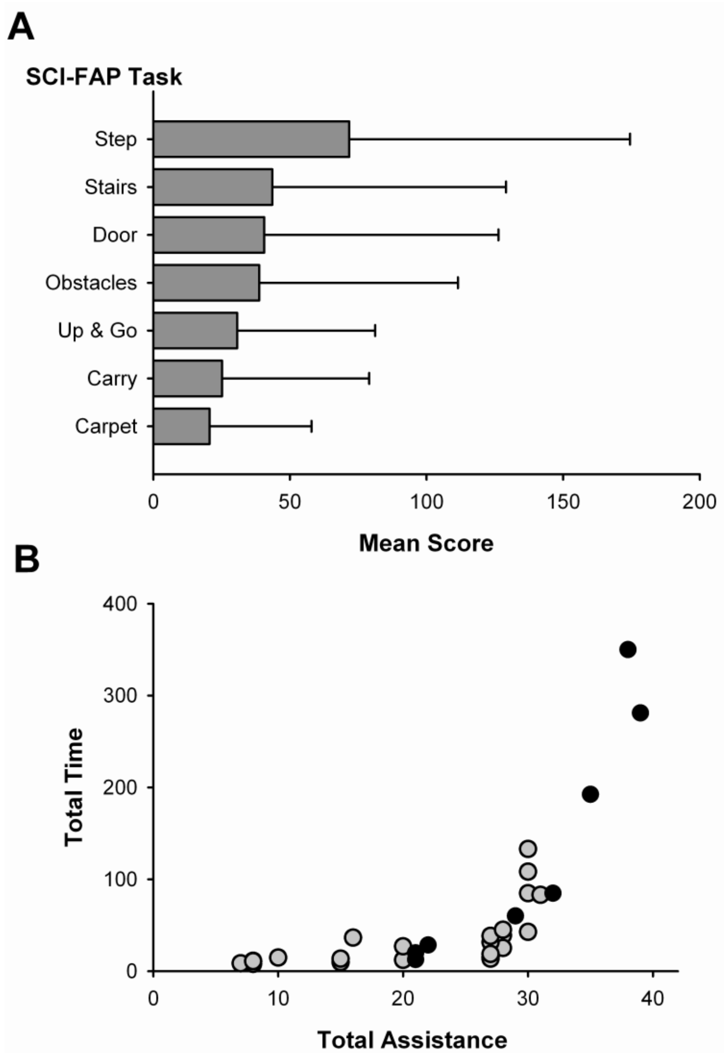


Figure 5-1: A) Mean score (+1 SD) on SCI-FAP tasks for all 32 participants with ISCI. Scoring is shown in equation [1]. Mean scores for able-bodied participants (not shown here) were 1.0 for each task. B) Total normalized time versus total assistance score for each participant with ISCI. Total refers to the sum of the normalized times or assistance ratings for the 7 SCI-FAP tasks. Each dot represents a participant with ISCI. Grey and black dots represent participants tested at the University of Alberta and the University of British Columbia, respectively.

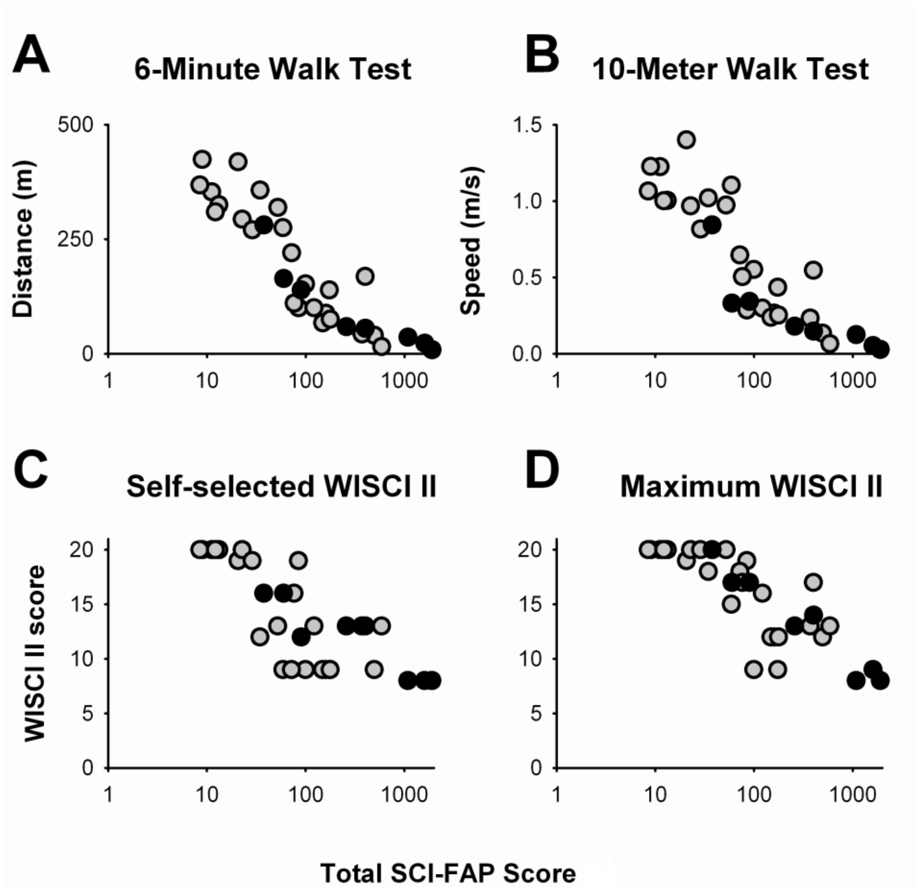


Figure 5-2: Total SCI-FAP score versus scores the 6-minute walk test (A), 10-meter walk test (B), self-selected WISCI II (C) and maximum WISCI II (D). SCI-FAP scores for all 32 participants plotted on a logarithmic scale because of the large range of SCI-FAP scores seen in these individuals. Each dot represents a participant with ISCI. Grey and black dots represent participants tested at the University of Alberta and the University of British Columbia, respectively.

5.5 Appendix

The Spinal Cord Injury Functional Ambulation Profile (SCI-FAP)

The SCI-FAP is composed of 7 tasks: (1) Carpet, (2) Up & Go, (3) Obstacles, (4) Stairs, (5) Carry, (6) Step, and (7) Door. Each participant is given a rest period between tasks long enough for the tester to explain and demonstrate the next task. Each participant is instructed to use an assistive device and/or brace(s) as needed. The tester provides instructions and answers the participant's questions. The tester provides physical assistance if needed. The tester times the participant during each task. The tester walks behind the subject, not beside, to prevent affecting the participant's speed. The tester provides feedback/encouragement only after the task is completed. The tester records the performance time for all 7 tasks on a data collection form (see scoring table below). If the participant cannot attempt a task, or does not complete a task, he/she is assigned the maximum time for that task, and an assistance rating of 6 ('unable to complete') (see scoring table below). If the participant takes longer than the maximum time to complete a task, he/she is assigned the maximum time, and the assistance rating that corresponds to the devices/assistance used for that task. Upon completion of all tasks, the tester calculates a total SCI-FAP score (see Scoring the Spinal Cord Injury Functional Ambulation Profile below).

Introduction

The tester provides an explanatory overview of the 7 tasks comprising the SCI-FAP. Prior to performance of each task, the tester explains and demonstrates the task. The participant is informed that performance of each task is timed and is instructed to ask for clarification at any time.

Although dimensions of the chair, obstacles, stairs, door, step, and bag have been described specifically, items having similar dimensions may be used, provided that the dimensions are noted and reproduced on subsequent testing.

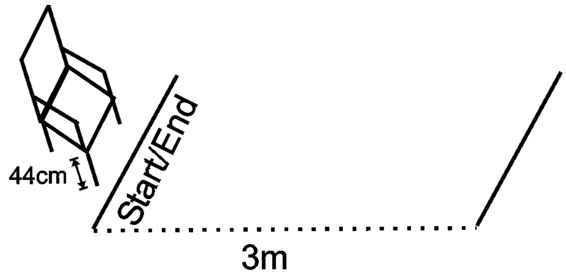
1) Carpet **Max time**: 220 seconds

Setup: Carpeted area or a piece of short pile carpet, no less than 7-m long and 2-m wide, securely taped to the floor. Starting point is marked with a 1-m strip of masking tape. End point is marked exactly 5-m from the starting point with a 2-cm piece of masking tape. Both starting point and end point are at least 1-m from the edge of the carpet.

1. Tester explains while demonstrating the Carpet task: "When I say 'go,' walk at your normal, comfortable pace until I say 'stop.' "
2. Tester assists participant as needed in placing toes on starting line tape.
3. Tester says "go," and presses stopwatch to begin timing.
4. Participant walks toward the end point. Tester walks alongside the participant as the participant traverses the 5-m distance.
5. Tester presses stopwatch to stop timing once both of the participant's feet have crossed the end point. Tester tells the participant to stop when he or she is beyond the end point.
6. Tester records time on data collection form.

2) Up & Go **Max time**: 455 seconds

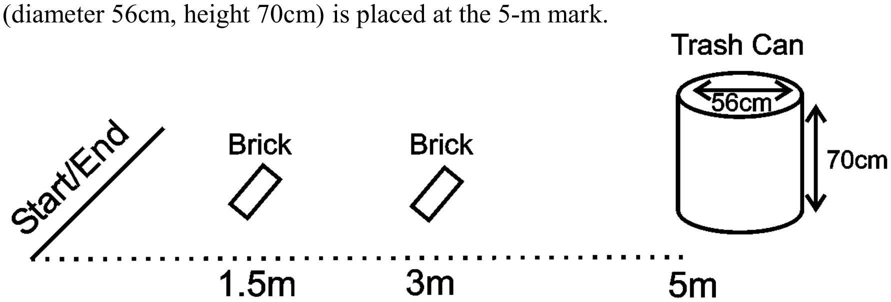
Setup: Standard armchair with a 44-cm seat height (from floor) is placed on the hard, non-carpeted floor. Three meters away, a 1-m strip of masking tape is placed on the floor.



1. Tester explains while demonstrating the Up & Go task: "You will sit in this chair with your back against the back of the chair and your arms resting on the armrests. When I say 'go,' you will stand up from the chair, walk at your normal comfortable pace past this line, turn around, walk back to the chair, and sit down, making sure your back is against the back of the chair."
2. Participant assumes sitting position in the chair. Tester stands beside the chair and prepares to walk with the participant.
3. Tester says "go," and presses stopwatch to begin timing.
4. Tester monitors line to ensure both of participant's feet cross the line before turning around.
5. Tester stops timing when participant is fully seated with back against the chair.
6. Tester records time on data collection form.

3) Obstacles* **Max time**: 570 seconds

Setup: A 1-m piece of masking tape is placed on a hard, non-carpeted floor to mark the starting point. A standard brick is placed on the floor at the 1.5-m mark and the 3-m mark. A trash can (diameter 56cm, height 70cm) is placed at the 5-m mark.

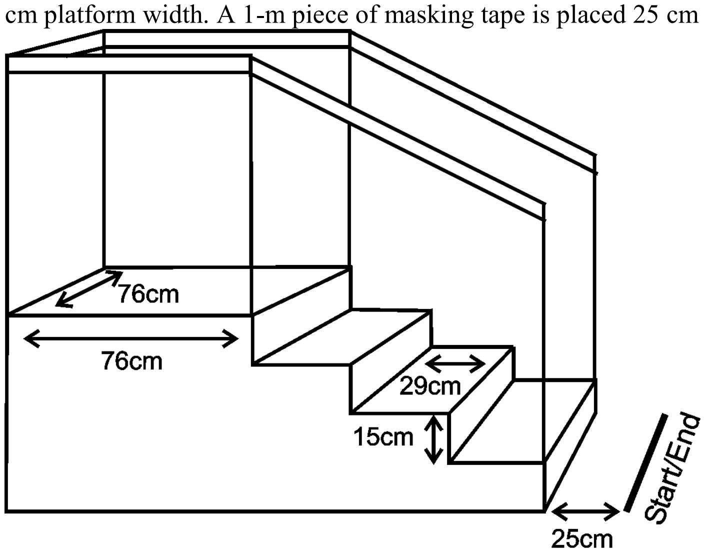


1. Tester explains while demonstrating the Obstacles task: "When I say 'go,' walk forward at your normal, comfortable pace and step over each brick. Then, walk around the trash can from either the left or right. Then walk back stepping over the bricks again. Do not hit the bricks or bin with your body or walking aid, if possible. Continue walking until I say 'stop.'"
2. Tester assists participant as needed in placing toes on starting line.
3. Tester says "go," and presses stopwatch to begin timing.
4. Tester walks with participant.
5. When both of the participant's feet have crossed the end line, tester presses stopwatch to stop timing. Tester tells the participant to "stop" when he or she is beyond the end line.
6. Tester records time on data collection form.

* If the participant hits one or more of the obstacles with his/her body or walking aid, 1 is added to the factor chosen for this task (e.g., if participant completed task with '1 cane/crutch' – a factor of 2, but he/she hits 1 or more obstacles, he/she is assigned a factor of 3).

4) Stairs* **Max time**: 310 seconds

Setup: Stairs with 4 steps, hand railings on both sides, and the following measurements are utilized: 29-cm stair depth, 76-cm stair width, 15-cm stair height, 76-cm platform depth, and 76-cm platform width. A 1-m piece of masking tape is placed 25 cm from the base of the first step.



1. Tester explains while demonstrating the Stairs task: "When I say 'go,' walk up the stairs at your normal, comfortable pace to the top of the stairs, turn around, and come back down. You may use the handrails if needed, but try to use them as little as possible."
2. Tester assists participant as needed in placing toes on starting line.
3. Tester says "go," and presses stopwatch to begin timing.
4. Tester follows participant up stairs to guard.
5. Tester presses stopwatch to stop timing when both of the participant's feet are in firm contact with the floor.
6. Tester records time on data collection form.

*Participant may use any technique to ascend and descend stairs (i.e., forwards, backwards, sideways), but must turn around at the top of the stairs so that he/she approaches the descent from the forwards direction. The technique used is recorded under the "Comments" section of the scoring form.

5) Carry **Max time**: 220 seconds

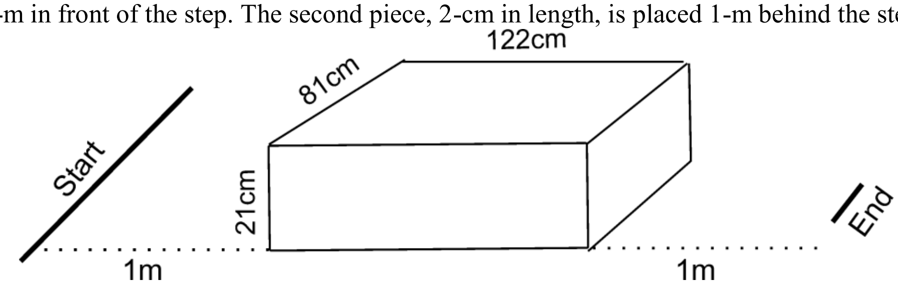
Setup: A 1-m strip of masking tape is placed on the hard, non-carpeted floor at the starting point. Five meters ahead of the starting point, a 2-cm piece of masking tape marks the end point. A shoulder bag, 36-cm long, 24-cm wide and 16-cm deep with a 5-lb weight placed inside, is worn by the participant. The shoulder strap should measure 4-cm in width, is adjusted so that the top of the bag is at the level of the iliac crest. The bag should hang across the participant's body so that if the bag is over the left shoulder it would hang on the right side of the participant's torso. The bag should hang either in front, beside, or behind the participant's torso while the participant is ambulating, according to the participant's preference. The position of the bag must be documented (under the "Comments" section of the scoring form) so that this may be replicated during subsequent trials.

1. Tester explains while demonstrating the Carry task: "When I say 'go' walk at your normal, comfortable pace, while carrying this bag over either shoulder, until I say 'stop'."
2. Tester assists the participant as needed in placing toes on the starting line, and can assist in placing the bag over either of the participant's shoulders.
3. Tester says "go" and presses stopwatch to begin timing.

4. Participant walks toward the end point. Tester walks alongside the participant as the participant traverses the 5-m distance.
5. Tester presses stopwatch to stop timing once both of the participant's feet have crossed the end point. Tester tells participant to stop when he or she is beyond the end point.
6. Tester records time on data collection form.

6) Step **Max time**: 185 seconds

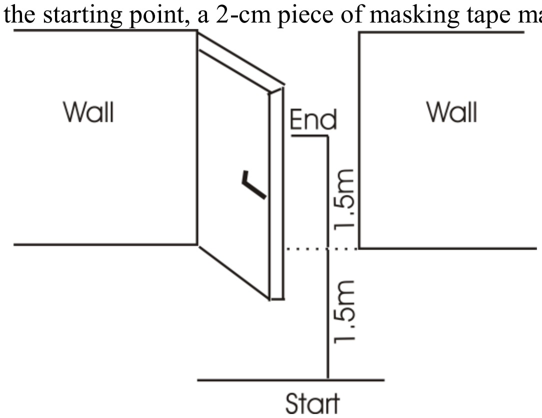
Setup: A step with the measurements shown in the diagram below is used. Two pieces of masking tape are placed on the floor to indicate the start and finish points. The first, 1-m in length, is placed 1-m in front of the step. The second piece, 2-cm in length, is placed 1-m behind the step.



1. Tester explains while demonstrating the Step task: "When I say 'go', walk towards the step, up and over, and continue walking until I say stop."
2. Tester assists participant as needed in placing toes on the starting point.
3. Tester says "go" and presses stopwatch to begin timing.
4. Participant walks toward the end point. Tester follows participant through the task for safety.
5. Tester presses stopwatch to stop timing when both of the participant's feet have crossed the end point.
6. Tester records time on data collection form.

7) Door **Max time**: 250 seconds

Setup: A wooden door with a latch handle, non-spring loaded, with the following measurements: 4-cm door depth, 95-cm door width, and 211-cm door height (see diagram below). The floor should be the same hard, non-carpeted surface on both sides of the door with no breaks or rises. The starting point is a 1-m strip of masking tape, which is placed on the floor 1.5-m from the door. Three meters ahead of the starting point, a 2-cm piece of masking tape marks the finish point.



1. Tester explains while demonstrating the Door task: "When I say 'go', walk forwards at your normal, comfortable pace, **pull*** open and go through the door, leave the door

open, and walk to the end point”. **Note:** participants can use any method they normally use to open the door.

2. Tester assists participant as needed in placing toes on the starting point.
3. Tester says “go” and presses stopwatch to begin timing.
4. Tester follows participant through the door for safety.
5. Tester presses stopwatch to stop timing when both of the participant’s feet have crossed the end point.
6. Tester records time on data collection form.

*Participant may use any part of his/her own body or walking aid to open the door. This will not be considered any differently in the scoring. The method of door opening is recorded under the “Comments” section of the scoring form.

Scoring the Spinal Cord Injury Functional Ambulation Profile

1) Tester multiplies time recorded for each task by appropriate assistance rating (see below) according to assistive device or assistance required during that task, and records the total in the appropriate cell in Row D.
2) Tester divides the number calculated in Row D by the mean time of able-bodied individuals (Row E).
3) Tester sums the 7 task scores to obtain the total SCI-FAP score.

Task (max time)	Carpet (220s)	Up&Go (455s)	Obstacles (570s)	Stairs (310s)	Carry (220s)	Step (185s)	Door (250s)
A. Time							
B. Assistance							
C. Hit Obstacle (+1)	/	/		/	/	/	/
D = A x (B + C)							
E.	4.4	9.1	11.4	6.2	4.4	3.7	5.0
Task Total = D/E							

Total SCI-FAP score = ___________

Assistance

1 = independent
2 = 1 cane/crutch/rail
3 = 2 canes/crutches/rails
4 = walker
5 = assist of 1
6 = unable to complete

Independent refers to walking without any walking aids or assistance. Walker refers to standard walker or 2- or 4-wheeled walker; **assist of 1** refers to physical assistance of 1 person whether minimum, moderate or maximum assist.

Comments

Carpet____

____

____

Up & Go____

____

____

Obstacles ____

____

____

Stairs ____

____

____

Carry ____

____

____

Step ____

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Door ____

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5.6 References

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Chapter 6: Discussion

In this chapter we discuss the implications (section 6.1) and limitations (section 6.2) of the research presented in chapters 2 through 5, followed by considerations for future work (section 6.3), and future directions of the research (section 6.4).

6.1 Implications

The research in this thesis provides greater insight into how the human nervous system learns walking movements, with an emphasis on how very young children learn. Furthermore, novel approaches for the training and assessment of walking after incomplete spinal cord injury (ISCI) were addressed.

Motor adaptation in young children

There are a number of implications from our work presented in chapter 2. First, we found that adaptation of the temporal coordination of the legs was seen in most infants older than 8.5 months of age, suggesting that the training of temporal adaptation will likely be successful in children older than 8-9 months.

Second, we showed that adaptation of a temporal measure (i.e., double support time) does not occur in parallel with adaptation of a spatial measure (i.e., centre of oscillation). Perhaps the mechanisms underlying adaptation of double support time and centre of oscillation are distinct. Others have suggested that different areas of the cerebellum or motor cortex are involved in temporal and spatial adaptation of interlimb coordination (Choi et al. 2009, Malone and Bastian 2010). Furthermore, perhaps the two components mature at different rates. Our findings suggest that the ability to adapt in time is present before the ability to adapt in space. This is further supported by study of split-belt adaptation in older children. Vasudevan and others (2009) found that while all children aged 3-5 years showed adaptation in temporal measures, none of these children showed adaptation to centre of oscillation.

Third, since it takes longer for children to adapt than adults, children may need to perform more repetitions when training. The adult data fit best with a double-exponential curve – reflecting fast and slow components of adaptation (Smith et al. 2006). The time courses of the children were best fit to a straight line, perhaps suggesting their learning involves only the slow component, which is believed to be more enduring than the fast component (Smith et al. 2006). If this were true, we would expect de-adaptation to take longer in the children. Unfortunately, most of our children could not walk long enough to study the de-adaptation rate, however, Jansen-Osmann and colleagues (2002) showed that children took longer than adults to de-adapt after training a novel arm movement.

Fourth, baseline asymmetry in step length or double support time was temporarily corrected with split-belt walking in our children. This correction has been previously reported for adults with stroke (Reisman et al. 2007) and older children with hemispherectomy (Choi et al. 2009), but not for children <3 years old. Thus, split-belt training may be beneficial for young children who walk with an asymmetric gait.

Lastly, our findings suggest that young children may show greater learning when the error driving the learning is small. Previous work in healthy adults has shown that when errors in arm movements are introduced gradually, rather than abruptly, the aftereffects are greater and more enduring (Klassen et al. 2005, Kagerer et al. 1997, Michel et al. 2007). Furthermore, patients with cerebellar damage are able to adapt a reaching movement when the perturbation is increased gradually over many trials, but not when the full perturbation is introduced abruptly (Criscimagna-Hemminger et al. 2010). Perhaps very young children, whose nervous systems are not fully mature, are like cerebellar patients in that they cannot adapt step length when the error is large.

Long-term training of interlimb coordination in human infants

The results from chapter 3 suggest that kicking and stepping share some controlling circuitry. These movements have been shown to respond similarly to load-related feedback (Musselman and Yang 2007), providing further indirect evidence for shared circuitry. Likewise, human infants can make gradual transitions between forwards, sideways and backwards stepping when held over a moving treadmill belt (Lam and Yang 2000), suggesting that the circuitry controlling walking in different directions may have shared components.

We also showed that a movement learned in a weight bearing position can transfer to a non-weight bearing position. This has implications for motor training. For example, initially following an ISCI, patients often do not have sufficient cardiovascular stability to begin upright walking training. During this period, perhaps walking movements could be successfully trained in a recumbent position.

Walking training after ISCI

General conclusions cannot be drawn from chapter 4, a case series study, but we can comment on the trends observed in our four participants. First, we found that the two individuals with very chronic injuries (i.e., >4 years) showed greater improvements with skill training, whereas the two participants who were ~1 year post-injury showed roughly equal benefit from skill training and BWSTT. This suggests that time since injury may be an important factor to consider when planning a walking training program. To date there has been little comparison of the effects of walking training in acute and chronic ISCI (Wernig et al. 1998).

Second, since our participants showed continual improvements in walking ability with long-term training (i.e., ≥6 months), it suggests that it may be beneficial to extend the period of training beyond the typical 3 months. Furthermore, two participants did not show improvements in walking until after 3 months of training. If training had stopped after 3 months, these individuals would be considered ‘nonresponders’ (Norton and Gorassini 2006). However, they were capable of responding to training if given sufficient time.

Lastly, our participants with ISCI maintained their walking gains post-training if they continued to walk at home. Ways to promote walking practice after training should be considered. Also, perhaps individuals should not be discharged from training until they reach a level of walking ability that will allow continued practice at home.

Assessing walking after ISCI

The Spinal Cord Injury Functional Ambulation Profile (SCI-FAP, chapter 5) addresses the need for a measure of functional walking for ISCI (reviewed in Lam et al. 2008). Since it measures a unique dimension of walking ability, it has the potential to be a valuable addition to the measures commonly used to assess walking after ISCI (e.g., 10-meter walk test, Walking Index for Spinal Cord Injury II).

6.2 Limitations

The limitations specific to each project are discussed in their respective chapters. Here we discuss general limitations of the thesis. First, two projects in this thesis used very young children (i.e., <1 year old) to study how the nervous system learns walking movements. The human infant is thought to be an excellent model for the study of spinal and brainstem control of walking (Yang et al. 2004); however, we do not know for certain the functional state of the many descending inputs that are undergoing maturation. The sequence of developmental events in the human nervous system is largely known, based on work done in non-human vertebrates (i.e., rodents and chicks) and confirmed with histological evidence from young humans (reviewed in Altman and Bayer 2001). The precise timing of the developmental events for the human is not known, and there is likely considerable variation between individuals, which cannot be measured at present.

There is sufficient evidence to suggest that the human nervous system is immature in the first year of life. There is little myelin in the hemispheres of the cerebrum at the time of birth (Yakovlev and Lecours 1967). After birth, significant changes in the cerebrum occur, including the growth of dendrites (Marin-Padilla 1970), changes in synapse morphology (Huttenlocher 1979, 1994), and development of myelin (Yakovlev and Lecours 1967, Lebel et al. 2008). An important descending tract from the motor cortex, the corticospinal tract, is not fully myelinated for some time after birth (Yakovlev and Lecours 1967, Brody et al. 1987, Eyre et al. 1991, Khater-Boidin and Duron 1991, Szelenyi et al. 2003, reviewed in Altman and Bayer 2001). The corticospinal tract is believed to be the last descending tract to mature (reviewed in Altman and Bayer 2001). Likewise, the cerebellar hemispheres and middle cerebellar peduncles are mostly unmyelinated at birth (Triulzi et al. 2006). In contrast, the pathways of the inferior and superior cerebellar peduncles, flocculonodular lobe and superior vermis have myelin at birth (Triulzi et al. 2006). Myelination in the cerebellum takes longer than that in the cerebrum (Saksena et al. 2008). The rate of myelination slows at 24 months and 36 months of age in the cerebrum and cerebellum, respectively (Saksena et al. 2008). By 12 months of age the three-layered structure of the cerebellum exists (Lavezzi et al. 2006).

Second, two projects involved a small number of individuals with ISCI. Thus, the conclusions drawn from these projects cannot be generalized beyond the study participants. Furthermore, our participants were a heterogeneous group of subjects (i.e., had varying levels of injury, time since injury, etc.). High inter-subject variability reduces a study's power and introduces confounding variables (Portney and Watkins 2000). A study involving a large number of homogeneous subjects is ideal, but often unrealistic for clinical research.

6.3 Considerations for Future Work

Studying motor adaptation with a split-belt treadmill

For future work related to this thesis, there are a number of things that we will do differently based on our past experience. When using a split-belt treadmill to study motor adaptation (i.e., chapter 2), we will use a 3:1, rather than 2:1, speed differential to increase the likelihood of inducing a perturbation in interlimb coordination. We will collect centre of oscillation data for all children, using the Optotrak system, since centre of oscillation, unlike step length, is a pure spatial measure. We will also experiment with the split-belt walking protocol to determine how to reliably manipulate the error size. Perhaps it is the speed differential or amount of body weight support that contributes to the size of the perturbation.

Long-term motor training for young children

If we undertake another long-term training study with young children (i.e., chapter 3) we will document the training dosage in much more detail. For example, we could have parents bring the child to the lab for practice sessions, or a researcher could visit the child's home to assist with the training. Another option is to give the parents a video camera and have them create a video log of the practice sessions. In all of these scenarios a researcher would be able to document the quality and duration of training – information we did not have for the study presented in chapter 3.

Retraining walking after ISCI

In future training studies involving individuals with ISCI, we will improve upon the study design described in chapter 4. First, walking ability varies day to day amongst these individuals due to fluctuations in muscle tone, pain, fatigue, etc. Considering this, we will perform repeated baseline assessments to ensure the individual's baseline ability is stable before beginning training. Second, if we use an alternating treatment design again, we will have a rest period between training phases. When training phases are presented back-to-back, the effects of one phase could carry-over into the subsequent phase. Third, we will include a measure of participation in walking in the home and/or community. For example, we could quantify the amount of walking done by the participants by having them wear a pedometer (e.g., the StepWatch) at home. Fourth, work in spinal cord-injured rats has shown that locomotor outcomes are better when the number of repetitions performed during training is high (Cha et al. 2007). Thus, when comparing two training methods, it is important to document the number of steps made. In the future we will have participants wear a pedometer during training.

Outcome measure development

If we develop a new outcome measure again (i.e., chapter 5), we will spend more time assessing the test items during the development phase. For example, if we had tested the SCI-FAP on more individuals with ISCI during its development, we could have looked at the redundancy within the measure (i.e., inter-task correlations) and identified which tasks should be re-designed prior to the testing of reliability and validity.

6.4 Future Directions

Effect of error size on adaptation

The findings presented in chapters 2-5 have led to interesting ideas for future work. In chapter 2 we showed that there is a relationship between error size and the ability to adapt step length. We are currently investigating this possibility by comparing adaptation to split-belt walking in young children under 2 conditions, 1) when the speed differential is increased very slowly, and 2) when the targeted speed differential is introduced instantaneously, to determine if there is a difference.

Retention and generalization of split-belt walking

One goal of studying adaptation to split-belt walking is to use it as a training method. To be used for training, the effects of split-belt walking need to be retained and transferred to realistic walking environments. We know that there is partial transfer of learning from split-belt walking to over-ground walking, and that the transfer is twice as great in individuals with stroke compared with healthy adults (Reisman et al. 2009). Children can transfer an adapted upper extremity movement to an untrained workspace (Jansen-Osmann et al. 2002), but the extent of transfer possible for a walking task is unknown in this group. We plan to quantify the amount of transfer between split-belt and over-ground walking in young children. We would also like to determine whether the adaptation learned on the split-belt treadmill is retained beyond the first exposure to split-belt walking. If there is retention, the rate of adaptation should be quicker at subsequent exposures and the size of the initial error should be smaller (Martin et al. 1996, Shadmehr and Brashers-Krug 1997, Gordon and Ferris 2007). Furthermore, with continued practice, can young children learn to make instantaneous switches between the walking patterns needed for tied-belt and split-belt walking? This has been shown for health adults performing a throwing task with and without wedge prism glasses (Martin et al. 1996).

Correcting gait asymmetries with split-belt walking

Children with hemiplegia, resulting from stroke or cerebral palsy, often have an asymmetric gait pattern (Norlin and Odenrick 1986). Split-belt walking can correct these asymmetries for a short time in children with hemispherectomy (Choi et al. 2009). Can very young children with stroke or cerebral palsy also produce a symmetric gait pattern after walking on a split-belt treadmill? If yes, it would be interesting to study the retention and generalization of this learning to assess its suitability as a training method.

Transfer of training effects from non-weight bearing to weight bearing movements

In chapter 3 we showed that the effects of training a movement in weight bearing could transfer to a non-weight bearing position. Can learned behaviours transfer in the other direction, from non-weight bearing to weight bearing? This direction of transfer is more clinically relevant. As a first step in addressing this issue, human infants could be trained to move the legs synchronously in a supine position (e.g., kicking play with the legs attached to one another), and we could test whether the synchronous coordination transfers to weight bearing movements on the treadmill.

Interlimb coordination in infants with injury to the CNS

We have also described the interlimb coordination of kicking and stepping movements of healthy infants aged 3-9 months. Do infants with damage to the central nervous system show abnormal interlimb coordination at this young age? Fetters and colleagues (2004) showed that there are distinct differences in intralimb coordination between pre-term infants with and without white matter disorder.

Regression of walking ability after training

Not all of our subjects with ISCI maintained their walking gains after the end of training. It would be interesting to identify the factors that contribute to this regression in walking ability. For example, there may be a minimum walking speed, below which functional walking is not realistic (as mentioned in Chapter 4). There are many factors to investigate – muscular strength, postural control, cardiovascular fitness, depression, motivation, time since injury, etc. To address this question, individuals with ISCI who are ambulatory could be followed for at least one year after discharge from an inpatient rehabilitation setting. Performance on a variety of physical and walking-related measures could be compared for individuals who show regression of walking ability over time and those who do not. This will allow identification of the factors contributing to the regression. With this information we can learn how to prevent the regression of walking ability, and identify individuals at risk.

Continued assessment of the SCI-FAP as a measure of functional walking

We plan to continue investigating the SCI-FAP as a measure of functional walking. First, we will re-design the carry and obstacles tasks in an effort to reduce the redundancy in the measure. We also plan to compare SCI-FAP performance when participants walk at a comfortable speed and at their fastest speed for all the tasks. Perhaps the ceiling effect of the SCI-FAP will be reduced if participants walk at their fastest speed. We are currently assessing the SCI-FAP's sensitivity to change and its minimal clinically important difference. Preliminary work suggests that the SCI-FAP is sensitive to changes in walking ability following endurance and precision training in individuals with ISCI (Musselman et al. 2010). We would like to assess whether the SCI-FAP is a useful measure for individuals with acute and sub-acute ISCI. This will involve assessing the SCI-FAP's validity, reliability and sensitivity to change in these groups. Likewise, the SCI-FAP may be a useful measure for other patient groups, such as stroke, but its psychometric properties will need to be assessed in these groups. Measures of functional walking are lacking for stroke (Lord and Rochester 2005).

6.5 Concluding Remarks

There are four main findings of this thesis. First, very young children can make short-term adaptations to their walking, and separate mechanisms may underlie the adaptation of temporal and spatial measures of walking. Second, weight bearing (i.e., stepping and jumping) and non-weight bearing (i.e., kicking) rhythmic movements in human infants may share some neural circuitry. Furthermore, training over 1 month can change the interlimb coordination of these movements. Third, skill training is effective at improving walking speed, skill, endurance and confidence after ISCI. Lastly, the SCI-FAP is a valid and reliable measure of functional walking for individuals with chronic ISCI. This thesis contributes to our understanding of how the human nervous system controls and learns walking movements, and suggests new directions for training and assessing walking after ISCI. Collectively the findings will contribute to the optimization of walking training programs and consequent greater recovery of independence in walking for individuals with damage to the CNS.

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