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Effects of overground walking with a robotic exoskeleton on lower limb muscle synergies

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Effects of overground walking with a robotic exoskeleton on lower limb muscle synergies

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Résumé

Les exosquelettes robotisés de marche (**ERM**) représentent une intervention prometteuse dans le domaine de la réadaptation locomotrice. Sur le plan clinique, les ERM facilitent la mise en application de principes de neuroplasticité. Jusqu'à présent, la majorité des études analysant les effets de l'ERM a été menée avec des ERM fournissant une assistance robotique complète le long d'une trajectoire de mouvements prédéfinie des membres inférieurs (**MI**) de façon à reproduire la marche de façon quasi parfaite à très basse vitesse. La nouvelle génération d'ERM, maintenant disponible sur le marché, propose de nouveaux modes de contrôles qui permettent, entre autres, une liberté de mouvement accrue aux MIs (c.-à-d. trajectoire non imposée) et une possibilité d'offrir une assistance ou résistance aux mouvements de différentes intensités surtout pendant la phase d'oscillation du cycle de marche. Cependant, les effets de ces modes de contrôles sur la coordination musculaire des MI pendant la marche au sol avec l'ERM, caractérisé via l'extraction de synergies musculaires (**SM**), restent méconnus. Cette thèse mesure et compare les caractéristiques des SM (c.-à-d. nombre, profils d'activation, composition musculaire et contribution relative des muscles) pendant la la marche au sol sans ou avec un ERM paramétré avec six différents modes de contrôle chez des individus en bonne santé (articles #1 et #2) et d'autres ayant une lésion médullaire incomplète (**LMI**) (article #3). Les signaux électromyographiques (**EMG**) des différents muscles clés des MI, enregistrés lors de la marche, ont été utilisés afin d'extraire les SM avec un algorithme de factorisation matricielle non négative. La similarité des cosinus et les coefficients de corrélation ont caractérisé les similitudes entre les caractéristiques des SM. Les résultats montrent que: 1) les profils d'activation temporelle et le nombre de SM sont modifiés en fonction de la vitesse de marche avec, entre autres une augmentation de la vitesse de marche entrainant une fusion de SM, chez les individus en bonne santé marchant sans ERM ; 2) lorsque ces derniers marchent avec un ERM, les différents modes de contrôle testés ne dupliquent pas adéquatement les SM retrouvées lors de la marche sans ERM. En fait, uniquement le mode de contrôle libérant la contrainte de trajectoire de mouvements des MIs dans le plan sagittal lors de la phase d'oscillation reproduit les principales caractéristiques des SM retrouvées pendant la marche sans ERM ; 3) le nombre et la composition

musculaire des SM sont modifiés pendant la marche sans ERM chez les personnes ayant une LMI. Cependant, parmi tous les modes de contrôle étudiés, seul le mode de contrôle libérant le contrôle de la trajectoire de mouvements des MI et assistant l'oscillation du MIs (c.-à-d. HASSIST) permets l'extraction de SM similaire à celles observées chez des individus en santé lors d'une marche sans ERM. Dans l'ensemble, cette thèse a mis en évidence le fait que différentes demandes biomécaniques liées à la marche (c.-à-d. vitesse de marche, modes de contrôle de l'ERM) modifient le nombre et les caractéristiques de SM chez les personnes en santé. Cette thèse a également confirmé que la coordination musculaire, mise en évidence via l'analyse de SM, est altérée chez les personnes ayant une LMI et a tendance à se normaliser lors de la marche avec l'ERM paramétré dans le mode de HASSIST. Les nouvelles preuves appuieront les professionnels de la réadaptation dans le processus de prise de décision concernant la sélection du mode de contrôle des MIs lors de l'entrainement locomoteur utilisant avec un ERM.

Mots-clés : Coordination musculaire, lésion de la moelle épinière, marche, réadaptation, technologie.

Abstract

Wearable robotic exoskeletons (**WRE**) represent a promising rehabilitation intervention for locomotor rehabilitation training that aligns with activity-based neuroplasticity principles in terms of optimal sensory input, massed repetition, and proper kinematics. Thus far, most studies that investigated the effects of WRE have used WRE that provide full robotic assistance and fixed trajectory guidance to the lower extremity (**L/E**) to generate close-to-normal walking kinematics, usually at very slow speeds. Based on clinicians' feedback, current commercially-available WRE have additional control options to be able to integrate these devices into the recovery process of individuals who have maintained some ability to walk after an injury to the central nervous system. In this context, WRE now offer additional degrees of movements for the L/E to move freely and different strategies to assist or resist movement, particularly during the gait cycle's swing phase. However, the extent that these additional WRE control options affect L/E neuromuscular control during walking, typically characterized using muscle synergies (**MSs**), remains unknown. This thesis measures and compares MSs characteristics (i.e., number, temporal activation profile, and muscles contributing to a specific synergy [weightings]) during typical overground walking, with and without a WRE, in six different control modes, in abled-bodied individuals (Articles #1 and #2) and individuals with incomplete spinal cord injury (**iSCI**; Article #3). **Surface EMG** of key L/E muscles were recorded while walking and used to extract MSs using a non-negative matrix factorization algorithm. Cosine similarity and correlation coefficients characterized, grouped, and indicated similarities between MS characteristics. Results demonstrated that: 1) the number of MSs and MS temporal activation profiles in able-bodied individuals walking without WRE are modified by walking speed and that, as speed increased, specific MSs were fused or merged compared to MSs at slow speeds; 2) In able-bodied individuals walking with WRE, few WRE control modes maintained the typical MSs characteristics that were found during overground walking without WRE. Moreover, freeing the L/E swing trajectory imposed by the WRE best reproduced those MSs characteristics during overground walking without the WRE; and 3) After an iSCI, alterations to the number and the composition of MSs were observed during walking without WRE. However, of all WRE control modes that were

investigated, only HASSIST (i.e., freeing WRE control over L/E swing trajectory while assisting the user's self-selected trajectory) reproduced the number and composition of MSs found in abled-bodied individuals during overground walking without WRE. Altogether, the results of this thesis demonstrated that different walking-related biomechanical demands (i.e., walking speed) and most of the WRE control modes can alter some MSs, and their characteristics, in able-bodied individuals. This research also confirmed that impaired muscle coordination, assessed via MSs, can adapt when walking with a WRE set with specific control options (e.g., HASSIST). These MS adaptations mimicked typical MS characteristics extracted during overground walking. The evidence generated by this thesis will support the decision-making process when selecting specific L/E control options during WRE walking, allowing rehabilitation professionals to refine WRE locomotor training protocols.

Keywords: gait, muscle coordination, rehabilitation, spinal cord injury, technology.

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ASIA	American spinal cord injury association
CNS	Central Nervous System
EMG	Electromyography
iSCI	incomplete Spinal Cord Injury
L/E	Lower extremity
MSs	Muscle synergies
NNMF	Non Negative Matrix Factorization
SCI	Spinal Cord Injury
VAF	Variance Accounted For
WRE	Wearable Robotic Exoskeleton

What we do together, that we cannot do it alone.

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CHAPTER 1 – INTRODUCTION

Walking is a complex task requiring the appropriate activation and coordination of several central nervous system (**CNS**) structures, and particularly the spinal cord, to generate walking-related muscle activations, and joint and limb movements to facilitate optimal locomotor adaptations to the environment. The disruption of sensory and motor signals across a lesion affecting the spinal cord, referred to as a spinal cord injury (**SCI**), constitutes a life-disrupting condition after which functional abilities, particularly walking and walking-related abilities (e.g., sit-to-stand transitions, ascending and descending stairs), are generally reduced (Behrman, Ardolino, & Harkema, 2017). After SCI, these impairments and disabilities often result in devastating consequences to social participation and life satisfaction (Ditunno, Patrick, Stineman, & Ditunno, 2008; Organization & Society, 2013).

Approximately 86 000 people live with an SCI across Canada, with approximately 4 300 new SCI cases each year. The cost associated with living with an SCI is substantial, with estimates of the average lifetime cost of direct care ranging from 1.5 to 3 million CAD. The estimated cost (including health care, equipment, and modifications) for traumatic SCI for newly injured Canadians is over 2.7 billion per year (Rick Hansen Institute, 2018). In Quebec, the incidence of new cases of SCI in 2018 was 1 035, with over 20 690 individuals living with an SCI that year alone. Moreover, those living with an SCI are 2 to 5 times more likely to die prematurely than those without SCI. Among SCIs, partial spinal cord lesions make up 72% of cases and complete lesions constitute 28% (Rick Hansen Institute, 2018). This higher proportion of incomplete SCI (**iSCI**) has important significance in the rehabilitation field, as the incompleteness of the lesion is associated with a better prognosis for walking, especially if the Lower Extremity Motor Score is greater than 20/50 (Waters, Adkins, Yakura, & Sie, 1994).

For many years, locomotor training approaches to restoring walking after an iSCI have focused on adapting or creating movement strategies based on assistive devices (i.e. walkers, canes or crutches), neglecting potential neural mechanisms for recovery. For example, use of a walker requires forward trunk flexion and arm use, thereby reducing lower extremity (L/E)

loading. However, this compensatory posture constrains hip extension during gait and therefore alters key sensory input needed from hip receptors for stance-swing gait phase transitions (Grillner & Rossignol, 1978). In other words, a compensatory-based rehabilitation approach for functional gains has been favored over a neurorecovery-based rehabilitation approach. However, recent progression in understanding how the CNS compensates and recovers from injury has created a paradigm shift in rehabilitation towards a restorative approach in recovering function through meaningful neurological change (Dietz, 2012; Hubli & Dietz, 2013).

In recent years, robotic-assisted walking with an exoskeleton has developed substantially, progressively transitioning from research laboratories to clinical practice. Most currently available wearable robotic exoskeletons (WREs) generate flexion and extension at the hips and knees via electrically actuated motors, while the ankles are controlled with a non-motorized dynamic orthosis or passive spring joints. A first-generation of robotic assisted walking devices was initially developed for treadmill walking, offering fully motorized control of the L/E (Wirz, Bastiaenen, de Bie, & Dietz, 2011). However, the fully motorized control often lead to participants becoming rapidly accustomed to assisted walking, resulting in a very limited active engagement or participation from the user and reduced movement variability (Morawietz & Moffat, 2013). The emergence of a second generation of WREs now allow users to perform overground walking and offer a wider range of L/E control modes (Kolakowsky-Hayner, Crew, Moran, & Shah, 2013; Mekki, Delgado, Fry, Putrino, & Huang, 2018). For example, it is now possible to reduce or completely remove the fully motorized control and allow the user to voluntary select L/E trajectory. This feature would in turn allow an active participation of the user during assisted walking and allows for step-to-step variability (Figure 1). The self-selection of L/E trajectories feature of this generation of WREs translates to the ability to assist or resist the hip or knee joints across a large range of forces during the swing phase of walking. These recent advancements are intended to allow rehabilitation professionals to offer the best and most effective locomotor training program to individuals who have sustained a neurological injury (e.g., SCI, stroke). This type of training is ideal for those who have minimally or partially recovered their ability to walk or perform walking-related activities (e.g., sit-to-stand transfers).

Although WRE with these features represents a promising neurorehabilitation intervention, the effects of these recent features offered by the second generation of WRE on the effectiveness of rehabilitation practices is unknown. Indeed, it is unclear how to prioritize features when developing a locomotor training program with a WRE (Figure 1).

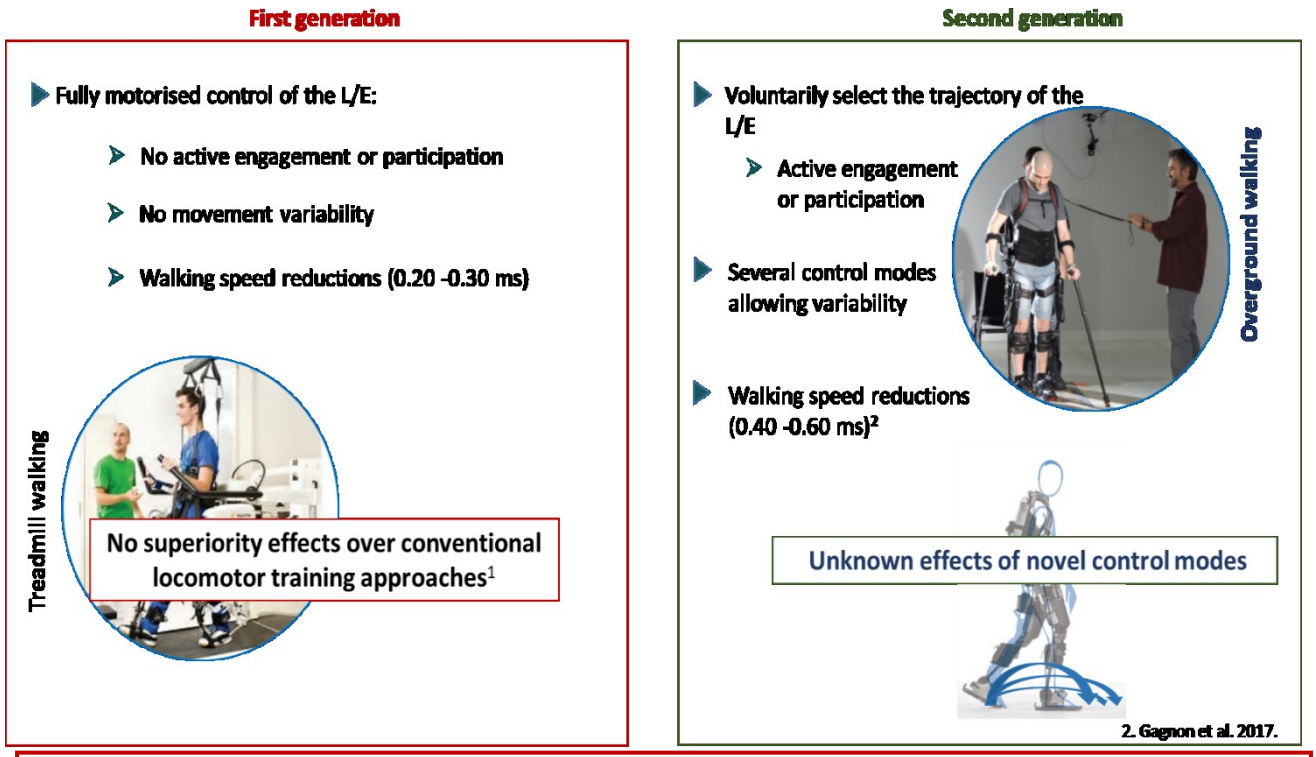

Figure 1. – Main features of the first and second generation of wearable robotic exoskeletons.

While the effectiveness of rehabilitation using WRE has predominantly been assessed using performance-based measures during clinical practice (i.e. walking speed, step length) (Bolliger et al., 2018), this approach does not allow rehabilitation professionals to adequately distinguish actual neuromuscular recovery. This is important because after an CNS lesion, changes to walking performance can be achieved by adopting various compensatory strategies that maintain abnormal patterns of muscle coordination (Maegele et al., 2002). However, these potential compensatory strategies are often neglected by therapists.

Within this context, this thesis explored the effects of various WRE control modes on L/E muscle coordination during walking using surface electromyographic (**sEMG**) analysis, both with and without a WRE, in able bodied adults and individuals with iSCI. Moreover, as a reference, different walking speeds without WRE in able-bodied individuals were also investigated as walking speeds are drastically reduced when walking with a WRE (Gagnon, Da Cunha, Boyer-Delestre, Bosquet, & Duclos, 2017). Finally, recruitment and synergy of specific L/E muscles were investigated using sEMG and muscle synergies (**MSs**), considered the basic neural control for muscle coordination. Through assessment of MSs, clinicians can determine whether specific motor subtasks are accessible and properly modulated by the CNS with an iSCI. The results of this work offer the first evidence of the effects of various control modes that comprise the second generation of WRE, providing a first step towards enriching the clinical decision-making process for rehabilitation professionals who use WRE for locomotor training.

CHAPTER 2 – LITERATURE REVIEW

2.1 Neural control of locomotion

Walking, while appearing to be an easy task, is the expression of a specific series of cyclical and sequential motor actions that require coordinated muscle activation patterns. Due to is cyclical nature, walking can be analyzed using the gait cycle. A gait cycle, defined as the time between two successive contacts of the same foot, can be subdivided into the stance and swing phases. When a gait cycle is time-normalized (i.e. from 0 to 100%), the stance phase is the period between 0% (i.e., foot contact) and 60% (i.e., toe-off of the same foot) (Winter, 2009). Stance phase represents the period where the limb is in contact with the ground, supporting the body's weight and propelling the body forward. At the end of stance, the limb is lifted from the ground (toe-off at 60% of the gait cycle), swung forward using hip flexion, and finally is again placed upon the ground (100% of the gait cycle). This period is called the swing phase and represents 40% of a gait cycle (Winter, 2009).

Walking is a result of intricate and dynamic interactions between a central program (i.e. from the brain and spinal cord) and peripheral feedback mechanisms. The feedback to generate and adapt locomotion to the environment originates from muscle and skin afferents as well as from primary sensory organs (i.e. visual, auditory, vestibular) and supraspinal sensory integration areas and is modulated by a central spinal program to adapt the locomotor pattern to the environmental requirements (Rossignol, Dubuc, & Gossard, 2006). The study of each of these components reveals the autonomy and the interdependence of the various control parts that contribute to the understanding of recovery after disruptions at the central nervous system (CNS).

2.1.1 Spinal circuits for locomotion

The central program for walking relies on a genetically determined spinal neural network capable of generating much of the basic timing and pattern of complex, coordinated muscle activities required during walking (Rossignol and Frigon, 2011). For locomotion, the "central pattern generator" (CPG) indicates a set of neurons whose properties and connectivity are

hypothesized to give rise to these rhythmic motor patterns. Almost four decades ago, Grillner proposed that the mammalian locomotor CPG is composed of interconnected modules that coordinate activity around specific joints (Grillner, 1981). This unit of modules may or may not be dissociated from the rhythm-generating circuitry and a multilayered spinal locomotor CPG, in which rhythm-generation and pattern formation are functionally separated, has been proposed (McCrea and Rybak, 2008). Therefore, in this two-level CPG, the rhythm generator controls rhythm features (i.e., cycle period, phase durations and transitions) and projects to the pattern-formation level, which coordinates and distributes activity to individual or group of motor pools.

The CPG represents a central concept over which we construct and assess models of plasticity, such as those that would aid recovery after a spinal lesion. For instance, animals and humans share locomotor control mechanisms, such as the spinal CPG, that are reproducible across species (Côté, Murray, & Knikou, 2018; Grillner & El Manira, 2019). The spinal CPG is at the core of the locomotor control system and it can be altered or modulated by sensory inputs (e.g. propiospinal and/or cutaneous) and descending signals from supraspinal structures (i.e. cortical or subcortical) that can modulate, trigger, stop, and steer locomotion (Rossignol and Frigon, 2011). CPGs, sensory inputs and supraspinal structures are in constant interaction to drive the appropriate commands to specific muscles to adapt locomotion to external situations. Furthermore, interneurons within the spinal cord could potentially participate in this modulation, before the command reaches its respective motoneurons that results and the intended coordinated activation of muscles to achieve walking (Figure 2). In sum, these neural networks for walking are modulated by both afferent and descending pathways.

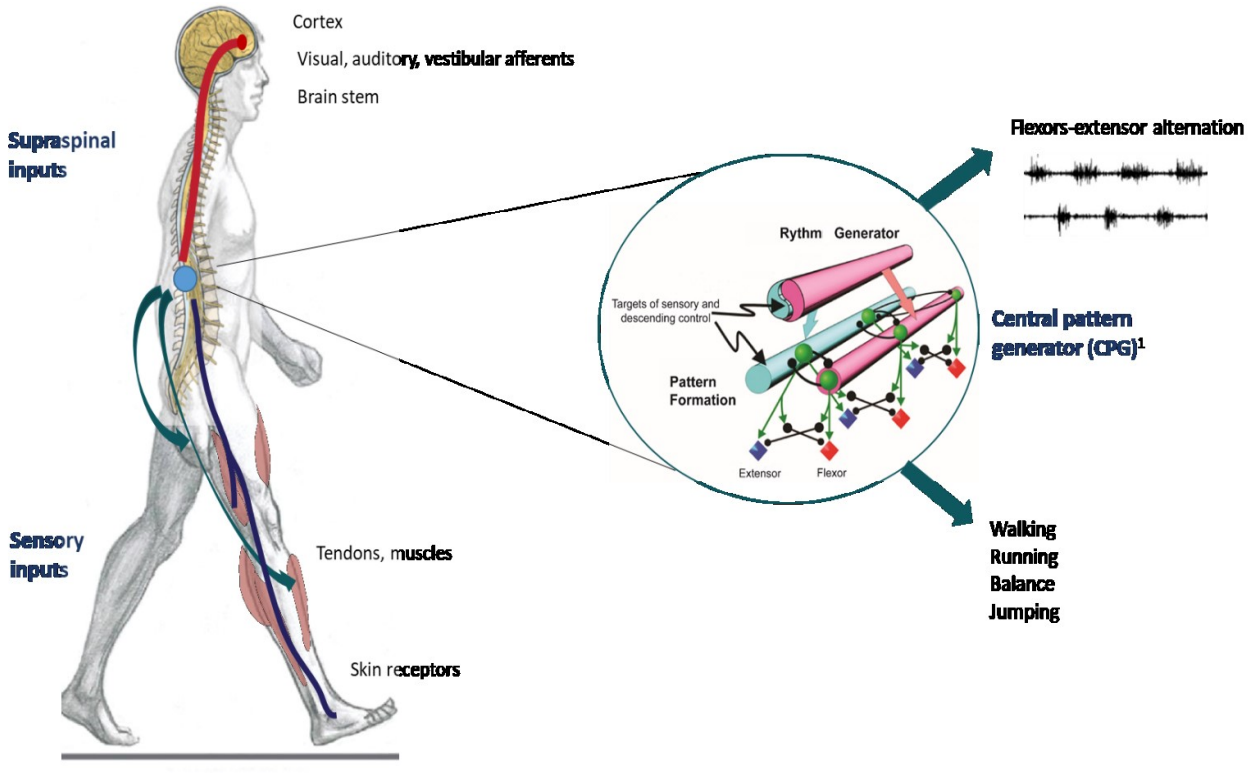

Figure 2. – Neural control of locomotion. The spinal CPG generates the rhythm and pattern commands for locomotion and is modulated by both sensory and supraspinal inputs.

2.1.2 Afferent inputs

The most relevant sensory feedback inputs for walking arise from afferents signaling hip position and from load-sensitive mechanoreceptors located in extensor muscles and skin afferents in the foot (Hubli & Dietz, 2013). Hip joint and L/E afferent inputs that signal load during stance are essential for activating spinal neuronal circuits underlying locomotion (V. Dietz, 2012), leading to appropriate L/E activation and amplitude of extensor muscles (Hubli & Dietz, 2013). For instance, studies in humans have shown that generating locomotor-like movements of the L/E by manual assistance were not sufficient to generate leg muscle activation in able-bodied individuals or individuals with spinal cord injury (Harkema et al., 1997; V. Dietz & Harkema, 2004). However, when load is added to the leg, mimicking the load-bearing function of stance phase, manually-assisted leg movements lead to an appropriate leg stepping pattern activation (Dietz &

Harkema, 2004). Furthermore, the amplitude of leg muscle activation is directly related to the level of loading during stepping on a treadmill, demonstrating the importance of load-bearing during the stance phase to walking pattern generation (Harkema et al., 1997; Sinkjær, Andersen, Ladouceur, Christensen, & Nielsen, 2000). Based on experiments of unilateral hip obstruction during walking, afferent input from hip joints initiates the transition from stance to swing phase (V. Dietz & Harkema, 2004). For instance, when one hip's movement is obstructed, it completely suppresses the rhythmicity of the L/E of the same side, while the other L/E continues to be rhythmically active (Grillner and Rossignol, 1978). Other studies have demonstrated that in chronic spinalized cats as well as in pre-walking human infants, preventing hip extension impedes the initiation of the swing phase by inhibiting the activity of the flexor muscles during stance phase (Pang & Yang, 2000; Van de Crommert, Mulder, & Duysens, 1998). These studies have presented evidence reflecting the importance of sensory inputs, especially during stance phase, in the modulation of efferent outputs during the generation of human and animal locomotion.

2.1.3 Supraspinal control of locomotion

Supraspinal control of locomotion can be viewed as initiation of locomotion by structures in the brain stem (Shik, Severin et al., 1966) or the control of posture and corrections to the walking pattern to adapt to the environment. Several spinal structures, including reticulospinal, corticospinal and vestibulospinal pathways, are capable of influencing locomotor neural circuits within the spinal cord (Drew, Jiang et al., 2002a). For example, the reticulospinal and vestibulospinal pathways are implicated in producing the requisite muscle tone necessary to support the body during walking, ensuring lateral stability, and producing step by step regulation in muscle activity. Furthermore, recordings of motor cortex cells and their projections to the spinal cord through corticospinal pathways are strongly modulated during precision walking, playing a key role in adaptations of the limb trajectory to more difficult locomotor tasks, such as obstacle avoidance and uneven terrain (Beloozerova & Sirota, 1993; Drew & Marigold, 2015). In humans, electrophysiological and imaging studies have demonstrated the importance of the motor cortex and supraspinal pathways during walking. For instance, studies involving transcranial magnetic stimulation (TMS) have indicated that corticospinal pathways are most active for flexor muscle control during steady-state walking. However, during walking tasks

requiring an increased attentional demand to the level of motor activity, corticospinal pathways are equally active for both flexor and extensor muscles throughout the entire gait cycle (Capaday, Lavoie, Barbeau, Schneider, & Bonnard, 1999). Moreover, low intensity TMS which activates intracortical inhibitory circuits, can suppress L/E muscle activation during walking (Petersen et al., 2001) demonstrating the importance of supraspinal structures in the control of both flexor and extensor muscle activation during locomotion.

2.2 Spinal cord injury

2.2.1 Symptoms and classification

Disruption of spinal cord function after an iSCI would highly impair the dynamic interactions between a central program for walking and both peripheral and supraspinal feedback mechanisms (Rossignol, Dubuc, & Gossard, 2006). This disruption would then lead to a decline in supraspinal command transmission to L/E motoneurons and impaired processing of afferent input by the spinal locomotor networks responsible for locomotion. Consequently, symptoms after a SCI are highly variable among individuals and depend on the severity of injury and its location within the spinal cord.

An SCI can arise from traumatic (e.g. physical injury) or non-traumatic causes (e.g infection, disease, cancer/tumor) or from degenerative musculoskeletal diseases, (e.g. osteoarthritis, congenital conditions) (Organization & Society, 2013). SCI can cause partial or complete loss of sensory or motor function of upper extremities, lower extremities and/or trunk, as well as the autonomic regulation of heart rate, blood pressure, bowel and bladder control, and sexual function (Stahel, 2013). In general, the higher the lesion's location within the spinal cord, the greater the sensorimotor impairments of the trunk and extremities. Thus, after a cervical level lesion, sensorimotor impairments affect the trunk and all four extremities, a condition known as tetraplegia, while sensorimotor impairments secondary to damage at thoracic, lumbar or sacral segments of the spinal cord will affect the trunk and L/E, sparing the upper extremities (Stahel, 2013).

The extent of impairments after a SCI not only depend on the lesion level but also on whether the lesion is “complete” or “incomplete”. This criteria is scored according to whether there is any sensory or motor preservation below the level of the lesion. The most common SCI reporting and classification method is the American Spinal Injury Association (ASIA) Impairment Scale (AIS) (Table 1). Injuries are classified as neurologically “complete” (cSCI) or “incomplete” (iSCI) based upon the sacral motor and sensory sparing definition. For instance, ASIA A and B are defined as no preservation of sensory function in the sacral segments. For grades C or D (i.e., motor incomplete), the individual must have either voluntary anal sphincter contraction or sacral sensory sparing (i.e. preserved sensation when applying deep anal pressure) with sparing of motor function below the level of the lesion. The ASIA lower extremity muscle score (LEMS) is commonly used to manually evaluate muscle strength by evaluating five lower extremity muscle groups representing each neurological level from lumbar to sacral spinal segments. Thus, both sensory and motor sparing and muscle strength are used together to classify SCI.

Table 1. – ASIA classification of spinal cord injury.

A = Complete. No sensory or motor function is preserved in the sacral segments S4-S5.
B = Sensory incomplete. Sensory but not motor function is preserved below the neurological level of injury (NLI) and includes the sacral segments S4-S5, AND no motor function is preserved more than three levels below the motor level on either side of the body.
C = Motor incomplete. Motor function is preserved below the neurological level, and more than half of key muscle functions below the single NLI have a muscle grade less than 3 (Grades 0–2).
D = Motor incomplete. Motor function is preserved below the neurological level, and at least half (half or more) of key muscle functions below the NLI have a muscle grade >3.
E = Normal. If sensation and motor function as tested with the International Standards for Neurological Classification of Spinal Cord Injury (ISNSCI) are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without a SCI does not receive an AIS grade.

This thesis recruited individuals with chronic paraplegic iSCI (i.e., ASIA motor incomplete C or D) with lesions occurring more than 12 months previously. While spontaneous recovery of motor function in patients with cSCI is limited, iSCI patients present the highest probability of recovery and improvement in locomotion through the use of rehabilitation tools or experimental therapies (Fawcett et al., 2007). Compared to individuals with acute iSCI, chronic iSCI participants present with the least amount of change in functional capacity one year after their injury and provide a stable baseline for assessing therapeutic interventions and distinguishing neurological improvement from spontaneous recovery (J. Ditunno, Little, Tessler, & Burns, 2004).

2.3 Changes to neural mechanisms after iSCI

2.3.1 Spinal changes after iSCI

Although the underlying mechanisms for spinal changes after SCI are still unclear, the chronic deprivation of supraspinal influence to spinal neurons and inappropriate peripheral inputs after SCI give rise to progressive neuronal excitatory function degradation of the spinal cord (Dietz, 2010). This leads to an imbalance and a shift towards more centrally controlled inhibitory signaling to the locomotor CPGs (Dietz, 2010). In both animals and humans, this inhibitory signaling to the spinal CPG after a SCI has been associated with the facilitation of long-latency reflex pathways. In turn, this facilitation results in the inhibition of the normal early spinal reflex component, an increase in the late spinal reflex component, and a reduction in electromyographic (EMG) amplitude after SCI (Frigon & Rossignol, 2006; Hubli, Bolliger, & Dietz, 2011). The hypothesis that changes in locomotion and spinal reflex components are due to a predominant inhibition, and not purely due to a progressive degeneration of neuronal circuits after a SCI, is based on locomotor networks continuing to function many years after a SCI, and the dominance of the early over the late spinal reflex component in iSCI individuals who are able to perform stepping exercises (Smith & Knikou, 2016).

In humans, chronic degradation and inhibitory signaling to spinal circuits are also reflected by a phenomenon called EMG exhaustion, known as a decline to nearly EMG noise level amplitude

after approximately five minutes of assisted locomotion. This phenomenon is thought to originate from a pre-motoneuronal (i.e., spinal level) as motoneurons can still be strongly activated when muscle spasms occurred (Dietz, 2010). Furthermore, EMG exhaustion is observed in the presence of long-term L/E immobility, regardless of SCI completeness. However, iSCI individuals who regularly perform stepping movements do not show EMG exhaustion, and the inhibitory control over spinal circuits is decreased (Smith & Knikou, 2016). This lack of degradation for individuals performing regular stepping indicates the importance of locomotor training for individuals with iSCI.

2.3.2 Supraspinal changes after SCI

After an SCI, cortical neuronal activity, while partially deprived of inputs from their target spinal neurons, undergoes adaptive changes. These changes to supraspinal pathways after SCI include an increase in cortical activity as a result of a shift from stereotypical gait movements, towards more skilled, but dysfunctional, L/E movements (Dobkin, 2000). Animal models have demonstrated that after an iSCI, spared axons, especially those from the corticospinal and reticulospinal tracts, can bypass the injury site via new collaterals, and innervate previously inaccessible spinal targets (Brus-Ramer, Carmel, Chakrabarty, & Martin, 2007; May et al., 2017; Wiessner et al., 2003). Cortical reorganization characterized by expanded territories of the leg or hindlimb cortical representations after an SCI have also been observed in rats and humans (Bruehlmeier et al., 1998; Endo, Spenger, Tominaga, Brene, & Olson, 2007).

2.3.3 Neuromuscular deficits after iSCI

To achieve an efficient walking pattern, a healthy motor system has the ability to coordinate many muscles crossing multiple joints to. However, motor command disruptions to the spinal cord after an iSCI limits this appropriate muscle coordination during overground walking, translating into the observed clinical deficits (Gorassini, Norton, Nevett-Duchcherer, Roy, & Yang, 2009; Maegele, Müller, Wernig, Edgerton, & Harkema, 2002). These deficits vary widely among iSCI participants and depend, among other factors, on the severity, level of injury, and the disrupted spinal pathways that in turn make each iSCI individual unique in their motor deficits. However, individuals with iSCI will present with some common motor impairments characterized

by an incapacity to adjust to environmental perturbation, and therefore experience a greater prevalence of falls than those without an SCI(Brotherton, Krause, & Nietert, 2007). Single-joint movements can be limited in individuals with SCI, providing a clear indication of the limited capacity of the supraspinal commands to access specific muscles, leading to impaired muscle coordination. Individuals with SCI may adopt compensatory strategies to overcome single-joint movements by instead employing multijoint flexion or extension movements or co-contractions of the entire limb (Maegele et al., 2002). Importantly, these compensations cause reductions in walking abilities such a decrease in walking speed (Dobkin, 2003) and walking related abilities (Figure 3).

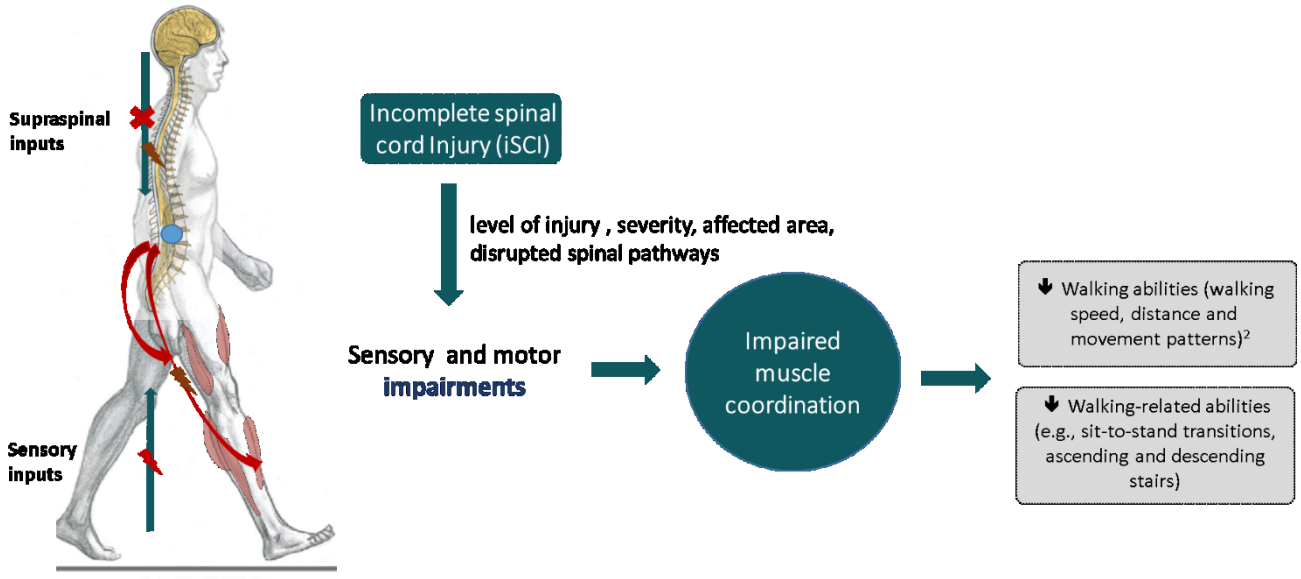

Figure 3. – Neuromuscular deficits after iSCI. Supraspinal and sensory disruption after an iSCI lead to impaired muscle coordination.

2.4 Locomotor training and rehabilitation principles

Neuroplasticity, whereby "neuronal circuits can be modified by experience, learning or injury" (R. Nudo, 2003), provides the underlying framework for neurologically based rehabilitation. First, it must be understood how the neural element constituting locomotion can be accessed and changed and second, how the ability to make use of the interactions between spinal, supraspinal, and sensory interactions can be best used to promote recovery after an iSCI.

The appropriate integration of spinal, supraspinal, and sensory aspects are of critical importance for recovery, since the loss of motor capacity after SCI could become greater if spinal circuits are not activated by functional inputs (V Dietz & Harkema, 2004).

2.4.1 Neurophysiological basis for locomotor training

Locomotor training is based on the principle that, by increasing functional sensory afferent and supraspinal inputs, a particular therapy could benefit from nervous system flexibility and plasticity to recover gait function (Harkema et al., 2012). Animal models have demonstrated that locomotor training can induce functional changes within the spinal cord by altering locomotor circuit excitability and configuration (Rossignol et al., 2015). For instance, Martinez et al. (2013) observed that after hemisection of the spinal cord, cats were able to be re-trained until motor recovery of walking. After a second, and now complete section of the spinal cord was performed below the first hemisection, all trained cats could walk at high speeds after 24 hours, a process that typically takes weeks to appear. This early re-expression of locomotion demonstrated that training helped maintain the spinal circuits in an active functional state after hemisection. The changes observed after repetitive locomotor training were likely related to the movement-related activation of sensory afferents that can participate in the regulation of muscle discharge amplitude and the control of step cycle characteristics (i.e. onset and offset of swing and stance) (Martinez, Delivet-Mongrain, & Rossignol, 2013). In humans, locomotor training after an iSCI can be attributed to enhanced L/E muscle activity, which was closely correlated to improved locomotor function (V Dietz & Harkema, 2004).

Spared pathways originating from propriospinal structures (i.e., interneurons interconnecting various levels within the spinal cord) can play an active role in recovery and in restoring some voluntary L/E control (Rossignol, Dubuc et al., 2006). However, descending pathway compensations may take different forms. While damaged pathways may regenerate, undamaged pathways may sprout or change their transmission efficacy (Rossignol and Frigon, 2011). In doing so, new circuits could result either from new anatomical connections or from enhanced connectivity of existing circuits (Rossignol and Frigon, 2011).

The importance of supraspinal inputs in locomotion recovery by increasing voluntary movements is highlighted by cortical changes and locomotor improvements after locomotor training. Functional magnetic resonance imaging (MRI) analysis in individuals with iSCI, demonstrated that while both voluntary and passive forefoot flexion movement training expanded cortical areas representing the L/E, voluntary training induced larger cortical area expansions, including changes in premotor and supplementary motor areas (Dobkin, 2000). Furthermore, a study that aimed to increase iSCI supraspinal activity by concentrating on voluntary activation of the lower limbs during treadmill training, demonstrated that overground walking function improved after a three to five month treadmill training therapy (Thomas & Gorassini, 2005).

Although mechanisms for recovery are present in spinal, sensory, and supraspinal aspects of locomotion, to exploit neural plasticity and generate functional and meaningful recovery, these circuits must be trained in a relevant manner. Universally accepted principles among rehabilitation researchers and professionals stipulate that, to generate neuroplasticity and to optimize meaningful gains in walking ability and walking-related abilities, any locomotor training must (Behrman et al., 2005; Forrest et al., 2008; Harkema, 2001; Harkema et al., 2012; Shea & Kohl, 1990):

- Provide an appropriate afferent input (i.e. task-specificity);
- Provide the possibility of massed repetition of a relevant task;
- Allow task variability and an increased voluntary engagement;
- Be performed over time.

2.4.2 Rehabilitation principles applied to iSCI locomotor training

2.4.2.1 Adequate afferent inputs and task-specificity

The adequate afferent inputs principle of rehabilitation dictates that iSCI locomotor training should aim to activate spinal locomotor circuitry by providing appropriate afferent feedback, both involving the facilitation and assistance of L/E stepping-like movements and body weight support (V. Dietz, 2012). These aspects represent key components for locomotor recovery

since spinal circuit plasticity is both task- and use-dependent. This has been demonstrated in animal experiments where, after a complete SCI, cats trained only to stand regained the ability to support their body weight but were not capable of stepping (De Leon, Hodgson, Roy, & Edgerton, 1998). This evidence demonstrates that a particular task could be successfully learned and executed after SCI if that particular task was specifically practiced.

Considering that the most important afferent inputs for walking arise from the stretch- and load-receptors, efficient therapies for walking must increase hip and load receptor activity. Hubli et al. (2013) observed that only after training unsupported stepping movements could individuals with iSCI show gait improvements during overground walking. These findings confirm the importance of extensor muscle loading for recovery of walking. Furthermore, studies have also demonstrated that decreased L/E unloading is positively correlated with flexor and extensor muscle EMG signals, regardless of the presence or absence of injury (i.e., more unloading, greater EMG amplitude) (Gorassini et al., 2009). Thus, the amount of appropriate or inappropriate sensory inputs are a key component for locomotor recovery (V. Dietz, 2012).

2.4.2.2 High repetition

To induce structural neurological changes after a CNS lesion, a high number of repetitions of appropriate task-specific afferent inputs during locomotor training must be included. For gait-specific training, studies in animals have demonstrated that approximately 1000 to 2000 steps per training session are required to improve lower limb coordination and step quality. A study of a locomotor training program in rats demonstrated that only the group that trained 1000 steps per session, compared to 100 steps per session, significantly improved step quality and the ability to adjust to different load and treadmill speed-related conditions (Cha et al., 2007). However, whether automatic and consistent repetition requires more active cognitive processing to induce neuroplasticity and motor learning is still under debate. For example, a study of individuals with stroke compared two groups performing a finger-tracking task (Carey et al., 2007). While one group performed an easier task, requiring only repetition, the other group performed a more difficult cognitive processing task requiring visuospatial tracking. Although both groups improved finger-tracking performance, only the group with the easier task performed better on functional testing. It was hypothesized that even though both groups performed the same task, the group

performing the easier task performed actually more repetitions than the group who was challenged by the cognitive task, leading to an improvement in performance (Carey et al., 2007). Contrary to these results, increased cognitive function during more complex locomotor training tasks may also induce neuroplasticity. Animal studies have demonstrated that, after a cortical lesion, fewer repetitions (i.e. 400-600) were required when they included a challenging motor task (i.e. fine-motor grasping) to induce changes in cortical hand representation (R. J. Nudo, Milliken, Jenkins, & Merzenich, 1996). Despite these differences in related to task difficulty, it is clear that more repetitions leads to improved function.

2.4.2.3 Variability and increased voluntary control

Although repetitive sensory information during locomotor training represents a favorable outcome for motor learning and function improvement, excessive movement variability (i.e., inconsistency or inappropriate intralimb kinematics) would diminish gains in muscle coordination and create step to step instability that could lead to increased risk of falling (Lewek et al., 2009). However, in a context when adequate limb kinematics with appropriate and repetitive sensory inputs is provided, allowing some variability during locomotor training may represent a key feature for gait improvements (Shea & Kohl, 1990). Natural variability is observed during both steady-state and more complex gait tasks (i.e. obstacle avoidance, steering), even in able-bodied individuals. Moreover, variability facilitates retention during motor learning as voluntary participation is expected to increase (Shea & Kohl, 1990). Compared to fixed, rigid limb guidance training, variability in training would allow the CNS to fully explore distinct movement options, inducing the most appropriate adaption to different environmental conditions (Cai et al., 2006; Lewek et al., 2009; Lotze, Braun, Birbaumer, Anders, & Cohen, 2003).

In the context of variability, increased exploration during specific motor task learning leads to more generalizable responses that can be transferred to other tasks (Shea & Kohl, 1990). Thus, in rehabilitation, one of the main goals should be to aim to induce sufficient functional changes so that locomotor function gains can be translated into more varied environmental conditions, as often found in the community. This ability would allow the CNS to access the proper tool or skills learned during locomotor training to successfully adapt to external conditions. Hence, allowing variability during locomotor training provides a wider range of motor schemes for individuals to

perform novel task variations of the learned tasked. For example, a study compared two trained groups during force production throughout visual-motor tracking tasks, where the group that experienced errors induced during the task had higher task retention than the group that repeated the same pattern without any induced error. However, variability alone without a proper task criterion (i.e., a specific task to follow) would not lead to improvements in task retention and adaptability (Heitman, Pugh, Kovaleski, Norell, & Vicory, 2005). Studies that have compared performance of the task alone and performance of highly variable movement have demonstrated that only the group that performs the task that is tested had task retention gains (Heitman, Pugh, Kovaleski, Norell, & Vicory, 2005).

2.4.2.4 Maintained through time

To preserve locomotor training benefits, locomotor activity must be maintained in the long term. Dietz and Harkema (2004) demonstrated that when locomotor training in individuals after SCI was maintained for several months, it led to a long-lasting increased capacity to generate coordinated stepping movements, increased leg extensor EMG activity, and improvements during overground walking. In contrast, EMG activity was significantly reduced in individuals with iSCI who stopped locomotor training, and locomotor task performance degraded. This same outcome also occurred in spinalized cats (Edgerton et al., 1997).

2.5 Locomotor principles and clinical reality

Despite advancements in understanding key neurophysiological aspects and principles to induce CNS plasticity, many of the locomotor training programs currently offered in publicly funded specialized SCI rehabilitation programs across Canada do not align with the aforementioned locomotor training principles. The barriers to the implementation of locomotor training programs in Canada include time and productivity constraints generally encountered in clinical practice, increased physical demand of physiotherapist to safely support individuals with trunk and L/E weakness while simultaneously assisting stepping during manual stepping therapies, limited availability of rehabilitation aids or technicians during locomotor training, and scarcity of equipment options for locomotor training (e.g., motorized treadmill, body weight support systems). A study of locomotor training in individuals with hemiparesis following a stroke

found that the number of repetitions performed during physiotherapy sessions did not approach the number of repetitions recommended to induce neuroplasticity to achieve meaningful recovery after neural injury (Kimberley, Samargia, Moore, Shakya, & Lang, 2010). Another study found that patients only received 40-60 repetitions per session, compared to the 400 to 600 repetitions recommended to induce neural plasticity (R. J. Nudo, Milliken, Jenkins, & Merzenich, 1996). Interestingly, the number of repetitions performed was strongly associated with therapist experience, with more experienced therapists allowing for more repetitions per session compared to inexperienced therapists. These aspects represent examples of the lack of consistency in rehabilitation therapy applications among clinicians as a consequence of standardized protocols for locomotor training (Kimberley, Samargia, Moore, Shakya, & Lang, 2010).

New and promising locomotor training approaches may aid in overcoming clinical practice obstacles related to physical demand (for trunk support and manually assisted stepping) to be able to induce proper task specificity and adhere to massed practice recommendations. For instance, many mobility assistive technologies have been developed in recent years to enable individuals with various types of neurological injuries to ambulate overground. Robotic gait-training devices, such as the powered lower extremity wearable exoskeletons investigated in this thesis, may provide a trainingalternative to overcome therapist limitations and to adhere to the locomotor training principles previously described.

2.5.1 Wearable robotic exoskeletons

Wearable robotic exoskeletons (WRE) are attached to the individual's trunk and lower extremities to provide constant or variable external mechanical assistance, unilaterally or bilaterally at the hip, knee, and/or ankle joints to enable standing, sit-to-stand transitions, and overground walking (Figure 4).

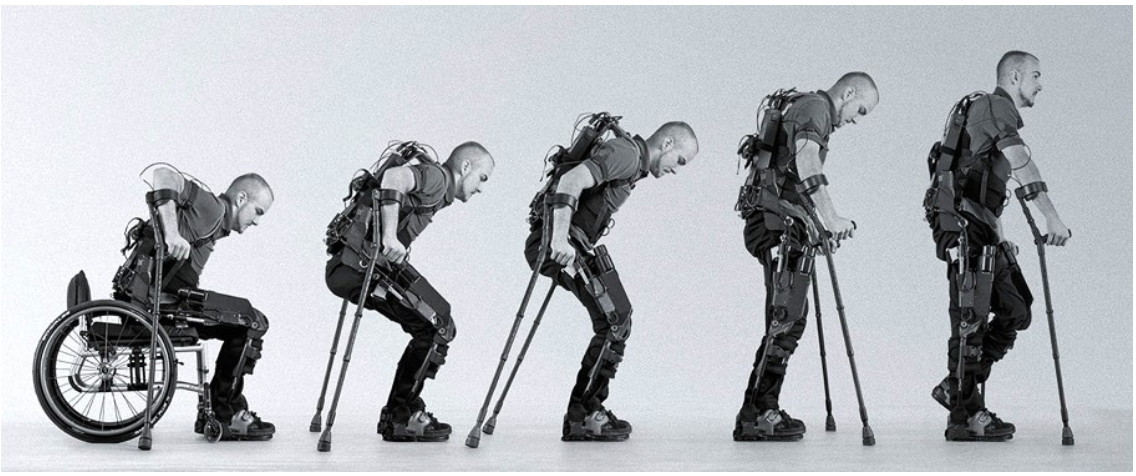

Figure 4. – The WRE enables standing, sit-to-stand transitions, and overground walking.

WREs enable individuals with an iSCI to practice walking over longer periods of time in a safe manner, compared to conventional physiotherapy locomotor training approaches (Esquenazi, Talaty, Packel, & Saulino, 2012; Talaty, Esquenazi, & Briceno, 2013; Zeilig et al., 2012). Moreover, these devices provide repetitive walking patterns that supply the specific sensory inputs (i.e., the joint and limb trajectories mimic those of individuals without neurological injury) which, in theory, strengthen neural pathways by generating coordinated patterns for locomotion (Colombo, Joerg, Schreier, & Dietz, 2000; Hesse, Uhlenbrock, & Sarkodie-Gyan, 1999). At the same time, WREs can minimize the intensive and repetitive physical demands required of physiotherapists during locomotor training and, ultimately, work-related injury risk (Freivogel, Schmalohr, & Mehrholz, 2009). However, the limited and sometimes contradictory knowledge of the efficacy of WRE locomotor training programs constitutes a major barrier for clinical implementation.

The few pre-clinical and clinical exploratory studies of WRE locomotor training programs completed to date that have demonstrated promising outcomes, have also highlighted potential shortcomings. For instance, WRE locomotor training in individuals with iSCI increased overground walking speed and step length during clinical assessments (Arazpour et al., 2012; Esquenazi et al., 2012; Zeilig et al., 2012). Furthermore, biomechanical assessments of walking while using WREs revealed 'stereotypical' and consistent gait movement patterns with reduced compensations (Arazpour et al., 2012; Talaty et al., 2013) and lower limb muscle activation patterns consistent with those expected during typical steady state walking (Hornby, Zemon, & Campbell, 2005; Nooijen, Ter Hoeve, & Field-Fote, 2009). From a clinical perspective, WREs can provide consistent support across locomotor training sessions, regardless of the attending physiotherapist (Galvez, Budovitch, Harkema, & Reinkensmeyer, 2011). However, given the mechanical assistance provided, WREs have been found to reduce the muscular, cardiorespiratory, and metabolic demands of walking (Kawashima, Sone, Nakazawa, Akai, & Yano, 2003). Walking with a WRE for individuals with a complete SCI is a moderate intensity exercise (Escalona et al., 2018), a level recommended to preserve physical fitness, with further potential positive effects on musculoskeletal and bone health when following a locomotor training program (Karelis, Carvalho, Castillo, Gagnon, & Aubertin-Leheudre, 2017).

Despite these advantages and benefits, WRE locomotor training has not yet demonstrated superiority over conventional physiotherapy approaches to improve walking ability in individuals with iSCI (Swinnen, Duerinck, Baeyens, Meeusen, & Kerckhofs, 2010; Tefertiller, Pharo, Evans, & Winchester, 2011). Indeed, a systematic review comparing different locomotor training approaches, including body-weight–supported treadmill training (BWSTT), electrical stimulation, manual assistance, or conventional physiotherapy and BWSTT robotic gait training in iSCI populations concluded that even though all approaches clearly demonstrated improvement after training for walking capacity, velocity, and duration, and quality of gait, none were clearly superior (Morawietz & Moffat, 2013). However, most of the studies were performed using a first generation of WRE that offers fully motorized L/E controlled trajectories and robotic parameters set to 100% passive guidance. This mode of WRE assisted training "maintained homogeneity of the intervention parameters between participants" (Morawietz & Moffat, 2013). This passive

mode rapidly accustomed individuals with SCI to the task, resulting in locomotor training that wasunchallenging, effortless, and/or not specific enough for those individuals (Morawietz & Moffat, 2013). Moreover, locomotor training using a robotic device over a treadmill (i.e., Lokomat [Hocoma, Inc., Zurich, Switzerland]) also did not show improvement in intralimb coordination (i.e. consistency of hip and knee kinematic trajectories) in individuals with iSCI while therapist-assisted treadmill training demonstrated improvement of this same parameter. A lack of step variability provided by the passive and rigid guidance of the lower extremities of the robotic device may explain the lack of improvement in walking coordination with robotic gait assistance , further supporting the hypothesis that the increased stepping variability provided by the therapist assistance leads to the improvement in motor coordination after a CNS lesion (Lewek et al., 2009).

To some extent, the divergence in the efficacy of WRE training results may relate, to the control modes or settings used during locomotor training programs. Very few of these body weight support robot studies allowed for step-to-step variability or increased voluntary demand required for a repetitive, consistent, but flexible, movements to induce important changes to locomotor capacities. Several L/E control mode options have emerged to allow a more flexible stepping control by the user and increased perceived utility and acceptability of the WRE in the neurorehabilitation community. For instance, other than the fixed swinging L/E trajectory offered by the first generation of WREs, a new generation of recently developed WREs now offers control options where the motorized input to the L/E can be removed and the swing path is not pre-programmed. In this modes of control, there would be no imposed trajectory during the swing phase. With these features, it is now possible to provide, different levels of assistance and resistance to individual users who can then self-select L/E motion during swing. To the best of our knowledge, no study has explored how these recently developed control modes affect L/E muscle neural control during walking. To achieve this goal, the concept of muscle synergies (MSs) was selected to quantify and describe neural changes to muscle control related to the adaptation of these additional WRE modes.

2.6 Muscle synergies

An EMG signal represents the summation of multiple active motoneurons that give rise to a motor unit action potential, providing an indirect measure of the motoneuron activity in the spinal cord at a given time during gait (Grasso et al., 2004). Since muscle activation reflects nervous system output, muscle activation patterns may provide indication of the flexibility of neural mechanisms among different tasks, and the adaptability of the CNS to external constraints. Collecting EMG signals in able-bodied and sensorimotor impaired individuals is relatively uncomplicated, however it becomes problematic when collecting signals at or around assistive devices, as the device causes excessive noise that precludes muscle signal analysis.

Human locomotion requires complex coordination and precise muscle control of a redundant musculoskeletal system to successfully adapt to specific environmental conditions. This redundancy in the musculoskeletal system originates from the large number of highly nonlinear muscles, complexity of dynamic coupling between body segments using biarticular muscles, and multiple joints with many degrees of freedom (Haghpanah, Farahmand, & Zohoor, 2017). Furthermore, this redundancy requires a high level of CNS control, increasing the probability of movement error.

Instead of controlling thousands of motor units or multiple muscles individually, the CNS can produce a predetermined movement by grouping muscles into motor modules, and in doing so, control a smaller number of variables (Drew, Kalaska, & Krouchev, 2008; Lacquaniti, Ivanenko, & Zago, 2012; Singh, Iqbal, White, & Hutchinson, 2018; Tresch, Saltiel, & Bizzi, 1999). These motor modules are considered the basic neural control or "building blocks" for muscle coordination. This modular organization, also known as MSs, is hypothesized to simplify highly complex tasks both in terms of neural activation and biomechanical adaptation (Safavynia, Torres-Oviedo, & Ting, 2011). Thus, a single supraspinal neural command (i.e., cortex, brain stem) could select, combine, and modulate the activation amplitude of a specific MS at a specific time within a spinal-level controller. Each of these synergies, or motor modules, contain a consistent ratio of muscle co-activations to coordinate motor segments and accomplish a specific biomechanical task (Figure 5) (Hayes, Chvatal et al. 2014; Bizzi & Cheung, 2013).

Evidence of this modular organization within the spinal cord, and the linear summation of motor commands represent the basis for MSs, originated from electrical stimulation of the spinal cord of spinalized frogs (Mussa-Ivaldi, Giszter, & Bizzi, 1994). Each stimulation resulted in a specific force fields (i.e., force vectors moving in a specific space location), and when two different locations were stimulated simultaneously, the resultant force field was a summation of each individual force field, creating a different and more complex motor output (Bizzi, Mussa-Ivaldi, & Giszter, 1991; Mussa-Ivaldi, Giszter, & Bizzi, 1994). These same principles can be applied to EMG activity analysis, where EMG physiologically corresponds to a summation of motor unit action potentials. The EMG signal is then used to extract muscle synergies by employing decomposition algorithms, which will be explained in this section.

By using such a modular organization, the CNS can produce reproducible, simplified, and consistent movements that are shared across the gait cycle. Indeed, these synergistic movements have been shown to be consistent, both in terms of muscle timing and composition across a wide range of different locomotor and voluntary tasks (d'Avella, Saltiel, & Bizzi, 2003; Ivanenko, Cappellini, Dominici, Poppele, & Lacquaniti, 2005) including walking (Lacquaniti et al., 2012; Singh et al., 2018), reaching (d'Avella, Portone, Fernandez, & Lacquaniti, 2006), running (Cappellini, Ivanenko, Poppele, & Lacquaniti, 2006) and balance tasks (Chvatal & Ting, 2013). This consistency has been demonstrated regardless of the factorization algorithm used to identify MSs (Tresch, Cheung, & d'Avella, 2006). Such a consistency across tasks and across extraction methods further supports the hypothesis of a common neural modular control for locomotion.

2.6.1 Extracting muscle synergies

To understand the encoding mechanisms of control within the spinal cord, MSs must be extracted from the EMG signal as a linear combination of motor outputs (Singh et al., 2018). Several computational algorithms have been developed to reconstruct EMG activity output into a reduced number of MSs. Although there are many different algorithms available to extract MSs, such as the independent component analysis, factor analysis, and non-negative matrix factorization (**NNMF**), all these methods constitutes a dimensional reduction of EMG data to simplify large EMG data sets. Analysis of MSs depends on the number of muscles included, EMG

normalization, and algorithm type (Singh et al., 2018). The NNMF algorithm is widely used to linearly decompose and reconstruct EMG signals by combining parts of the original data set, providing an accurate reconstruction of muscle activity (d'Avella et al., 2003; Devarajan & Cheung, 2014). Reconstructing the data is performed to validate that the extracted MSs accurately represent characteristics of the original EMG data. NNMF is based on the time-invariant characteristics of MSs, where synergies are considered to be spatially fixed or synchronized in a temporal pattern (Devarajan & Cheung, 2014).

2.6.2 Characteristics and flexibility of muscle synergies

MSs can be described in terms of number, composition (i.e., number and relative weighting of active muscles per motor module), and activation (i.e., duration and amplitude) (Neptune, Clark, & Kautz, 2009; Pérez-Nombela et al., 2017b). For gait, a set of specific muscle synergies (typically four muscle synergies for walking tasks) are associated with a particular gait phase and muscle output related to leg stabilization, forward propulsion, swing initiation, and leg deceleration during swing to stance transitions (Neptune, Clark, & Kautz, 2009; Pérez-Nombela et al., 2017b; Torres-Oviedo, Macpherson, & Ting, 2006). Moreover, each MS represents a specific set of muscles related to a specific phase of the gait cycle (Figure 5). Overall, the number, composition and activation of MSs indicates whether specific motor subtasks are functional, accessible and properly modulated by the CNS (Safavynia, Torres-Oviedo, & Ting, 2011).

Although the muscles composing each MSs are linked to a specific temporal activation phase during the gait cycle, MSs allow for dynamic and flexible adaptations to the environment or to a specific task. Thus, in able-bodied individuals, new or existing synergies can be activated in different proportions to allow for adaptation to specific environmental constraints (McGowan, Neptune, Clark, & Kautz, 2010). Indeed, a simulation study demonstrated that even though the number and characteristics of MSs were consistent, altering body weight resulted in a flexible modulation of the recruitment intensity of MSs as well as changes to the activity of main muscles within a specific synergy to adapt to a task (McGowan, Neptune, Clark, & Kautz, 2010).

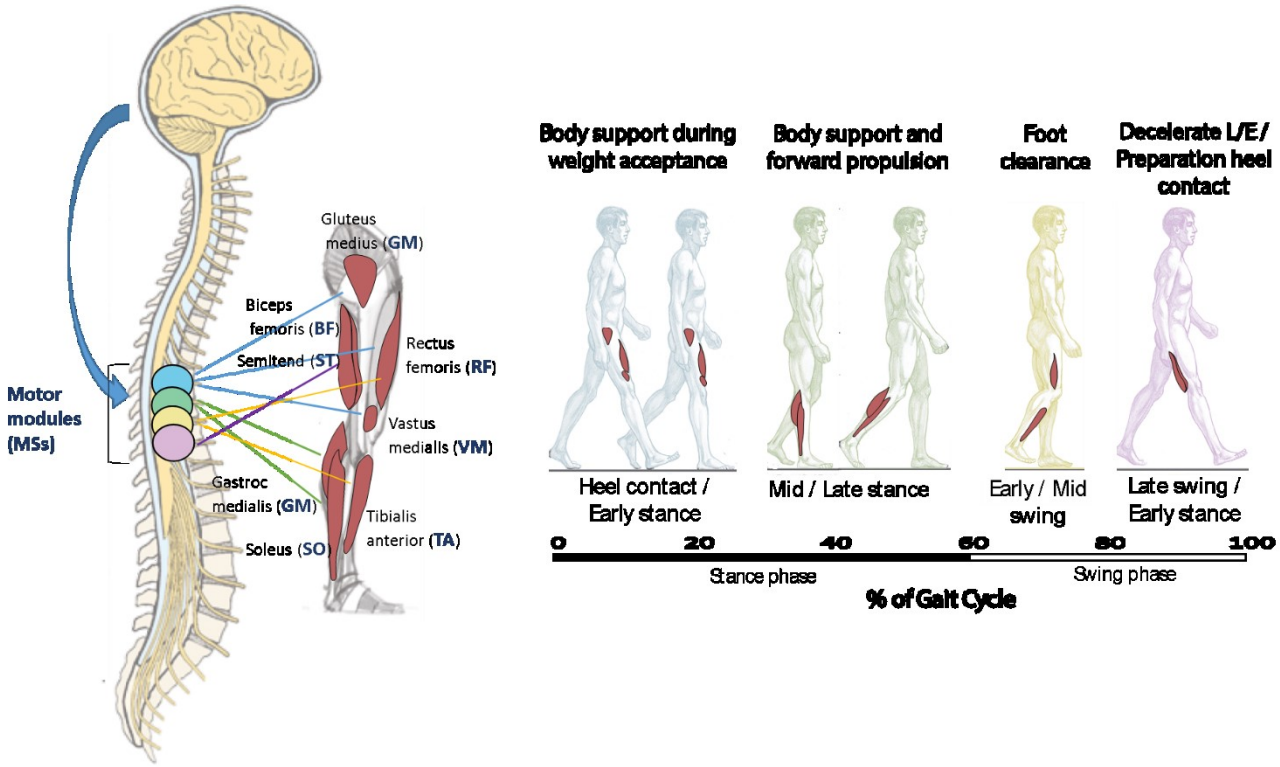

Figure 5. – Schematic representation of typical muscle synergies extracted during the gait cycle.

A study exploring MSs composition during walking with a WRE and unassisted overground walking in able-bodied individuals demonstrated that the muscles composing each synergy may vary between tasks (Li, Liu, Yin, & Chen, 2018). Moreover, new synergies can form during motor skill acquisition or the motor learning process. For example, while performing balance tasks, a subpopulation of individuals differed from the majority in using a knee-bending strategy to accomplish the task. Although common synergies were identified across balance tasks, in this subpopulation, different MS specific to the knee-bending strategy were found, despite all participants accomplishing the balance task properly (Torres-Oviedo & Ting, 2007). Thus, although MSs represent common motor programs, flexible adaptations and modifications can occur through training. This is very important to the rehabilitation process, since even impaired synergies could be modified, with a proper training approach, to achieve normal activation and

muscle composition, leading to a regulation of atypical neural function and consequently a likely recovery of motor function.

2.6.3 The arguments against muscle synergies

Although MSs are reproducible among different tasks, alternative control mechanisms for muscle activation have been suggested. For example, finger muscle control varied across tasks, indicating that muscles were recruited in a flexible manner and adapted to a target movement, and does not support the hypothesis of synergistic muscle activation (Kutch, Kuo, Bloch, & Rymer, 2008). Still, neural differences between fine movement control of the hands, which is more cortically controlled, and-rhythm control of distal structures such as L/E, which are more reliant on spinal structures, could explain different control mechanisms for muscle coordination. For instance, while most CNS motor control is accomplish by corticospinal pathways originating from premotor and motor cortical regions (Drew et al., 2008), hand control have monosynaptic connections projecting through ventral motor neurons on the spinal cord, providing more direct cortical control (Zinger, Harel, Gabler, Israel, & Prut, 2013). These arguments do not completely reject the muscle synergies concept because both fractionated control and MSs control of fine finger movements and gross hand and upper extremity limb movements exist together at the cortical level (Leo et al., 2016). More studies are needed to corroborate that multiple mechanisms of motor control are acting together to accomplish motor tasks, while also allowing for the flexibility needed to execute them.

2.6.4 Muscle synergies after a CNS lesion

After an iSCI, when motor commands are severely disrupted and limit the ability to coordinate multiple muscles during gait, evidence of alterations to MSs have been observed (Clark, Ting, Zajac, Neptune, & Kautz, 2010). Hence, the number, composition, and temporal aspects of different MSs utilized during a motor task, can shed light on whether motor subtasks are accessible and properly modulated by the nervous system. Indeed, reductions in the number of synergies have been associated with an inability to access a specific subtask, translating into motor deficits and abnormal motor outputs, thereby predicting the degree of impairment (Clark,

Ting, Zajac, Neptune, & Kautz, 2010; Hayes, Chvatal, French, Ting, & Trumbower, 2014; Singh et al., 2018).

When comparing MSs between eight individuals with iSCI and eight able-bodied individuals, Hayes et al. (2014) found that the iSCI group presented with a reduced number of MSs and inappropriate muscle components on each synergy, reflecting the heterogeneity of deficits in this population. This alteration in MSs was evidenced by an increase in co-activation or muscles activation that belonged to other synergies. In contrast, the specific and distinctive MSs that were found in able-bodied individuals are an indication of differential muscle control and therefore, greater muscle control complexity. A more recent study of individuals with iSCI demonstrated that fewer MSs and a different composition of MSs were found on the most affected lower limb, when compared to the less affected limb, and compared to able-bodied individuals (Pérez-Nombela et al., 2017a). In the same study, the most affected MSs, found in the individuals with iSCI presenting the most gait deficiencies, were synergies composed of the rectus femoris and tibialis anterior muscles related to the toe-off phase of the gait cycle, and a synergy composed mainly of the gastrocnemius medialis, related to the push-off during the gait cycle. These deficits in specific synergies could explain important gait impairments observed in individuals with iSCI compared to the MSs characteristics of able-bodied individuals. Another study of individuals with hemiparesis following a stroke found that the inability to independently recruit MSs on the paretic limb, and the extensive co-contraction of antagonist muscles, results from a reduced number and merged versions of the typical MSs found in the non-paretic limb, resulting in decreased walking speeds, reduce propulsion, and increased gait asymmetry (Clark et al., 2010). This evidence suggests that the more severe the neural injury, the less complexity in terms of independent activation of muscle groups. This would result in a reduced number or merging of MSs and translate clinically into greater deficits during overground walking. Merging of MSs in adults with stroke have also been associated with poor improvements in muscles strength and restricted joint range of motion, indicating poor motor coordination (Israely, Leisman, & Carmeli, 2018).

Although a reduced number of MSs is not always constant across subjects with similar injuries, Rouston et al. (2013) demonstrated an association between improvements in motor

function and the number and composition of MSs after a 12-week locomotor training program incorporating stepping on a treadmill (Routson, Clark, Bowden, Kautz, & Neptune, 2013). Hence, MSs could be used to understand the nature of locomotor impairments or motor compensations after a CNS injury and the degree of flexibility and adaptability of their motor patterns. Since MSs reflect the state of neural connectivity or CNS excitability, exploring new methods of rehabilitation using these changes to neural output may help inform the efficacy of a rehabilitation tool and guide therapeutic decisions.

To summarize the information presented in this chapter, after an SCI, disruptions in supraspinal commands as well as deficient sensory inputs lead to impairments in muscle coordination. These impairments translate into observable functional disabilities, especially affecting locomotor and locomotor-related abilities. While locomotor training principles are based on the premise that the CNS has a high capacity for plasticity and recovery, several constrains impede the application of these principles in clinical practice. The emergence of WRE represent a promising rehabilitation intervention for locomotor training that aligns with activity-based neuroplasticity principles in terms of specificity (e.g., optimal sensory input, proper movement patterns) and intensity (e.g., possibility to take > 1000 steps/session). The second generation of WRE offering different L/E control modes (e.g., assistance, adaptive, resistance) increase the perceived utility and acceptability of the WRE in the neurorehabilitation community. However, little is known about how these control modes affect L/E muscle neural control during walking. The heterogeneity of SCI, the pathways affected, the individual adaptations, and ensuing compensations demand subject-specific analysis of the neuromuscular mechanisms in the adaptation to these WRE control modes. This neural mechanisms of motor control could be unveiled through the study of MSs, a number of functional units responsible for a well-organized co-activation pattern of multiple L/E muscles associated to specific functions during the gait cycle. Understanding and quantifying the number, composition, and activation of these MSs during overground walking and walking with the WRE is vital for the evaluation of more targeted therapies for walking with an SCI.

CHAPTER 3 – OBJECTIVES

3.1 General objective

The general objective of the thesis is to evaluate how different WRE control modes that are acting mainly on the swing phase of the gait cycle, affect the neural control of L/E muscle coordination during overground walking with a WRE. This information is important when choosing a therapy targeted to a particular individual.

To meet this general objective, three separate studies were completed around two main components: the effects of various overground walking speeds on L/E muscle synergies for able-bodied individuals without a WRE and L/E muscle synergies in able-bodied and individuals with an iSCI during overground walking without and with a WRE.

3.2 Specific objectives and hypotheses

3.2.1. Study #1

This first study investigated, in able-bodied individuals, the effects on the number, temporal profiles, and compositions of MSs of three walking speeds: predetermined slow with rhythmic auditory cueing (SLOW), self-selected comfortable natural (NAT), and self-selected fast (FAST). The hypotheses being tested are:

- Temporal profiles, compositions, and number of MSs will remain similar between the NAT and FAST (Cappellini, Ivanenko, 2006).
- For SLOW, temporal profile, composition, and number of MSs will differ from NAT and FAST because of reduced ground reaction forces, reduced lower extremity inertial effects, reduced lower extremity muscular demand.

This project is relevant since one of the most important biomechanical constraints associated to WRE walking relates to large walking speed reduction resulting, in most part, from mechanical constrains (Gagnon, Da Cunha, Boyer-Delestre, Bosquet, & Duclos, 2017).

3.2.2. Study #2

The second study characterized and compared overground walking without and with a WRE set at six different L/E control options (i.e., a subset of trajectory-controlled and non-trajectory controlled options used for neurorehabilitation). Outcome measures were individual muscles activations and MSs (number, composition, activation profiles). The hypotheses being tested were:

- Walking with a WRE set to fixed trajectory controlled options will preserve typical MS characteristics (i.e., number, profile, muscle weighting) found during overground walking at a matched walking speed without a WRE
- Walking with the WRE set to non-trajectory control modes will lead to variable changes in MS characteristics depending on the mode used (e.g., resistance or assistance control modes).

This project is relevant since the most recently-developed WRE control modes will be investigated for the first time.

3.3.3. Study #3

The third study presents a case series to examine how various WRE trajectory and non-trajectory control modes affected L/E muscle synergies attributes (e.g., number of MSs, muscle weightings within a synergy) in individuals with iSCI during overground walking with a WRE. The hypotheses being tested are:

- The number and weighting of muscles composing each MS during overground walking without a WRE will differ between iSCI and able-bodied individuals
- Walking with a WRE set in a non-controlled trajectory mode will best reproduce the number of MSs and the weight of muscles composing each MS to levels comparable to those extracted in able-bodied individuals during overground walking.

This project is relevant since it represents an initial step to strengthen evidence in regard to L/E muscular coordination that will inform clinical practice on the effects of different control modes when planning personalized WRE locomotor interventions.

CHAPTER 4 – METHODS

Most of methodological aspects in this thesis have been well described in the results section. Therefore, this chapter covers exclusively key methodological elements that relate to the wearable robotic exoskeleton and the muscle synergy extraction process.

4.1 Wearable robotic exoskeleton for overground walking

The EKSO™ GT (Ekso Bionics, Richmond, CA, USA) is a ready-to-wear, battery-powered, motor driven robot that generates motion at the hips and knees in a sequenced manner. It provides important safety features in terms of trunk stabilization and stance phase knee support (Figure 6A-B). These features allow long and consistent stepping kinematics. Each joint is independently controlled by the information provided by sensors feeding the control panel linked to a small, portable, computerized control system attached to the flexible trunk module, housing the battery (see Figure 6C). Information, gathered from over 35 different sensors (e.g., accelerometers, speed controllers, gyroscopes, pressure sensors), feed a decisional algorithm allowing users to perform sit-stand-sit and walking in a straight line. The use of a rolling walker or forearm crutches are required for balance and body weight transfer while walking. For this research, all participants used crutches during all walking trials with the exoskeleton.

The Ekso GT™ provides various control modes to the swing and stand phases of walking, as selected by the physical therapist assisting the user. During swing phase, assistance modes applicable to the limb in motion can be grouped in two categories: Trajectory controlled or Non-trajectory controlled.

When in trajectory controlled mode, steps are initiated when the participant reaches proper lateral shift of his center of pressure (lateral target) and manages to initiate hip flexion. Body weight shifts are generated through active trunk and upper extremities (U/E) movements and facilitated using forearm crutches to ensure contact points with the ground. The Ekso automatically generates the step once these two requirements are met while the leg follows a swing trajectory determined by the programmed settings of the Ekso. Modes belonging to the

trajectory-controlled category used in the present thesis included, for the swing phase, total assistance (TOT), no assistance provided over an imposed trajectory (FIXED0) and an "assistance-as-needed" mode (ADAPT) in which assistance is adapted in response to the amount of force that a participant contributes to the limb motion. In the TOT assistance mode, the leg will move consistently through swing and is less susceptible to the participant's interaction. When in this mode participants were asked to leave control to the machine and not participate in the leg motion. In the FIXED0 mode, the exoskeleton provides a fixed ceiling of robotic assistance set at 0 (thereby the name FIXED0). When in this mode participants perform the L/E motion over an imposed, rigid foot trajectory imposed by the WRE with no robotic assistance. In the ADAPT mode, the exoskeleton automatically adapts to how much the participant influences the motor power of the exoskeleton, and will increase or decrease as needed throughout a predetermined trajectory during the swing phase of gait. A feedback provides the mean assistance level provided by the exoskeleton during the previous 5 consecutives steps.

For these trajectory-controlled modes, a certified therapist accompanying the user can control numerous walking features (e.g., swing speed, step height, step length). Of these parameters, step length and step height were modified by the therapist during trajectory-controlled modes, to reproduce natural gait in an optimal manner adapted for each participant according to their height and assure proper balance and to reproduce natural gait. The remaining parameter (i.e., swing speed) using trajectory-controlled modes was kept at the default setting.

When in non-trajectory controlled, steps are actively initiated and completed by the user. The swing path is not controlled by a program (i.e., no imposed trajectory during swing phase) and the motors at the hip and knee only provide assistance to counteract the weight of the exoskeleton and potential inertial effects. Therefore, the participant is free to move his leg as he wishes in terms of kinematics (i.e., step height, length and speed). Non-trajectory controlled included a high assistance (HASSIST), high resistance (HRESIST) and NEUTRAL modes that provides an assistance, a resistance or no assistance nor resistance during the swing phase, respectively.

For the stance phase, modes included very high, high, medium and low assistances, each contributing to a certain amount to the supporting moment generated at the hip and knee joints. In addition, the stance phase assistance can limit knee flexion up to 45° for safety features. This last setting was used with all participants and exoskeleton modes recorded.

The EKSO™ GT exoskeleton weighs about 28 kg and can reach, in theory, a maximal walking speed of 1.6 m/s. In 2012, following clinical trials, the EKSO™ received the Food and Drug

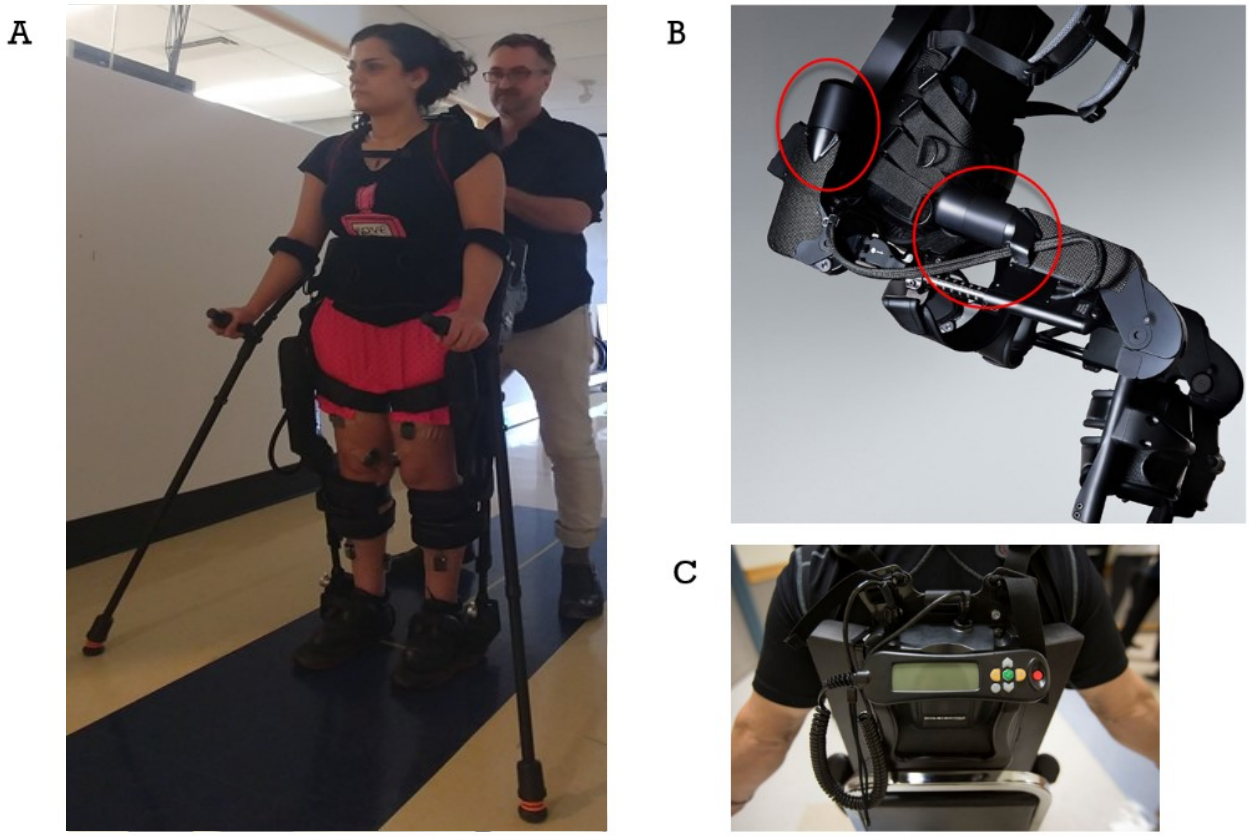

Figure 6. – EKSO™ GT. **A.** Experimental setup and EMG sensors placement in a participant with iSCI. **B.** the EKSO is motorized at the hip and knee joints. **C.** computerized control system attached to trunk from which control modes are selected.

Administration (FDA) approval for hospital use in the United States (Rupal, Singla, & Virk, 2016) and Health Canada approval for clinical use.

4.2 Inclusion and exclusion criteria for the robotic exoskeleton

Clinical, demographic, and specific inclusion and exclusion criteria are described in each of the scientific articles in the methods sections. During the screening process, the research physiotherapist evaluated each participant using the inclusion and exclusion criteria (Table 2).

Table 2. – Participant and exoskeleton-specific inclusion and exclusion criteria.

Inclusion criteria	**Exclusion criteria**
Participant-specific:	***Participant-specific:***

• Adults (≥18 year old)
• Normal cognition (Montreal Cognitive Assessment Score ≥26/30)
• Understand and communicate in English or French
• Reside within 75 km from a research site
 	
<u>Participants with iSCI</u>
• Chronic incomplete SCI
  ○ AIS C or D
  ○ traumatic or non-traumatic SCI below the C5
  ○ > 18 months pre-enrollment
• Capacity to walk overground for at least 10 meters with an assistive device
	• Other neurological impairments aside from those linked to the SCI (e.g., severe traumatic brain injury)
	• Concomitant or secondary musculoskeletal impairments
	• Unstable cardiovascular or autonomic system
	• Pregnancy
	• Any other conditions that may preclude L/E weight-bearing, walking, or exercise tolerance in the WRE

Exoskeleton-specific:	***Exoskeleton-specific:***
• Body mass ≤100kg • Height= 1.52-1.93 m • Pelvis width= 30-46 cm • Thigh length= 51-61.4 cm • Lower leg length=48-63.4 cm • Standing tolerance ≥ 30 minutes with full lower extremity weight-bearing	• Inability to sit with hips and knees ≥90° flexion • Lower extremity passive range of motion limitations (hip flexion contracture ≥5°, knee flexion contracture ≥10°, and ankle dorsiflexion ≤-5° with knee extended • Moderate-to-severe lower extremity spasticity (>3 modified Ashworth score) • Length discrepancy (≥ 1.3 or 1.9 cm at the thigh or lower leg segment) • Skin integrity issues preventing WRE use

4.3 Muscle synergy extraction using Non-negative Matrix Factorization algorithm

In this section, MSs extraction by NNMF are presented. Details of the surface EMG equipment, data processing, and MSs extraction procedures are summarize in the methods section (Article #1).

4.3.1 The NNMF algorithm

Using the NNMF algorithm, MSs are a compressed version of the original EMG data set where muscle activity is represented as a linear summation of motor modules (Lee & Seung, 1999). The NNMF algorithm is a reliable algorithm that provides accurate reconstructions of muscle activity by combining parts of the original EMG data showing a consistent accuracy across a broad range of motor tasks as shown in previous work, accurate (Clark, Ting, Zajac, Neptune, & Kautz, 2010; Rodriguez, Roemmich, Cam, Fregly, & Hass, 2013). This algorithm imposes nonnegative constraints on the synergies and the activation profiles which consider the physiological signaling of the CNS as being a straight forward command without anything being subtracted from it (non-negative components in a signal).

Muscle synergy extraction procedures are defined by means of original data, decomposition, and reconstruction of the original data set.

4.3.1.1 ORIGINAL DATA

The original raw EMG signal from eight L/E muscles collected at 1926 Hz, filtered (Butterworth bandpass 20-400 Hz) and smoothed (continuous Root Mean Square (RMS) using a centered 250 msec moving window) for each muscle was time normalized using 101 temporal data points (0% to 100%). Three consecutive gait cycles presenting the lowest mean coefficient of variation (CV) computed for all the muscles EMG envelopes were selected using a custom-made Labview. Then, the selected consecutive three cycles were averaged together prior to initiating the muscle synergy analysis. For each participant, the RMS signals from each muscle was normalized to its own maximum peak value for each walking trial. This original EMG data matrix, referred to as experimental EMG (**EMGexp**) (Figure 7A), can be defined by $\mathbf{EMG}_{\mathbf{exp}}^{\mathbf{m.t}}$, where *m*

is the number of muscles (8 muscles per L/E) and *t* represents the number of time samples (101 points from time normalization of the EMG data to fit 100% of the gait cycle).

4.3.1.2 DECOMPOSITION

NNMF decomposes the EMG_{exp} into three matrices: $\mathbf{EMG_{exp} = W^{m.s} \cdot H^{s.t} + e}$ (Figure 7B). The W matrix represents weightings of muscle contributions for each MSs (product of *m* (number of muscles) by *s* (number of synergies found)). For visualization and to better characterize muscle composition in each synergy, each W matrix was normalized to the maximum muscle contribution during the whole gait cycle such that each muscle contribution ranged from 0 to 1. The H matrix represents the amplitude of each MSs activation across the time-normalized gait cycle. This matrix is the product of *s* (number of synergies) by *t* (101 time point samples). Finally, the *e* matrix represents the reconstruction error and is the product of *m* (number of muscles from the W matrix) by *t* (time points from the H matrix). For the extraction of MSs to be considered optimal, the reconstruction error must be minimal or reach values close to 0. The less reconstruction error there is, the better the reconstruction process reflects accurate MSs.

4.3.1.3 RECONTRUCTION

To validate that the W matrix accurately represents the data within EMG_{exp}, an evaluation of the proximity between EMG_{exp} and the reconstruction error is necessary. The original data is reconstructed by linearly combining parts of this decomposed data. Thus, the algorithm will run 500 times to evaluate the validity of the reconstructed data relative to the original EMG_{exp} matrix while the algorithm search for an optimal solution to minimize the reconstruction error. A potential MS occurs when reconstruction error values are lower than 1e-8 during 20 consecutive passes of the algorithm. To corroborate the finding of a MS and to estimate the validity of the reconstructed EMG data ($\mathbf{EMG_{rec}}$), Variance Accounted For (VAF) is used to measure the differences between the original matrix EMG_{exp} and the EMG_{rec} (Figure 7C). The closer VAF values are to 1, the more accurate the reconstruction process.

A threshold method was used to calculate the number of MSs, where a threshold value on the VAF curve was set to find the number of synergies for extraction. Thus, VAF was calculated for each muscle ($\mathbf{VAF_m}$) and the product of all VAF_m was defined as global $\mathbf{VAF_g}$. VAF_m values were

acceptable if they exceeded 0.9 (90%). The computation stopped when VAF_g exceeded 0.80 (80%). This whole procedure was repeated while the algorithm identified the reconstruction error and the VAF value criteria. For example, if the VAF criteria had only been identified three times, then the number of MSs found were three.

Out of these procedures, extracted MSs were grouped and classified in terms of number, composition (weightings), and activation timing profiles; this is presented in the scientific articles.

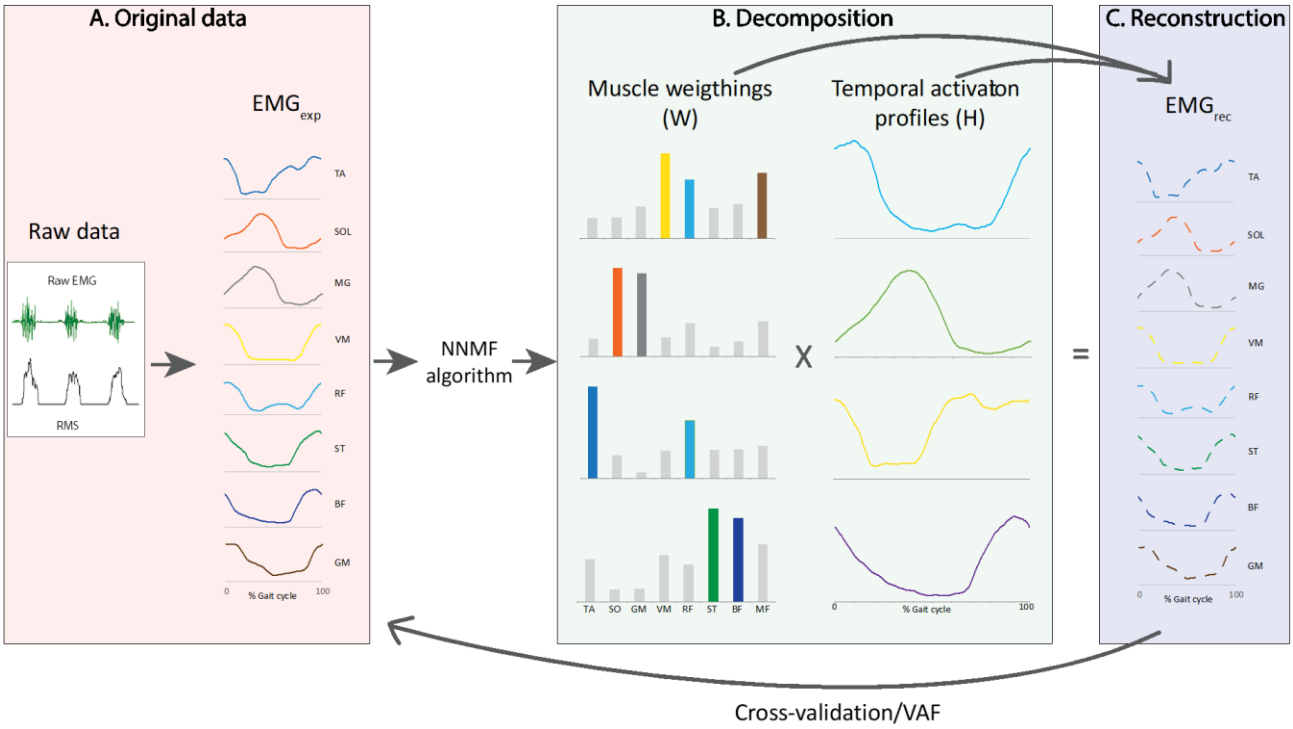

Figure 7. – Muscle synergies extraction procedure.

CHAPTER 5 – RESULTS

The main results of this thesis are presented in three scientific papers that are submitted to scientific journals.

1. ***Effects of varying overground walking speeds on lower extremity muscle synergies in healthy individuals.*** Journal of Motor Control. Manuel J. Escalona, Daniel Bourbonnais, Damien Le Flem, Michel Goyette, Cyril Duclos, Dany H. Gagnon.
2. ***Effects of different robotic exoskeleton control options on lower limb muscle synergies during overground walking in able-bodied adults.*** Clinical Neurophysiology. Manuel J. Escalona, Daniel Bourbonnais, Damien Le Flem, Michel Goyette, Cyril Duclos, Dany H. Gagnon.
3. ***Wearable exoskeleton control modes selected during overground walking affect muscle synergies in adults with a chronic incomplete spinal cord injury.*** Spinal Cord Series and Cases. Manuel J. Escalona, Daniel Bourbonnais, Michel Goyette, Cyril Duclos, Dany H. Gagnon.

5.1. Article #1: Effects of varying overground walking speeds on lower extremity muscle synergies in healthy individuals

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Article submitted in the Journal of Motor Control on January 2020.

As first author, I contributed substantially to the conception and development of the methodology, data collection, analysis, and interpretation of the results. I also wrote the original draft of the manuscript. Dr. Bourbonnais contributed expertise related to muscle synergies, analysis, and results interpretation. Mr. Leflem contributed to the data collection and data processing. Mr. Goyette contributed mainly to data processing and software development for data extraction and analysis. Professors Gagnon and Duclos contributed to methodology development, oversaw results analysis and interpretation, and manuscript writing. All authors contributed to revision of the manuscript's intellectual content and approved the final version for publication.

5.1.1. Abstract

The effects of walking speeds on lower extremity (L/E) muscle synergies (MSs) were investigated among 20 adults who walked 20-m at SLOW (0.6±0.2 m/s), natural (NAT; 1.4±0.1 m/s), and FAST (1.9±0.1 m/s) speeds. Surface EMG of eight L/E muscles were recorded before extracting MSs using a non-negative matrix factorization algorithm. Increasing walking speed tended to merge MSs associated with weight acceptance and limb deceleration whereas reducing walking speed do not change the number and composition of MSs. Varying gait speed, particularly decreasing speed, may represent a rehabilitation strategy needing additional attention given its effects on MSs.

Keywords: Electromyography, gait, locomotion, motor control, movement, walking

5.1.2. Introduction

Human locomotion is a complex task that requires coordinated and precise neural control of muscle activation. This coordination is most likely governed by a sequence of motor modules, also referred to as 'muscle synergies (MSs)', that co-activate multiple lower extremity (L/E) muscles in a reproducible, simplified, and consistent way to generate movements linked to specific locomotor-related subtasks during walking (Lacquaniti, Ivanenko, & Zago, 2012; Singh, Iqbal, White, & Hutchinson, 2018). MSs may be shared across various motor tasks such as standing balance (Chvatal & Ting, 2013), walking (Lacquaniti, Ivanenko, & Zago, 2012; Singh, Iqbal, White, & Hutchinson, 2018), and running (Cappellini, Ivanenko, Poppele, & Lacquaniti, 2006). This coherence in the repertoire of MSs found across various motor tasks supports the idea of a common neural modular control. Hence, MSs analysis may provide insights on the neural control during walking that most laboratory (e.g., kinematics or kinetics) or clinically-based tests fail to do by only characterizing attributes of movements or of performance (Safavynia, Torres-Oviedo, & Ting, 2011), respectively.

Previous clinical and simulation studies have confirmed that neural control during walking can be explained, in most part for able-bodied individuals, by a repertoire of four to five MSs, each associated with a specific sub-phase of the gait cycle (*i.e.*, leg stabilization, forward propulsion, swing initiation, and leg deceleration) (Clark, Ting, Zajac, Neptune, & Kautz, 2010; Neptune, Clark, & Kautz, 2009). Moreover, studies with able-bodied individuals have demonstrated that these MSs adapt to faster or slower speeds during walking: For examples, Ivanenko *and al.* (2004) and Capellini *and al.* (2006) reported that a set of five lower extremity MSs can characterize treadmill walking across speeds ranging from slow (0.27 m/s) to fast (2.5 m/s) while Clark *and al.* (2010) reported that a set of two to five muscle synergies explain treadmill locomotion at speeds ranging from 0.3 m/s to 1.8 m/s, respectively. These small differences when reporting solely the number of MSs are not yet fully understood, although they may relate to locomotor task specificity (e.g., treadmill versus overground walking) and familiarization time for treadmill walking (Meyer et al., 2019). Different adaptations between treadmill and overground walking explain, in most part, spatiotemporal (e.g., greater treadmill walking angular velocities, increase stance phase time with speed decreases), kinetic (e.g.,

treadmill walking changes in muscular activation and smaller ankle dorsiflexors and knee extensor moments and powers (Lee & Hidler, 2008)), and electromyographic (EMG) differences (e.g., positive association between walking speed and muscular recruitment amplitude (Den Otter, Geurts, Mulder, & Duysens, 2004)). Thus, further analysis of MSs (i.e., number, profiles and composition) during overground walking will increase the ecological validity of the current evidence since most studies assessing the effects of speed on MS changes have been gathered during treadmill walking to date.

A detailed analysis on the number and characteristics of MSs during overground walking among able-bodied individuals remains highly relevant, especially that able-bodied individuals are often used as control in studies investigating individuals who sustained a neurological event, such as a spinal cord injury or a stroke, and typically experience a significant and meaningful reduction in walking speeds (Clark et al., 2010; Pérez-Nombela et al., 2017). Hence, the present study aims to investigate the effects of three distinct walking speeds on the number, temporal profiles, and compositions of MSs in healthy individuals: 1) predetermined slow with rhythmic auditory cueing (SLOW), 2) self-selected comfortable natural (NAT), and 3) self-selected fast (FAST). It was hypothesized that the temporal profiles, compositions, and the number of MSs will remain similar between the NAT and FAST walking speeds (Cappellini et al., 2006) and that MSs may change at a predetermined slow speed due to increased motor control complexity and attentional cost (Lajoie, Jehu, Richer, & Tran, 2016). This might be reflected on some MSs characteristics when comparing SLOW to NAT and FAST speeds.

5.1.3. Methods

5.1.3.1. Participants

A convenience sample of 20 healthy adults was recruited (Table 1). Potential participants were 18 to 60 years of age, without neuromusculoskeletal impairments affecting their lower extremities, without conditions limiting their capacity to walk, ability follow simple verbal command, and sufficient auditory ability. The study was conducted at the Pathokinesiology Laboratory of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) located at the CIUSSS du Centre-Sud-de-l'Île-de- Montréal (Institut universitaire sur la

réadaptation en déficience physique de Montréal). All participants provided written consent to participate after being informed of the study's objectives and nature of their participation. The Research Ethics Committee of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal approved the study (CRIR-1083-0515).

5.1.3.2. Walking Tasks

Participants walked at self-selected comfortable natural speed (NAT), fast speed (FAST), and slow (SLOW) speeds. For SLOW, 0.6 m/s was targeted and rhythmic auditory feedback was provided with a metronome (60 bpm) to cue walking cadence and decrease speed-related step time variability associated with slow speeds (Beauchet et al., 2009). This selected slow speed matches the natural walking speed of individuals with sensorimotor impairments (*i.e.,* 0.58 m/s) (Wing, Lynskey, & Bosch, 2012). Participants walked 20-m on a level tiled corridor. Data between 5 and 15-m lines highlighted on the floor (i.e., 10m) was analyzed. Following a familiarization period, participants walked the 20-m distance once at each speed in a random order and a rest period of at least one minute was provided between each trial.

5.1.3.3. Surface Electromyography

Surface EMG of eight muscles was recorded at the right lower extremity: gluteus medius (GM), rectus femoris (RF), vastus medialis (VM), semitendinosus (ST), biceps femoris (BF), tibialis anterior (TA), medial gastrocnemius (MG) and soleus (SO). After the skin surface was shaved and cleaned, Delsys Trigno™ wireless EMG electrodes (Delsys Inc., Boston, MA, USA) were fixed directly to the skin with double-sided tape and positioned in accordance with the SENIAM recommendations (www.seniam.org). These electrodes recorded EMG at 1926 Hz and 3D acceleration at 148 Hz.

Raw EMG were filtered using a fourth-order Butterworth zero-lag bandpass filter, with cut-off frequencies at 20 Hz and 400 Hz before a centered 250-msec sliding root mean square (RMS) window was used to generate continuous EMG envelopes for each muscle. To define gait cycle timing, consecutive foot contacts were identified using a Teager-Kaiser Energy Operator (TKEO) to determine rapid deceleration in the longitudinal direction of the lateral malleolus

sensor. The deceleration peaks were visually inspected and foot contact times adjusted as needed.

Each gait cycle, starting from right foot contact, was time normalized using 101 temporal data points (0% to 100%) from which the stance (0 to 59%) and swing (60-100%) phases were depicted. Among all cycles analyzed, the three consecutive gait cycles presenting the lowest mean coefficient of variation (CV) for all the muscles EMG envelopes over each data point were automatically selected using custom-made Labview software. The consecutive three cycles were averaged together prior to muscle synergy analysis. The use of three gait cycles was deemed optimal because adding gait cycles could minimize variability and potentially reduce the number of modules to be found. For each participant, each RMS signal from each muscle was normalized to its own maximum value.

5.1.3.4. Muscle Synergies

A non-negative matrix factorization (NNMF) algorithm using the Gamma model based on J divergence, a reliable method that generates higher coefficient of correlation and confidence levels compared to other methods (Devarajan & Cheung, 2014), was incorporated into the custom-made Labview EMG analysis software and employed to extract MSs during walking. First, an experimental EMG (EMG_{exp}) data matrix that represented the mean time-normalized EMG of all muscles investigated was constructed for each participant before being submitted to the NNMF algorithm. This algorithm decomposed the EMG_{exp} into two matrices that were multiplied to generate the reconstructed EMG (EMG_{rec}) throughout a complete gait cycle: the muscle weighting matrix coefficients (W= $m \times s$) where W represents the contribution of each muscle (m) within each synergy (s), and the temporal patterns (H= $s \times t$) where H represents the activation muscle synergies (s) profiles during the gait cycle for each time-normalized point (t), as well as error of reconstruction (e). The relative maximum value of each W was constrained to 1 to decrease factorization indeterminacy e (Serrancolí, Monllau, & Font-Llagunes, 2016). Agreement between EMG_{rec} and EMG_{exp} was evaluated via the "variance accounted for" (VAF) for each muscle *m* using the following equation:

$$VAF_m = 1 - \left(\sum \left(EMG_{exp} - EMG_{rec}\right)^2 / \sum EMG_{exp}{}^2\right)$$

The number of MSs was determined by choosing the least number of synergies that could account for an VAF in each muscle (VAF_m) greater than 0.9 (90%) and a global VAF (VAF_g), calculated as the product of all VAF_m, greater than 0.8 (80%). Whenever these criteria were reached, the agreement of this reconstruction was deemed acceptable and the computation stopped. When the absolute difference of the coefficient of determination between the current and last pass was lower than $1\times e^{-8}$ for 20 consecutive passes, or when 500 passes were done without convergence, the algorithm stopped. This procedure was done twenty times, and the result of the lowest reconstruction error with the lowest number of synergy modules within the validation criteria were considered adequate.

Muscle synergies were classified based on the similarities in muscle weightings (W) across participants and walking conditions using a cosine similarity analysis (Hagio & Kouzaki, 2014; Kibushi, Hagio, Moritani, & Kouzaki, 2018). For this analysis, the inner product of the compared MSs vectors was calculated and the cosine angle between those two compared synergies was measured. Whenever cosine similarity value (r) is closer to 1, the greater the similarity in the directions of the two compared vectors. To group muscle synergies, the cosine similarity was calculated between a reference muscle synergy taken from an arbitrary reference participant, to any other muscles synergy. Whenever the cosine similarities of W between the reference muscle synergies and other muscle synergies were over 0.868 ($p < 0.05$) (Nishida, Hagio, Kibushi, Moritani, & Kouzaki, 2017), muscle synergies were considered similar. Likewise, when two MSs at the same walking speed were classified into the same muscle synergy group, these two synergies were considered to be fused together or "merged". The synergy with the lowest correlation was considered to be merged to the main synergy presenting the highest correlation value (See fig. 1).

5.1.3.5. Statistical Analyses and Interpretation

Walking speed was compared across speed conditions using a repeated measures analyses of variance ($p < 0.05$) with pairwise post-hoc comparisons using an adjusted p-value (p=0.05/3 pairwise comparisons=0.017). To verify to what extent the temporal profiles of MSs and of muscle timing activations profiles across walking speeds were comparable between the SLOW, NAT, and

FAST speeds, Pearson product-moment correlation coefficients (*r*) were calculated. The *r* values were interpreted as being very high (≥.90), high (0.70 to 0.89), moderate (0.50 to 0.69), and low (0.30 to 0.49) (Mukaka, 2012). All statistical analyses were performed using SPSS v.24 (SPSS Inc., Chicago, IL, USA).

5.1.4. Results

5.1.4.1. Walking speeds

Walking speeds at SLOW= 0.60 m/s ± 0.16, NAT=1.42 m/s ± 0.11, FAST=1.88 m/s ± 0.10 were significantly different ($p < 0,017$) from each other. These speeds highlight a reduction and augmentation of –57.9% and +33.4% when walking at SLOW or FAST speeds in comparison to NAT speed, respectively.

5.1.4.2. Number of muscle synergies and merged synergies

Two to four muscle synergies were found when reconstructing unilateral lower extremity muscle activation across walking speeds (VAF > 0.8 for all conditions) and are illustrated in Figure 3. Each muscle synergy was characterized by a specific set of predominantly activated muscles (group mean muscle weighting ≥0.3) across all walking speeds: Synergy 1 composed mainly by GM, VM and, to a lesser extent, RF; Synergy 2 composed mainly by SO and MG; Synergy 3 composed mainly by TA and RF, and Synergy 4 composed mainly of the hamstring activity (ST and BF) (Fig. 2).

The analysis on each of these extracted MSs is presented in Table 2. Synergy 1 was identified in most participants (85%) at SLOW walking speed but was only rarely identified during NAT (55%) and FAST (50%) walking speeds. This is confirmed by the cosine similarities values (Fig. 3) in which Synergy 1 was the least consistently identified synergy for NAT (r= 0.74±0.09) and FAST speeds (r= 0.75±0.09). Synergy 2 was identified in almost all participants across all walking speeds (≥95%) and was the least affected synergy (r≥ 0.86) by the walking speeds (*i.e.,* most consistent synergy). Synergy 3 was also identified in the majority of participants across all walking speeds (≥85%) and was the second least affected synergy (r≥ 0.80) by walking speeds. Lastly, synergy 4 was identified in the majority of participants (95%) at SLOW walking speed and

progressively decreased as walking speed increased, although still present and consistent (r≥ 0.83) in the majority of participants (NAT=80%; FAST=75%). Hence, changes in speed predominantly affected synergy 1 and, to a lesser extent, synergy 4. Also of interest, only during SLOW walking speed all four MSs were consistently identified (r≥ 0.85) across all participants and across the group (Fig. 3).

Further analysis of changes in synergies 1 and 4 revealed that, during NAT and FAST walking speeds, all muscles belonging to these synergies merged into another synergy, in many participants. Merging of synergies 1 and 4 was observed mostly during NAT at 65% and FAST at 75% (table 2). As an example of this merging (Fig. 1), for participants 1 and 13, the muscles belonging to synergy 1 (VM, GM and to a lesser degree RF; r<0.86) co-activated or merged with synergy 4 (r ≥ 0.86). Overall, at NAT speed, 65% of the participants (13 out of 20) presented at least one merged synergy. From these 13 participants, 12 (92%) had their synergies 1 and 4 merged. Likewise, at FAST speed, 80% of the participants (16 out of 20) presented at least one merged synergy. From these 16 participants, 14 participants (87.5%) had their synergies 1 and 4 merged (Table 2).

5.1.4.3. Muscle synergy profiles

Synergy 1 was predominantly active during foot contact/early stance. Synergy 2 was active during mid/late stance. Synergy 3 was active during early swing. Synergy 4 active during late swing/early stance (Fig. 2). MSs activation profiles were similar across walking speeds, except during SLOW speed for synergies 1 and 4. For synergy 1, activation timing profiles during FAST (*r*=0.98) and SLOW (*r*=0.87) walking were very highly or highly similar to synergy 1 generated during NAT, respectively. Likewise, the FAST and SLOW profiles were highly similar (*r*=0.80). For synergy 2, activation timing profiles were very highly similar across all walking conditions (*r*≥0.96). For synergy 3, activation timing profiles were highly similar between NAT and FAST (*r*=0.87) whereas *r*=0.77 for SLOW and NAT and *r*=0.51 for SLOW and FAST. Although activation timing profiles differed, FAST and SLOW shapes of synergy 3 were somewhat comparable to NAT; however, synergy 3 activated earlier for FAST or later for SLOW. Synergy 4 activation timing profiles for NAT were very highly similar to FAST (*r*=0.99) whereas SLOW was different from NAT

(*r*=0.13) and FAST (*r*=0.17). The SLOW profile activated earlier (40 to 70% of the gait cycle) and had a different shape through most of the gait cycle (except at early stance).

5.1.4.4. Muscular activation profiles

EMG_{exp} activation profiles of each lower extremity muscle at three walking speeds are illustrated in Fig. 2. When comparing NAT and FAST, all muscles had very highly similar activation patterns ($r \geq 0.94$). NAT and SLOW activation patterns were very highly similar ($r \geq 0.91$) for some muscles (VM, SO, MG, RF) and r ranged from 0.15 to 0.78 for other muscles (GM, TA, ST, BF). The most different muscular activation profiles between SLOW and NAT were for ST (r= 0.25) and BF (r= 0.15), two muscles of synergy 4 with high weightings.

5.1.5. Discussion

The effects of walking speeds on the number of MSs, temporal profiles, and weightings were investigated when able-bodied individuals walked overground. Four MSs were revealed, which had similar temporal activation profiles and muscle weightings as MSs reported in previous studies (Clark et al., 2010; Lacquaniti et al., 2012; Neptune et al., 2009). The results also aligned with previous studies where walking speed influenced some MSs characteristic (Cappellini et al., 2006; Chvatal & Ting, 2013; Ivanenko, Poppele, & Lacquaniti, 2004).

In terms of temporal activation profiles, synergies 3 and 4 were the most affected by walking speed. MSs similarity analysis supported the idea that most differences from NAT occur for SLOW speed. Activation timing profiles demonstrated the greatest difference on synergy 4 at SLOW speed, with most activation during mid stance/early swing. In the same manner as synergy 3 where the late stance/early swing component was also observed later during SLOW compared to NAT/FAST conditions (Fig. 2). These findings are in line with other works, where the activation timing (i.e., center of activity) of muscle synergies related to swing initiation and leg deceleration (i.e., synergies 3 and 4 in our study), was shifted at slow speeds, thereby suggesting CNS modifications of motor control produce by speed changes (Kibushi 2019). Moreover, other studies during treadmill walking have also reported that MSs profiles across speeds were somewhat similar except that, as speed increases, temporal profiles were shifted to earlier phases

of the gait cycle, which may be explained by reduced stance phase duration with increased speed (Cappellini et al., 2006; Ivanenko et al., 2004).

Since MSs temporal activation profile differences occur because of individual EMG muscle activity differences, differences at SLOW speeds and muscles defining synergies 3 or 4 were expected. For all measured muscles, EMG amplitude tended to decrease with decreasing walking speed, but activation profiles remained stable across speeds (See. Fig 2), which is consistent with other studies (Den Otter et al., 2004; Ivanenko, Grasso, Macellari, & Lacquaniti, 2002). Significant differences between SLOW and NAT/FAST speeds were found, especially for the TA, ST and BF muscles. For TA, the overall amplitude reduction during swing phase might be associated with a reduced need of foot clearance, since at SLOW speeds leg stabilization during stance phase would be prioritized (Den Otter et al., 2004). The need for leg stabilization during stance is supported in part by ST and BF muscles that are normally active at late swing/early stance, but instead are mainly active during the whole stance phase at SLOW speed, even though their overall amplitude was less than NAT and FAST.

Biomechanical requirements differ during SLOW walking; therefore, it was expected that temporal activation patterns, individual EMG profiles, and muscle weightings would differ across speeds. Overall, four well identified synergies were found across all participants (Fig.3) reflecting the central organization of motor patterns for walking However, changes related to the discrepancy on the number of synergies were observed (Fig. 3). Discrepancy on the number of MSs among studies have also been reported, not only across subjects, but also across walking speeds (Chvatal & Ting, 2013; Clark et al., 2010). However, to our knowledge, the present study is the first to separately quantify synergies observed for each of the 20 healthy participants (Table 2). Two main findings were observed: 1) the faster the walking speed, the less MSs were found (i.e. a progressive reduction of MSs when speed increased from SLOW to NAT to FAST speeds) and 2) the reduction in the number of MSs affected synergies 1 (mainly active during weight acceptance) and 4 (limb deceleration) as speed increased.

The MSs cosine similarity analysis revealed that whenever a reduction of the number of MSs was observed, those “missing” MSs presenting poor cosine similarities values ($r < 0.80$) were

instead merged with other MSs. Fewer MSs, from module merging, have been associated with reduced walking abilities and muscle coordination complexity (Clark et al., 2010; Safavynia et al., 2011; Torres-Oviedo, Macpherson, & Ting, 2006), but reduced ability can be excluded since the study population was able-bodied individuals. The merged synergies in the present study are associated with walking speed differences (1.4 -1.9 m/s). In particular, merging synergies 4 and 1 was found among 75% of participants for NAT and 87.5% for FAST speed.

MSs characteristic differences, particularly at synergies 1 and 4 between SLOW and the other speeds, might be explained by two main factors. First, at SLOW speed, different biomechanical adaptations are required due to prolonged double support and reduced acceleration-deceleration of the lower extremity during swing (i.e., reduced inertial effects). Second, different walking speed may produce different adaptations that play an active role in shaping the behavior and recruitment of muscle synergies to the constrains imposed by a specific task (Cheung, d'Avella, Tresch, & Bizzi, 2005). Although the contribution of the volitional aspect required to match the slow speed was not investigated, the increased number of MSs during the SLOW speed might have been influenced by a combination of both reduced spatio-temporal parameters and joint kinematic variability, and to the prolonged double support and reduced acceleration-deceleration adaptations to the slow speed. The foot strikes matching the auditory cues provided by the metronome (i.e., auditory-motor anchoring) (Wright, Bevins, Pratt, Sackley, & Wing, 2016) would require an increased limb control and coordination, facilitated by a sensori-motor coupling strategy which translates into the activation of each of the four MSs at SLOW speed.

Future studies can explore whether imposing slow speed after a neurological event (*i.e.,* spinal cord injury, stroke) could be an effective strategy to increase the number of muscle synergies and reinforce normal neural activation of central structures before progressing to faster walking speeds during a neurorehabilitation program.

This study had several limitations. The number of MSs identified was proportional to the number of muscles investigated. Additional MSs could have been revealed if a more muscles were investigated (Ivanenko et al., 2004). NAT and FAST speeds were selected by the participant and

varied across participants whereas the SLOW speed was imposed and identical for all participants. As a result, the percentage of variations between speeds differed slightly across participants. For able-bodied participants to comply with the 0.6 m/s walking speed and minimize rhythm perturbations, auditory cues were needed and made it challenging to isolate the effects of SLOW speed. Foot strike and foot off events, used to define stance and swing phases, defined from accelerometer peaks may not perfectly aligns with events determined with an instrumented force plates or plantar pressure sensors. Because of the difficulty accurately identifying foot-off events from accelerometers signals, a preset stance-swing ratio (i.e., 60% stance, 40% swing) was used to time-normalized the MS and the EMG profiles. This could have introduced errors at the swing and stance transitions, which was especially relevant since this was where muscle synergies in this study were found. As a result, stance and swing duration analysis for each synergy was not performed, limiting our analysis on MSs timing in relation with stance to swing transitions. Since this time ratio may vary between participants and walking speeds, the results may have been affected.

5.1.6. Conclusion

Slow, natural and fast walking speeds altered the number, composition, and temporal profiles of lower extremity MSs in able-bodied individuals, for level overground walking. Slow walking speed had the same was found to consistently maintain the number and composition of four well-identified muscle synergies, whereas natural and, in a higher degree, fast walking tended to merge some synergies related to weight acceptance at early stance and limb deceleration at late swing . To assess the integrity of the underlying neural strategies supporting muscle activity during walking, research professionals should consider that muscle synergies adapt to speed. Hence, cautious is advised when MSs of individuals with sensorimotor impairments are compared with able-bodied counterparts, since people with movement deficits likely walk slower and differently.

5.1.7. Acknowledgements

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Conflict of interest

The authors have no conflicts of interest to report.

Table 1. – Demographic characteristics for all participants

Participants	Sex	Age	Height (m)	Weight (kg)	BMI (kg/m^2)
1	M	23	1.67	87.1	31.2
2	F	22	1.61	54.5	21.0
3	M	22	1.8	76.6	23.6
4	M	18	1.79	98.8	30.8
5	M	19	1.81	67.5	20.6
6	F	29	1.66	60	21.8
7	M	41	1.72	73.9	25.0
8	F	24	1.6	53.5	20.9
9	M	31	1.92	96.2	26.1
10	F	21	1.67	63	22.6
11	M	39	1.74	69.4	22.9
12	M	50	1.67	80.3	28.8
13	M	21	1.78	75	23.7
14	F	31	1.74	81	26.8
15	M	59	1.74	78	25.8
16	F	48	1.59	79.2	31.3
17	F	22	1.56	54	22.2
18	M	18	1.85	92.6	27.1
19	F	47	1.7	70.5	24.4
20	F	23	1.61	56	21.6
Mean	-	**30.4**	**1.7**	**73.4**	**24.9**
SD	-	**12.5**	**0.1**	**13.9**	**3.5**

M = male; F = female; BMI = body mass index

Table 2. – Summary of muscle synergies detected and merging of muscle synergies in each walking condition for all participants.

	Slow				Natural				Fast			
	Synergy				*Synergy*				*Synergy*			
Participant	***1***	***2***	***3***	***4***	***1***	***2***	***3***	***4***	***1***	***2***	***3***	***4***
1	✓	✓	✓	✓	~ #4	✓	✓	✓	✓	✓	✓	~ #1
2	✓	✓	✓	✓	✓	✓	✓	~ #1	~ #4	✓	~ #4	✓
3	✓	✓	✓	✓	✓	✓	✓	~ #1	✓	✓	✓	~ #1
4	~ #4	✓	✓	✓	~ #4	✓	✓	✓	~ #4	✓	✓	✓
5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	~ #1
6	✓	✓	✓	✓	✓	✓	✓	~ #1	~ #4	✓	✓	✓
7	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
8	✓	✓	✓	✓	~ #4	✓	✓	✓	✓	~ #1	✓	✓
9	~ #2	✓	✓	~ #3	~ #4	✓	✓	✓	~ #4	✓	✓	✓
10	✓	✓	✓	✓	✓	✓	✓	~ #1	~ #4	✓	~ #4	✓
11	✓	✓	✓	✓	✓	✓	✓	✓	~ #4	✓	✓	✓
12	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
13	✓	✓	✓	✓	~ #4	✓	✓	✓	~ #4	✓	✓	✓
14	~ #4	✓	✓	✓	~ #4	✓	✓	✓	~ #4	✓	✓	✓
15	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
16	✓	✓	✓	✓	~ #4	✓	✓	✓	~ #4	✓	✓	✓
17	✓	✓	✓	✓	~ #3	✓	✓	✓	~ #4	✓	✓	~ #4
18	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	~ #1	✓
19	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
20	✓	✓	✓	✓	~ #4	✓	✓	✓	✓	✓	✓	~ #1
Synergy presence	17/20	20/20	20/20	19/20	11/20	20/20	20/20	16/20	10/20	19/20	17/20	15/20
%	85%	100%	100%	95%	**55%**	100%	100%	**80%**	**50%**	95%	85%	**75%**
Merged synergies	3/20	0/20	0/20	1/20	9/20	0/20	0/20	4/20	10/20	1/20	3/20	5/20
%	15%	0%	0%	5%	**45%**	0%	0%	**20%**	**50%**	5%	15%	**25%**

✓= synergy detected, ~ #X = synergy merged with synergy x.

Figure legends

Figure 1. – Muscle synergy weighting compositions and examples of muscle synergy merging on three participants at SLOW, NAT and FAST walking speeds.

Colored bars represent muscles bellowing to a specific synergy as follows: Synergy 1: GM, VM and, to a lesser extent, RF. Synergy 2: SO and MG. Synergy 3: TA and RF. Synergy 4: ST and BF. Participant 12 shows a typical reconstruction where all 4 modules were found across all conditions. Low cosine similarity values ($r < 0.86$, participants 1 and 13) were considered synergy merging with another synergy with higher r values. Pale grey bars represent muscles contributing less to a specific synergy. Variance accounted for (VAF) values are showed for each participant and walking condition. TA= tibialis anterior, SO= soleus, MG= medial gastrocnemius, VM= vastus medialis, RF= rectus femoris, ST= semitendinosus, BF= biceps femoris, GM= gluteus medius.

Figure 2. – Group average (n=20) for each of the four muscle synergies found in healthy participants at SLOW (red), NAT (green) and FAST (yellow) walking speeds.

A. Activation timing profiles for each synergy over the gait cycle. **B**. Muscle synergies average and SD weightings. Muscles in bold represents the muscles defining a specific muscle synergy, being the muscles that contribute the most. **C.** Individual EMG activation profiles over the gait cycle. Each muscle activity was normalized by maximum activation across each walking speed. To evaluate similarity among activation profiles r values are presented between all walking conditions. TA= tibialis anterior, SO= soleus, MG= medial gastrocnemius, VM= vastus medialis, RF= rectus femoris, ST= semitendinosus, BF= biceps femoris, GM= gluteus medius.

Figure 3. – VAF and cosine similarity values.

A. Number of synergies determined by the VAF criterion for all participants and for each walking condition. **B**. Global VAF values for each walking condition and for each number of synergies found. **C.** Cosine similarity values (r) for the weightings of each muscle synergy.

Figure 1

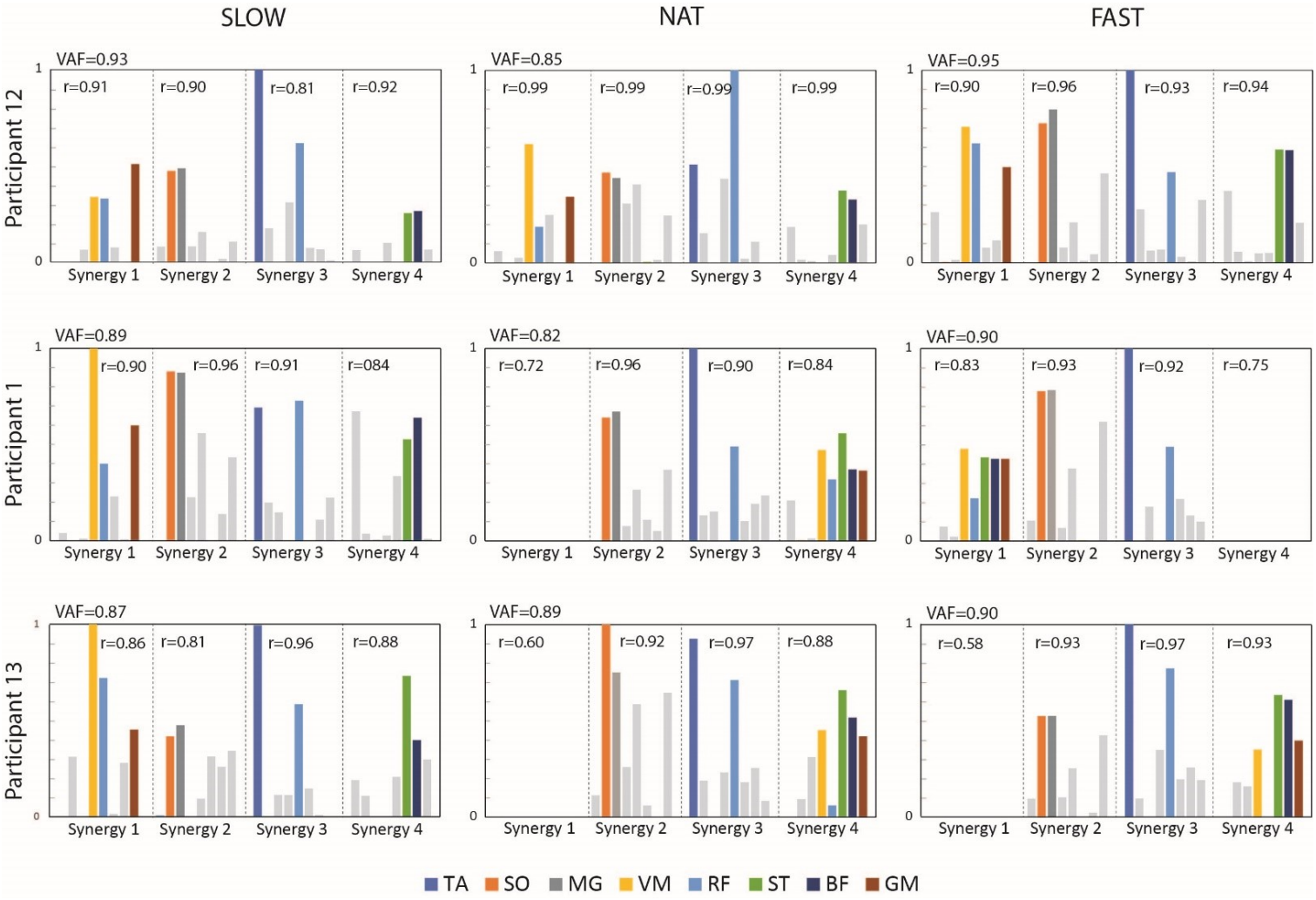

SLOW
NAT
FAST
Participant 12
Participant 1
Participant 13
VAF=0.93
r=0.91
r=0.90
r=0.81
r=0.92
VAF=0.85
r=0.99
r=0.99
r=0.99
r=0.99
VAF=0.95
r=0.90
r=0.96
r=0.93
r=0.94
VAF=0.89
r=0.90
r=0.96
r=0.91
r=084
VAF=0.82
r=0.72
r=0.96
r=0.90
r=0.84
VAF=0.90
r=0.83
r=0.93
r=0.92
r=0.75
VAF=0.87
r=0.86
r=0.81
r=0.96
r=0.88
VAF=0.89
r=0.60
r=0.92
r=0.97
r=0.88
VAF=0.90
r=0.58
r=0.93
r=0.97
r=0.93
Synergy 1
Synergy 2
Synergy 3
Synergy 4
TA
SO
MG
VM
RF
ST
BF
GM

Figure 2

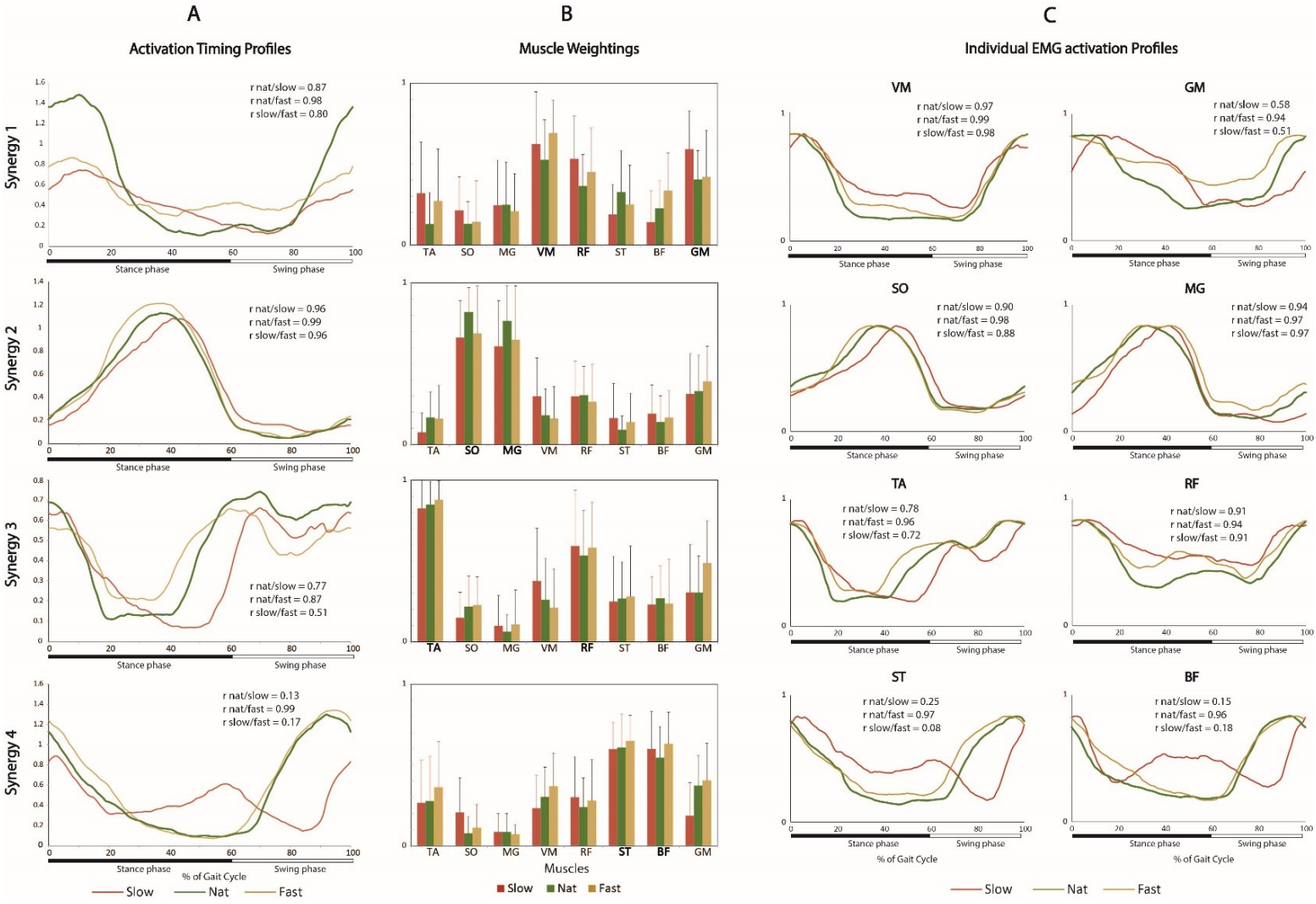
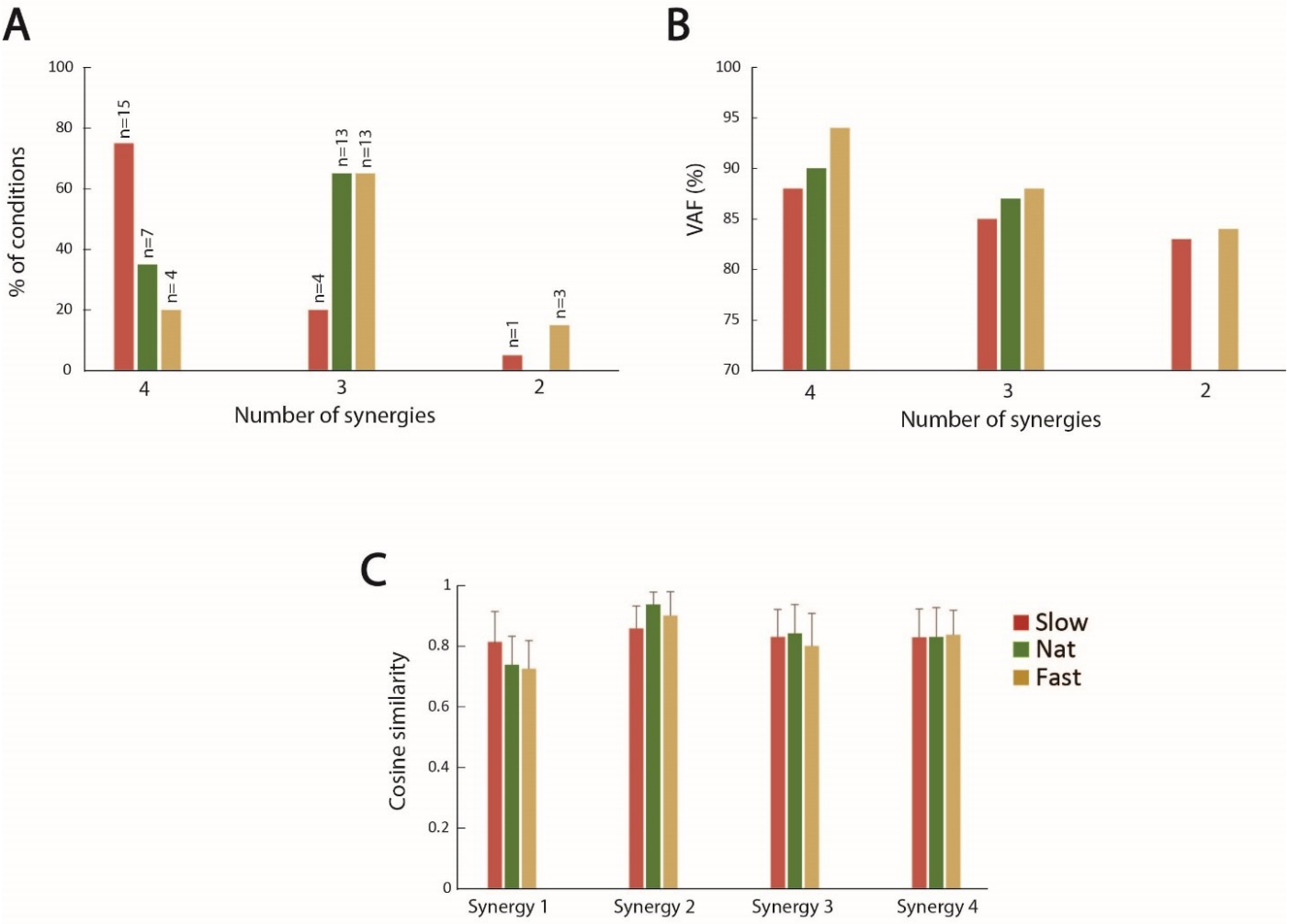

A
Activation Timing Profiles
B
Muscle Weightings
C
Individual EMG activation Profiles
Synergy 1
r nat/slow = 0.87
r nat/fast = 0.98
r slow/fast = 0.80
Synergy 2
r nat/slow = 0.96
r nat/fast = 0.99
r slow/fast = 0.96
Synergy 3
r nat/slow = 0.77
r nat/fast = 0.87
r slow/fast = 0.51
Synergy 4
r nat/slow = 0.13
r nat/fast = 0.99
r slow/fast = 0.17
Stance phase
Swing phase
% of Gait Cycle
TA SO MG VM RF ST BF GM
Muscles
Slow Nat Fast
VM
r nat/slow = 0.97
r nat/fast = 0.99
r slow/fast = 0.98
GM
r nat/slow = 0.58
r nat/fast = 0.94
r slow/fast = 0.51
SO
r nat/slow = 0.90
r nat/fast = 0.98
r slow/fast = 0.88
MG
r nat/slow = 0.94
r nat/fast = 0.97
r slow/fast = 0.97
TA
r nat/slow = 0.78
r nat/fast = 0.96
r slow/fast = 0.72
RF
r nat/slow = 0.91
r nat/fast = 0.94
r slow/fast = 0.91
ST
r nat/slow = 0.25
r nat/fast = 0.97
r slow/fast = 0.08
BF
r nat/slow = 0.15
r nat/fast = 0.96
r slow/fast = 0.18

Figure 3


A
100
80
60
40
20
0
% of conditions
n=15
n=7
n= 4
n=4
n=13
n=13
n=1
n=3
4
3
2
Number of synergies
B
100
95
90
85
80
75
70
VAF (%)
4
3
2
Number of synergies
C
1
0.8
0.6
0.4
0.2
0
Cosine similarity
Synergy 1
Synergy 2
Synergy 3
Synergy 4
Slow
Nat
Fast

5.1.8. References

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5.2. Article #2: Effects of Robotic Exoskeleton Control Options on Lower Limb Muscle Synergies during Overground Walking: An Exploratory Study Among Able-Bodied Adults

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Manuel Escalona contributed substantially to the conception and development of the methodology, data collection, analysis, and results interpretation. I also wrote the original draft of the manuscript. Dr. Bourbonnais contributed his muscle synergies expertise to the analysis and results interpretation. Mr. Leflem contributed to the data collection and data processing. Mr. Goyette contributed mainly to the data processing and to the software development for data extraction and analysis. Professors Gagnon and Duclos contributed to methodology development and oversaw the analysis, results interpretation, and manuscript writing. All authors contributed to revision of the intellectual content of the manuscript and approved the final version for publication.

5.2.1. Abstract

Background: The effects of lower limb (L/L) control options, developed for overground walking with a wearable robotic exoskeleton (WRE), on the neuromotor control of L/L muscles (*i.e.*, muscle synergies (MSs)) during walking remains uncertain. **Objective:** To gain initial insights regarding the effects of different control options on the number of MSs at the L/L and on their muscle weighting within each MS when walking with a WRE. **Methods:** Twenty able-bodied adults walked without and with the WRE set at two control options with a predetermined foot pathway imposed by the WRE, and at three other control options with free L/L kinematics in the sagittal

plane. Surface electromyography of eight right L/L muscles were recorded. MSs were extracted using a non-negative matrix factorization algorithm. Cosine similarity and correlation coefficients characterized similarities between the MSs characteristics. **Results:** Freely moving the L/L in the sagittal plane (*i.e*., non-trajectory controlled options) during WRE walking best duplicated typical MSs extracted when walking without WRE. Conversely, WRE walking while fully controlling the L/L trajectory presented the lowest correlations to all MSs extracted when walking without WRE, especially during early swing and L/L deceleration. **Conclusions:** Neuromotor control of L/L muscles is affected by the selected control option during WRE walking, particularly when a predetermined foot pathway is imposed. **Significance:** This exploratory study represents the first step in informing the decision-making process regarding the use of additional L/L control options when using WRE and calls for further research among adults with sensorimotor impairments.

Keywords: electromyography; gait; motor control; muscle coordination; locomotion; rehabilitation; task performance and analysis.

5.2.2 Introduction

Wearable robotic exoskeletons (WRE) allow people with sensorimotor impairments affecting their lower limb (L/L) to stand and walk and rehabilitation professionals to further adhere to the basic locomotor training principles to promote neuroplasticity. Overground walking with a WRE represents an activity-based rehabilitation intervention that may promote neurological and functional recovery after a central nervous system (CNS) lesion [13, 14]. Most of the first generation of WREs provided total and continuous motorized assistance at the hip and knee joints for the foot to follow a predefined planned trajectory during the swing phase. However, to meet the needs and expectations of neurorehabilitation professionals and end users, a wider range of control options are becoming available on the new generation of WREs. Among those, some recently-developed WREs now allow self-selected L/L movement trajectory during the swing phase of the gait cycle (i.e., non-trajectory controlled) that promote active participation of the user and allows stepping variability. This control option can also be combined with assistance or resistance being provided to the L/L. However, whether any of these new control options promote typical muscle activation patterns, or which of those control options could best

do it, remain unclear. The limited knowledge about what these new options could bring to the rehabilitation field impedes the development of evidence-based WRE locomotor training strategies during neurorehabilitation.

One way of investigating the effects of different WRE control options on the CNS is through muscle synergy (MSs) analyses. The MSs are a series of motor modules, each containing specific muscular activation patterns to simplify the neuromotor control of locomotion [9, 18, 32]. The CNS needs to control only a small number of these MSs, each containing a specific group of muscles associated with specific biomechanical function during the gait cycle [5, 26]. Simulation studies have shown, for example, that altering body weight and external conditions might lead to changes in MSs characteristics, providing evidence of the link between neuromotor control and specific neurobiomechanical adaptations to a task [22]. Hence, given the configuration of some WREs (i.e., backpack command center), it is plausible that the motor control when walking without and with a WRE differs.

Although previous studies have explored kinematic outputs and individual muscle activity during walking with robotic devices [15, 33, 35], few studies have explored MSs related to robot-aided walking, and these MSs studies have reported contradictory results. For example, the number of MSs and muscle weighting within each MS were similar when able-bodied individuals walked at different speeds on a treadmill with a WRE, with different amounts of weight support or various levels of robotic guidance [11, 24]. Another study showed that muscle weightings within MSs were modified when using passive guidance during overground walking with a WRE compared to without a WRE [20]. These studies are limited by the most commonly available WRE control options used during walking (i.e., total and continuous motorized assistance according to a predefined planned trajectory), and none of them include in their comparison the most recently developed non-controlled trajectory control options. The recently developed control options offering self-selected L/L trajectories that can be assisted or resisted to different extents by the WRE represent promising interventions for rehabilitation purposes, especially for those individuals that preserve the ability to walk after a CNS lesion. However, it is unknown which of these features are valuable and which ones might result in abnormal patterns of muscle coordination or compensatory strategies required to adapt to these control options. These

aspects first need to be investigated in able-bodied individuals to explore how an intact CNS might adapt to these conditions imposed by the WRE, before further exploring muscle patterns adaptations to these control options in individuals with sensory motor impairments.

The present exploratory study aims to gain initial insights regarding the effects of different control options on the number and profile of MSs at the L/L and on their muscle weighting within each MS, during overground walking without and with a WRE set at six different L/L control options (i.e., a subset of trajectory-controlled and non-trajectory controlled options used for neurorehabilitation). It is hypothesized that (1) all WRE control options will preserve MS characteristics extracted during overground walking without a WRE, as the intended L/L kinematics remain similar; (2) walking with the WRE set to non-trajectory control options will lead to variable changes in MS characteristics depending on the control option used, since these options allow increased voluntary participation and step variability by imposing different constraints on the L/L motion. Stronger evidence is needed to provide new insights into the effects of various control options on biomechanical and neural locomotor control [10], and to inform how different control options may be applied during locomotor training of individuals with sensorimotor impairments and limited walking ability following a neurological event.

5.2.3 Methods

5.2.3.1 Participants

A non-probabilistic convenience sample of 20 able-bodied adults (11 men, 9 women; mean age = 31.0 ± 12.5 years; height =1.70 ± 0.10 m; weight = 73.4 ± 13.9 kg; body mass index = 24.9 ± 3.5 kg/m2) was recruited. To be included in the study, participants had to be at least 18 years of age and present no neuromusculoskeletal impairments affecting their L/L or lower back, or any other conditions that could restrict their capacity to walk, follow simple verbal commands, or perceive auditory cues. The study was conducted at the pathokinesiology laboratory located at the Institut Universitaire sur la Réadaptation en Déficience Physique de Montréal. All participants provided written consent to participate after being informed of the study's objectives and the nature of their participation. The Research Ethics Committee of the CRIR approved the study (CRIR-1083-0515).

5.2.3.2 Robotic exoskeleton for overground walking

The Ekso GT™ WRE (EKSO Bionics, CA, USA) provides external support to L/L and generates flexion and extension movements at the hips and knees via motors in a sequence that replicates typical walking (Figure 1). The ankles are non-motorized and are fixed to dynamic orthoses. The WRE offers various L/L control options that can distinctively affect the swing and stance phases of walking and are pre-selected by the therapist before initiating or during walking. For the different swing phase control options that were investigated in the present study, they can be grouped into two key categories: trajectory-controlled and non-trajectory controlled (Table 1). The trajectory-controlled options were used with a total assistance (TOT) or a fixed amount of assistance (FIXED0) provided to help participants complete steps (i.e., swing phase) within a fixed amount of time, as the step length and velocity are predetermined. The non-trajectory controlled options (i.e., free joint movement) were used with a high assistance (HASSIST), gravity compensation assistance (NEUTRAL), NEUTRAL with the hip abduction exceptionally unlocked in the frontal plane (ABD), and high resistance (HRESIST) to engage participants to different extents when *freely* completing steps. The precise amount of torque provided by the electric actuators at the hips and knees is not provided while the control architectures and algorithms for the actuators are not disclosed by the manufacturer. As for the stance phase, the Ekso only restricted knee flexion beyond 45° as a safety measure provided by the manufacturer but did not provide any amount of assistance or resistance prior to reaching this limit.

5.2.3.3 Intervention

Participants completed four training sessions to learn to walk with the EKSO and to familiarize themselves with all WRE control options investigated (Table 1). At the end of the training sessions, participants were expected to walk at least 50 m along a tiled corridor with the WRE and only minimal or contact-guard assistance provided by a physical therapist for each WRE control o to qualify for the laboratory assessment. Each training session lasted 45–60 min and a 24-72-hour rest period was planned between training sessions.

5.2.3.4 Laboratory assessment

5.2.3.4.1 Walking conditions

Participants were asked to first walk overground without the WRE at a natural self-selected speed (REF-NAT) and at a speed matching WRE walking in ABD control option (REF-EXO). At REF-EXO speed, step cadence was guided using auditory cues from a metronome and was calculated for each participant during the last familiarization session by recording the time needed to complete 10 consecutive steps in ABD control option. This last option was selected as a reference since it allows an additional degree of freedom at the hip joints (i.e., abduction/adduction in the frontal plane), best representing overground walking kinematics considering the WRE movement constraints.

For all walking conditions, participants walked 20 m on a level, tiled corridor. Data were collected between the 5 and 15 m marks to assure steady-state walking. Walking speed was measured using the time needed to walk the 10-meter distance (i.e., 5 to 15 m marks) for each walking condition. All walking conditions were performed using a block randomized order (i.e., with or without WRE). Between each condition or control option, participants walked 20 m with the next WRE control option to be tested to eliminate any potential carry-over effects of the previous condition or control option (i.e., “wash-out” period).

5.2.3.4.2 Surface Electromyography

For each trial, using the Delsys Trigno Wireless System (Delsys Inc., Boston, MA, USA) surface EMG was recorded at eight right L/L muscles: tibialis anterior (TA), soleus (SO), medial gastrocnemius (MG), vastus medialis (VM), rectus femoris (RF), semitendinosus (ST), biceps femoris (BF), and gluteus medius (GM).The preparation of the skin and the placement of the hybrid sensors were carried out according to the recommendations of the Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) recommendations (www.seniam.org). These hybrid sensors enable surface EMG (1,926 Hz) and 3D acceleration (148 Hz) recording.

All raw EMG recordings were filtered using a fourth-order Butterworth zero-lag bandpass filter with cut-off frequencies set at 20 Hz and 400 Hz. EMG envelopes of each cycle were

generated via a 250 msec sliding root mean square (RMS) window. Foot contact events were determined from the 3D integrated accelerometer data peaks recorded with the SO sensor using the Teager-Kaiser Energy Operator (TKEO), and thereafter visually inspected and adjusted whenever needed. Thereafter, each gait cycle was time-normalized using 101 temporal data points (0% to 100%). Stance phase was set to 0–59% of the gait cycle and swing was set to 60–100% due to difficulty obtaining accurate foot-off events from the acceleration data. Finally, among all cycles analyzed, the three consecutive gait cycles presenting the best goodness of fit (i.e., lowest mean coefficient of variation (CV) computed for all muscle EMG envelopes over each temporal data point embedded within each time-normalized cycle) were automatically selected using a custom-made LabVIEW software and averaged together prior to initiating the muscle synergy analysis. For each participant, RMS signals from each muscle were also normalized to its maximum value reached during each trial. Averaging the EMG envelope of three gait cycles best reconstruct the original EMG datasets (i.e. highest Variability Accounted For – VAF) [28]. In fact, adding gait cycles minimizes variability of the EMG data to be analyzed and reduces the capability to determine if the muscles under study are neurally coupled (i.e., alteration in the number of MSs found and their muscle weighting) [29, 34]. Thus, if a group of muscles are coupled together as part of a neural control strategy, then not only should their muscle activity be correlated (i.e., task-related biomechanical constraints), but the variations in muscle activity in these muscles should also be correlated. Hence, three gait cycles were deemed appropriate to assess the effects of the WRE control options on muscle synergy during the experimental tasks, particularly when investigating the trajectory controlled options that may impose certain restrictions on the possible set of muscle activation patterns generating gait cycles.

5.2.3.5 Muscle synergies

For each participant, the experimental EMG data matrix, consisting of the mean of three consecutive gait cycles of each recorded muscle, was submitted to a non-negative matrix factorization (NNMF) algorithm. The number of muscle synergies was determined by the least number of synergies that could explain the variance accounted for (VAF) in each muscle ($\mathrm{VAF_m}$), with $\mathrm{VAF_m}$ greater than 0.9 (90%) and the product of all $\mathrm{VAF_m}$ (global VAF, $\mathrm{VAF_g}$) greater than 0.8 (80%). Muscle synergies were classified based on similarities in muscle weightings (W) across

participants and walking conditions using a cosine similarity analysis [6, 12, 17]. For this analysis, the inner product of the compared MS vectors was calculated, and the cosine angle between those synergies was measured. To group MSs, the cosine similarity was calculated between a reference MS taken from an arbitrary reference participant during REF-NAT and the obtained MSs of each recorded walking trial and for each participant. Whenever the cosine similarities of W between the reference synergy and other MSs were over 0.868 ($p < 0.05$) [27], the synergies were considered similar. Likewise, when two MSs at the same walking speed were classified into the same group, these two synergies were considered to be "merged". The synergy with the lowest correlation was deemed to be merged to the main synergy which presented the highest correlation value. These merged synergies were counted and their percentage of presence reported whenever an important quantity of these synergies appear on a specific walking trial. The number and total group percentage of the presence of each MS was calculated.

5.2.3.6 Statistical analysis and interpretation

To compare walking speeds across conditions, a repeated measures analysis of variance (ANOVA) with Bonferroni *post hoc* analysis determined differences between experimental and control options. Pearson product-moment correlation coefficients (*r*) characterized the association between MSs temporal activation profiles and individual EMG activity profiles across conditions. The *r* values were interpreted as very high (≥.90), high (0.70–0.89), moderate (0.50–0.69), and low (0.30–0.49) [25]. All statistical analyses were performed using SPSS v.24 (SPSS Inc., Chicago, IL, USA).

5.2.4 Results

5.2.4.1 Walking speeds

Walking speeds across all overground and WRE conditions are presented in Table 2. Walking speeds were similar ($p > 0.05$) between REF-EXO and most non-trajectory control options except for HASSIST ($p = 0.01$). By contrast, walking speeds were significantly different ($p < 0.05$) between REF-NAT and all WRE control options, with speed reductions between -84.4 ± 20.4% and -138 ± 8.9%. Overall, the slowest speed was TOT, being 76.9 ± 19.7% slower than REF-EXO and -138 ± 8.9% slower than REF-NAT.

5.2.4.2 Number and muscle weightings of muscle synergies

Overall, three to five MSs were extracted across all WRE walking conditions (VAF > 0.80 for all conditions; see Figure 2A). The four main MSs found during walking without the WRE were found in most WRE control options. These four synergies were: Synergy #1: mainly GM, VM and, to a lesser extent, RF; Synergy #2: mainly SO and MG; Synergy #3: mainly TA and RF; Synergy #4: mainly hamstring activity (ST and BF). Muscle weightings observed across all walking conditions are illustrated in Figure 3B.

All WRE control options showed good cosine similarity correlations with their overground walking without WRE comparators ($r \geq 0.86$), except for FIXED0 that had poor correlations for Synergies #1 ($r = 0.69 \pm 0.05$) and #3 ($r = 0.68 \pm 0.06$). Moreover, whenever three synergies were found, Synergies #1 and #3 were merged together in 45% of participants, especially in FIXED0, and poor correlation was obtained indicating differences on muscle weighting on synergies #1 and #3 when compared to trial without WRE. A fifth synergy (Figure 4) was also observed mostly during TOT and was active throughout the gait cycle, with a predominantly increased activity around mid-swing. This synergy was composed of a coactivation of several muscles where GM, RF and, to a lesser degree, ST were the most active. The percentage and number of participants presenting each of these MSs are summarized in Table 3 and Figure 2A, respectively. Note that synergies #1 and #3 were less frequently extracted during FIXED0 when compared to the other WRE control options. The fifth synergy was mostly identified during TOT, in eight out of the 20 participants.

5.2.4.3 Muscle synergy profiles

Synergy #1 was active during foot contact/early stance. Synergy #2 was active during mid/late stance. Synergy #3 was active during early swing. Synergy #4 was active during late swing/early stance (Figure 3A). No-WRE overground walking REF-NAT and REF-EXO profiles (e.g., targeted very slow speed) differed, with both used as comparators for the WRE control options (Figure 2C and 2D and in Table 4). For Synergy #1, activation profiles during all WRE walking conditions were highly similar to REF-NAT and REF-EXO , except for TOT that was moderately correlated with REF-EXO ($r = 0.62$). For Synergy #2 activation profiles were very highly similar across all WRE walking conditions ($r \geq 0.73$). For Synergy #3, activation profiles were highly similar

to REF-EXO ($r \geq 0.73$) whereas, when compared to REF-NAT, Synergy #3 was moderately correlated across almost all WRE conditions, except for HRESIST and ABD that had high correlations ($r \geq 0.75$). Synergy #4 activation profiles presented the most differences across conditions, showing no similarities ($r < 0.49$) between WRE walking conditions except HASSIST control options, which had moderate correlations ($r \geq 0.56$ and 0.65) between REF-NAT and REF-EXO. The overall profile of Synergy #4 differed the most between REF-NAT and the rest of the walking conditions. Overall, while the activation profiles tended to be consistent across most of the WRE conditions (Figure 3A), FIXED0 presented a highly distinctive increased activation from approximately 50 to 90% of the gait cycle. Interestingly, HASSIST was the only control option that maintained moderate to high correlations across all conditions, independent of the reference condition (REF-NAT or REF-EXO).

5.2.4.4 Experimental EMG muscular activation profiles

The EMG_{exp} activation profiles of each L/L muscle during all walking conditions are illustrated in Figure 3C. When comparing REF-NAT and REF-EXO to each WRE control option, VM and SO had the highest Pearson correlation coefficients ($r > 0.70$), confirming resemblances of the activation profiles (Table 4). The EMG_{exp} activation profiles of GM, MG and TA had very similar activation profiles across all walking conditions apart from two exceptions: (1) activation profiles during FIXED0 control option increased drastically during the swing phase, and (2) MG profile during all WRE control options was delayed or shifted when compared to the REF-NAT condition. EMG_{exp} activation profiles of RF, ST and BF in the WRE control options had the lowest correlations when compared to REF-NAT and REF-EXO. For both ST and BF EMG_{exp} activation profiles, all WRE conditions tended to be similar, except the FIXED0 condition that had high activation between 60 to 85% of the gait cycle.

5.2.5 Discussion

The present study investigated the effects of different WRE control options on MSs in terms of number, activation profiles, muscle weightings, and EMG profiles of individual muscles composing each MS. Although previous research investigating MS characteristics using robotic devices was limited to trajectory-controlled WRE passive and active control options [11, 20], to

our knowledge this is the first study investigating MSs during WRE walking with a range of WRE control options, including non-trajectory control options.

The four commonly reported MSs during overground walking in previous work [5, 18, 26], were found throughout each of the WRE control options explored in the present study. These findings reinforce the results of previous work reporting that MSs characteristics during normal walking is maintained while walking in a WRE [11]. However, Synergies #3 and #4 during the swing phase, when using trajectory-controlled options (TOT and FIXED0), differed from typical MSs in terms of temporal profile and muscle weighting and only partially support the first hypothesis that all WRE control options equally preserve the typical MS characteristics observed during overground walking without WRE. This finding contradicts results from previous studies that investigated treadmill walking with a WRE (LOKOMAT) using almost identical trajectory-controlled options to those explored in the present study (TOT and FIXED0) [11, 24]. In those studies, the MS activation profiles tended to be highly similar to profiles observed during overground walking without WRE. The differences in temporal profiles and muscle weightings found in the present study for Synergies #3 and #4 during trajectory-controlled options might be explained by human–machine interactions, such a greater need for limb deceleration at mid-late swing to counteract the passive or active L/L motion imposed by the WRE, which might differ from those adaptations induced by treadmill-based WRE walking [23].

Changes in speed might also explain the phase-shift activation patterns observed on almost all WRE control options on Synergy #4 compared to REF-NAT (Figure 3A), as reported in previous work [7]. Although previous research hypothesized that such changes may be associated with a reduction in ankle joint mobility when walking with a WRE that creates increased knee flexors activity during push-off [7], similar phase-shift activation patterns were also observed on synergy #4 when reducing walking speed during overground walking without a WRE (i.e., REF-EXO condition). Hence, speed reduction results in biomechanical adaptations that include a prolonged double support period that may alter the recruitment of MSs to adapt to the task [4]. Interestingly, when analyzing non-trajectory control options, only HASSIST presented high correlations independent of the reference condition (i.e., REF-NAT or REF-EXO), mainly supporting the second hypothesis that walking with the WRE set to non-trajectory control options

will lead to variable changes in MS characteristics depending on the control option used. HASSIST allows step variability and provides assistance to a self-selected L/L kinematics during the swing phase, leading to a similar muscle activation pattern to those observed without WRE walking regardless of the walking speed.

Low correlations between REF-NAT and REF-EXO for RF, BF and ST EMG muscle activation profiles (muscles forming Synergies #3 and #4) are in line with literature investigating EMG activity and robotic devices, which reported higher variability or differences in BF and ST muscle profiles [11, 33]. ST and BF muscular activities, highly involved in maintaining erect posture by producing a tonic activation against gravity [3] and normally active in late swing/early stance, instead showed increased and sustained activity during the entire stance phase across all WRE control options. This might be explained in part by the need for greater L/L stabilization during stance while the swinging leg is being affected by different WRE control options. Of all control options explored, FIXED0 presented the most changes and out-of-phase activation patterns, for all muscles except VM.

Synergy #5 extracted in TOT control option might be the result of speed-reduction changes reported in previous studies [8] in which lower speeds tended to modified EMG activation patterns, since TOT represented the lowest speed (0.26 ± 0.04 m/s) among all WRE conditions. Another possible explanation is that this synergy might be the result of increased muscle activity from trunk muscles, as reported by [11]; however, trunk EMG was not recorded in the present study. Lateral and forward weight transfers and trunk displacement are essential in this control option to trigger stepping. Thoracohumeral muscles, originating from the trunk, are also solicited when using walking aids during WRE walking, which may further increase muscular efforts.

A better understanding of human–machine interactions and biomechanical adaptations to specific available control options of the WRE is important if these devices are to be used more widely for locomotor training in the future. The trajectory-controlled options (TOT and FIXED0), which are used in most studies to compare or assess WRE with other interventions, differed the most from typical MSs reported during overground walking without WRE. In contrast, control options with a free WRE trajectory combined with L/L assistance or resistance best mimicked MSs

reported during overground walking, especially in HASSIST control option. The non-trajectory control options, especially when coupled with HASSIST, best mimicked typical MSs. HASSIST control option might also allow greater step variability requiring an increased involvement of end users, two key notions of motor learning and retention[31]. Greater step variability would allow the CNS to fully explore distinct movement options, inducing better adaptions to different environmental conditions compared to the used of fixed, rigid-limb guidance training conditions [1, 19, 21]. Based on this finding, future studies investigating individuals with sensorimotor impairments are warranted.

The present study has several limitations. Firstly, the number and content of MSs weightings are influenced by the number of muscles investigated. Additional MSs or enriched content could have been revealed if more muscles had been investigated [16]. Secondly, speed differences between walking without and with the WRE and across experimental tasks (i.e., REF-NAT vs REF-EXO; six different control options) might have limited interpretation of some results since walking speed can affect MSs [2, 30]. Thirdly, the event markers selected to define the stance phase of consecutive steps, and thereafter time-normalize the recorded EMG signals, were identified using the accelerometer deceleration spikes and may not perfectly align with those that could have been selected if pressure-sensitive mats or insoles had been used. Similarly, given the difficulty of accurately identifying toe-off events from accelerometer signals, stance was set to 60% of the gait cycle. Since the stance/swing proportions change with walking speeds, MS profiles may have varied between individuals and across experimental tasks, and their level of similarity may have been underestimated. Lastly, considering that some biomechanical requirements may change according to the control option selected, as well as the targeted rehabilitation objective in clinical practice, comparing all control options against overground walking without a WRE might undermine the potential utility of WRE. For example, the HRESIST control option may represent a unique opportunity to perform walking-specific muscular strengthening.

5.2.6 Conclusion

The number of MSs and their muscle weightings observed during typical overground walking is maintained when walking with various WRE control options, although their temporal

profiles vary to different extents. Non-trajectory-controlled options best duplicated the typical MSs found during overground walking, whereas the most commonly used controlled options (i.e., passive and active trajectory control options) presented the most differences in terms of muscle weightings and temporal profiles. This work represents the first step in informing the decision-making process regarding the use of additional L/L control options when using WRE. Meanwhile, the HASSIST control option may represent a promising feature and calls for further research among adults with sensorimotor impairments.

5.2.7 Acknowledgements

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Conflicts of interest

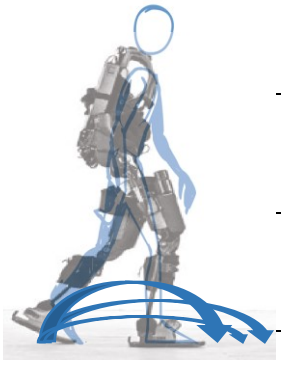
The authors have no conflicts of interest to report.

Table 1. – Description of all six different exoskeleton walking control options included in the present study

1. **Trajectory controlled:** The wearable exoskeleton (WRE) automatically initiates steps when the participant reaches both pre-determined lateral and forward body shift thresholds. Once the step is initiated, the exoskeleton swings and controls the lower limb (L/L) hip and knee kinematics for the foot to follow a specific pathway.

1.a. TOT	Provides total motorized assistance continuously to move the hip and knee joints according to a predefined hip and knee kinematics for the foot to follow a specific pathway during the swing phase.
1.b. FIXED0	Provides ceiling of robotic assistance from 0 to 100 where the higher the fixed assistance value, the more strictly the WRE controlled participant's leg trajectory. Fixed mode was set at 0 (thereby the name FIXED0) with no WRE assistance provided over an imposed swing trajectory.

2. Non-trajectory controlled ('free legs'): The participant initiates, swings and controls freely L/L kinematics (amplitude, velocity, acceleration) within the sagittal plane (i.e., no predefined trajectory) during the swing phase .



2.a. NEUTRAL	Provides no assistance and no resistance at the L/L hip and knee joints during swing phase.
2.b. HASSIST	Provides high assistance to facilitate L/L hip flexion and knee extension during swing phase.
2.c. HRESIST	Provides high resistance to augment L/L hip flexor and knee extensor muscular efforts during swing phase.
2.d. ABD	Frees L/L abduction in the frontal plane, reproducing a complete free swing trajectory.

Table 2. – Walking speeds (m/s) measured during all experimental walking conditions

	Walking conditions							
	Without exoskeleton		With exoskeleton					
			Control options					
Participants	**REF-NAT**	**REF-EXO**	**TOT**	**FIXED0**	**NEUTRAL**	**HASSIST**	**HRESIST**	**ABD**
1	1.39	0.58	0.27	0.47	0.66	0.65	0.60	0.71
2	1.49	0.38	0.22	0.28	0.37	0.28	0.33	0.35
3	1.53	0.40	0.23	0.30	0.38	0.26	0.35	0.48
4	1.25	0.43	0.25	0.41	0.41	0.39	0.32	0.48
5	1.40	0.58	0.29	0.35	0.40	0.38	0.38	0.45
6	1.6	0.69	0.26	0.32	0.46	0.48	0.41	0.59
7	1.37	0.94	0.36	0.51	0.77	0.62	0.79	0.74
8	1.20	0.59	0.22	0.32	0.34	0.36	0.32	0.56
9	1.62	0.85	0.27	0.50	0.85	0.79	0.82	0.88
10	1.38	0.51	0.25	0.29	0.40	0.36	0.40	0.36
11	1.41	0.87	0.26	0.45	0.63	0.60	0.62	0.66
12	1.38	0.59	0.18	0.36	0.45	0.39	0.58	0.56
13	1.39	0.54	0.25	0.36	0.56	0.46	0.47	0.50
14	1.46	0.57	0.22	0.35	0.44	0.45	0.40	0.55
15	1.34	0.40	0.26	0.39	0.43	0.52	0.53	0.43
16	1.52	0.75	0.24	0.40	0.74	0.54	0.62	0.73
17	1.32	0.53	0.29	0.38	0.58	0.48	0.51	0.68
18	1.55	0.69	0.37	0.47	0.73	0.77	0.77	0.94
19	1.34	0.58	0.25	0.40	0.47	0.41	0.46	0.46
20	1.47	0.58	0.28	0.39	0.52	0.56	0.65	0.65
Mean	**1.42**	**0.60**	**0.26**	**0.39**	**0.53**	**0.49**	**0.52**	**0.59**
SD	0.11	0.16	0.04	0.07	0.15	0.15	0.16	0.16

Table 3. – Muscle synergies found as percentage of participants for different control options.

Exoskeleton options	**Synergy #1**	**Synergy #2**	**Synergy #3**	**Synergy #4**	**Synergy #5**
REF-EXO	90%	100%	90%	95%	0%
TOT	95%	100%	90%	95%	**40%**
FIXED0	100%	95%	75%	100%	10%
NEUTRAL	85%	100%	100%	95%	10%
HASSIST	90%	100%	90%	100%	5%
HRESIST	100%	100%	90%	95%	10%
ABD	90%	100%	100%	85%	5%
Mean	93%	99%	91%	95%	11%
SD	0.06%	0.02%	0.08%	0.05%	0.13%

Table 4. – Correlation coefficients between overground walking without and with the exoskeleton set in different control options for the principal synergies investigated

			Synergy #1			Synergy #2			Synergy #3			Synergy #4		
		Control options		Muscle composition			Muscle composition			Muscle composition			Muscle composition	
	Trajectory		Profile	VM	GM	Profile	SO	MG	Profile	TA	RF	Profile	ST	BF
Comparator : REF-EXO	Controlled	TOT	0,62	0,86**	0,96**	**0,99**	**0,96*** **	**0,96*** **	0,74	0,77**	0,77**	-0,05	-0,28	-0,15
		FIXED0	0,86	**0,90*** **	0,35	0,88	0,80**	0,32	0,63	0,57*	0,81**	-0,16	-0,33	-0,26
	Non-controlled	NEUTRAL	0,84	0,84**	**0,93*** **	**0,97**	**0,96*** **	0,86**	0,88	**0,92*** **	-0,26	0,48	0,23	**0,90*** **
		HASSIST	0,80	0,88**	**0,92*** **	**0,96**	**0,95*** **	0,88**	0,84	**0,93*** **	0,13	0,65	0,31	0,64*
		HRESIST	0,74	**0,92*** **	0,72**	**0,96**	**0,98*** **	0,69*	0,89	**0,92*** **	0,69*	0,45	-0,18	0,10
		ABD	0,80	0,86**	**0,94*** **	**0,98**	**0,99*** **	0,83**	**0,91**	0,88**	0,02	0,40	0,37	0,88**
Comparator : REF-NAT	Controlled	TOT	**0,95**	0,87**	0,48	**0,97**	**0,96*** **	0,50*	0,57	0,84**	0,60*	-0,69	-0,72	-0,85
		FIXED0	**0,92**	**0,96*** **	0,57*	**0,73**	0,62*	-0,34	0,66	0,64*	0,69*	-0,31	-0,14	-0,37
	Non-controlled	NEUTRAL	**0,96**	0,89**	0,49	**0,92**	**0,99*** **	0,31	0,58	**0,90*** **	-0,05	-0,12	-0,37	0,57*
		HASSIST	**0,97**	**0,93*** **	0,41	**0,90**	**0,98*** **	0,35	0,50	**0,91*** **	0,08	0,56	0,46	0,70**
		HRESIST	**0,97**	**0,94*** **	0,28	**0,87**	**0,94*** **	0,03	0,88	0,84**	0,73**	-0,72	-0,52	-0,83
		ABD	**0,96**	**0,92*** **	0,44	**0,92**	**0,97*** **	0,27	0,75	**0,92*** **	-0,06	0,19	-0,06	0,46

Color legend :

***	**Very high** (r≥.90)
**	High (r=0.70 to 0.89)
*	Moderate (r=0.50 to 0.69)
	Low (r=0.30 to 0.49)

Both the colors (synergy) and stars (EMG) represents the strength of the association between the control option explored and the respective comparator condition.

Figure legends

Figure 1. – Photos of the wearable robotic exoskeleton used for overground walking.

Figure 2. – VAF and cosine similarity values for all exoskeleton control options explored.

A. Number of synergies determined by the VAF criterion for all exoskeleton walking control options. n= on the top of each bar indicates the number of participants presenting a determined number of synergies for each exoskeleton control option recorded. Note that most of the participants presented four muscle synergies. **B**. Cosine similarity values (r) for the weightings of each muscle synergy and for each exoskeleton condition. **C, D**. Cross-correlation values for the temporal activation profiles compared to non-exoskeleton overground REF-EXO (C) and REF-NAT (D) conditions.

Figure 3. – Group average (n=20) for each of the four muscle synergies found in able-bodied participants at REF-NAT (black), REF-EXO (red), and all exoskeleton walking conditions.

A. Activation timing profiles for each synergy over the gait cycle. REF-NAT and REF-EXO are presented in bold to define the reference to which each activation profile is compared. **B.** Muscle synergies average and weightings. Muscles in bold represent the muscles defining a specific muscle synergy, being the muscles that contribute the most. **C.** Individual EMG activation profiles over the gait cycle. TA = tibialis anterior, SO = soleus, MG= medial gastrocnemius, VM= vastus medialis, RF = rectus femoris, ST = semitendinosus, BF = biceps femoris, GM = gluteus medius.

Figure 4. – Activation timing profile and average (n=8) muscle weighting of the fifth synergy found during TOT exoskeleton control option.

Black line represents the average, while red pointed line represents the SD. TA = tibialis anterior, SO = soleus, MG = medial gastrocnemius, VM= vastus medialis, RF = rectus femoris, ST = semitendinosus, BF = biceps femoris, GM = gluteus medius.

Figure 1

Figure 2

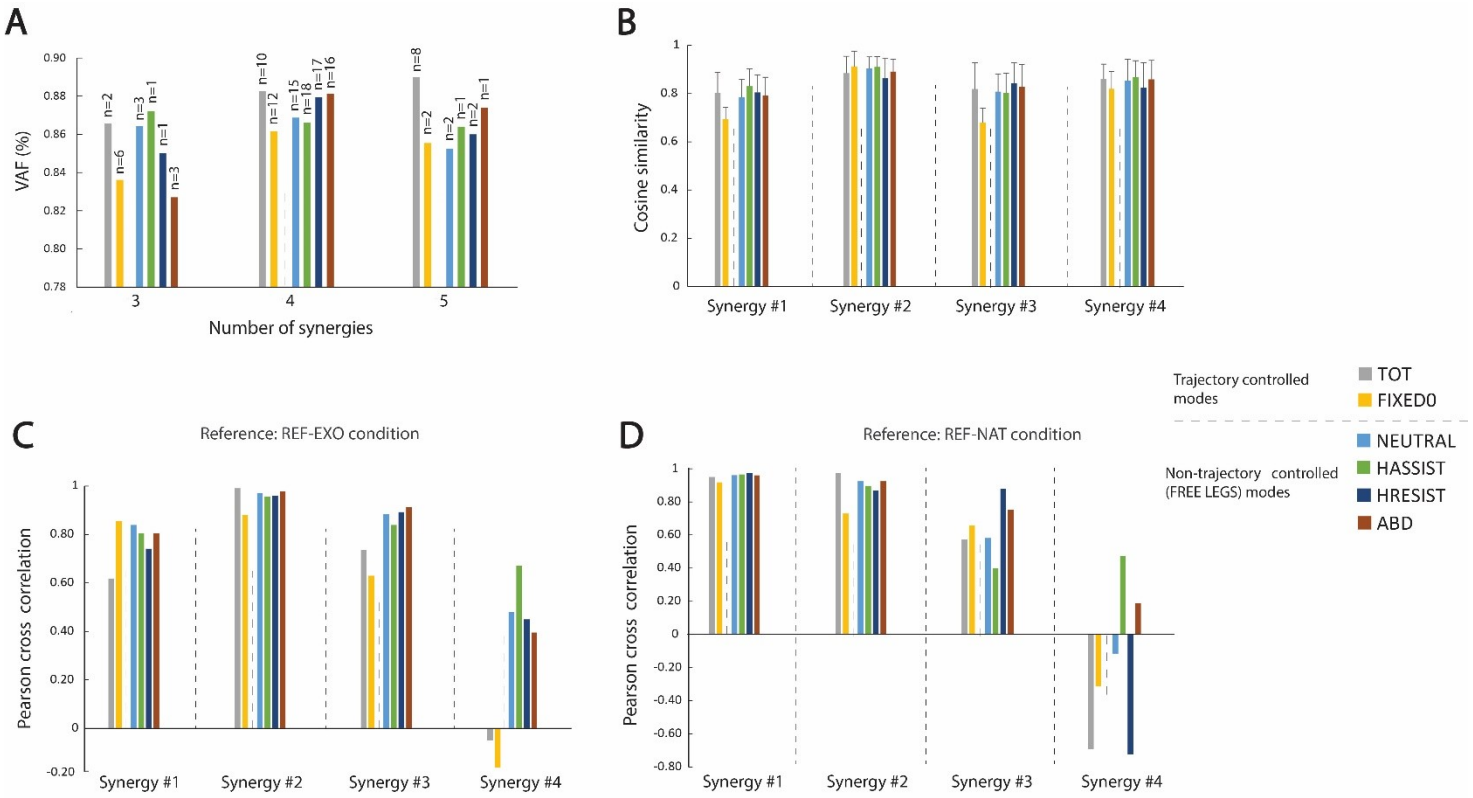

A
VAF (%)
Number of synergies
B
Cosine similarity
Synergy #1
Synergy #2
Synergy #3
Synergy #4
C
Reference: REF-EXO condition
Pearson cross correlation
D
Reference: REF-NAT condition
Trajectory controlled modes
Non-trajectory controlled (FREE LEGS) modes
TOT
FIXED0
NEUTRAL
HASSIST
HRESIST
ABD

Figure 3

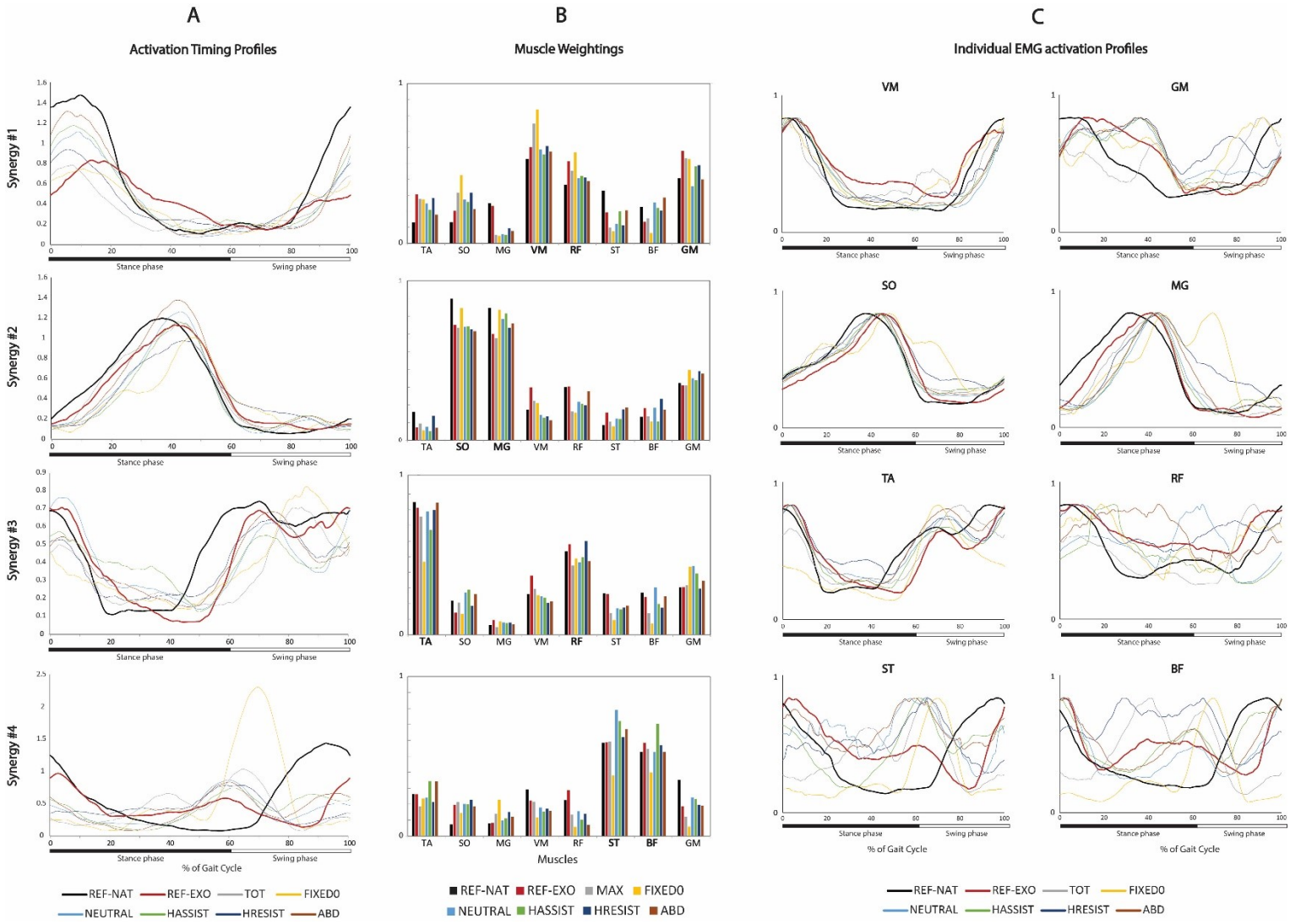
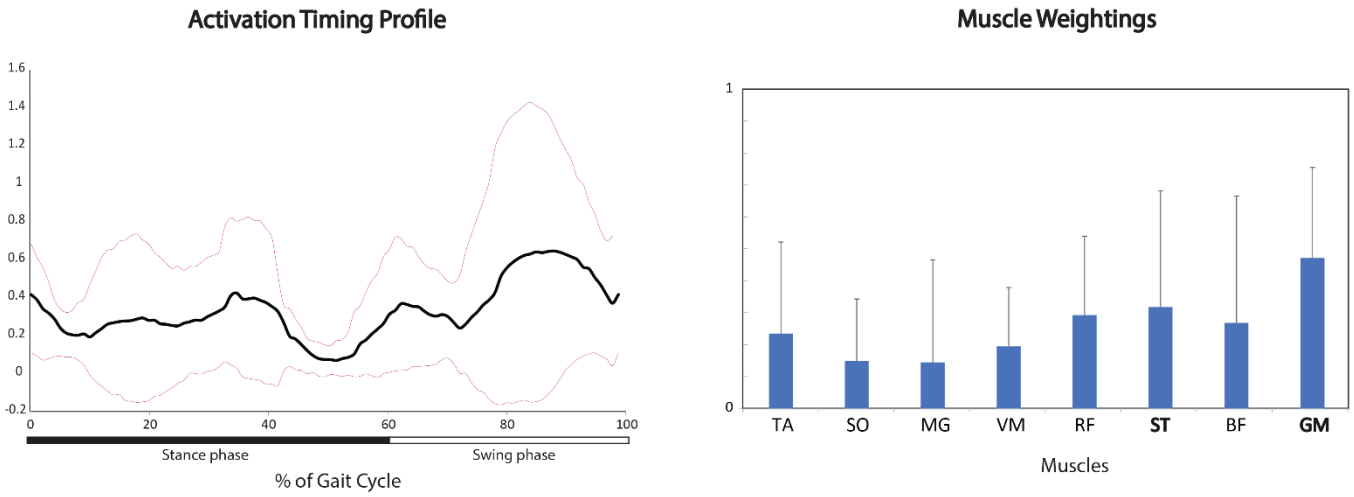

A
Activation Timing Profiles
B
Muscle Weightings
C
Individual EMG activation Profiles
Synergy #1
Synergy #2
Synergy #3
Synergy #4
Stance phase
Swing phase
% of Gait Cycle
TA SO MG VM RF ST BF GM
Muscles
VM
GM
SO
MG
TA
RF
ST
BF
REF-NAT REF-EXO TOT FIXED0
NEUTRAL HASSIST HRESIST ABD
REF-NAT REF-EXO MAX FIXED0
NEUTRAL HASSIST HRESIST ABD
REF-NAT REF-EXO TOT FIXED0
NEUTRAL HASSIST HRESIST ABD

Figure 4


Activation Timing Profile
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
-0.2
0
20
40
60
80
100
Stance phase
Swing phase
% of Gait Cycle
Muscle Weightings
1
0
TA
SO
MG
VM
RF
ST
BF
GM
Muscles

5.2.8 References

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5.3. Article #3: Wearable exoskeleton control modes selected during overground walking affect muscle synergies in adults with a chronic incomplete spinal cord injury

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As first author, I contributed significantly to the conception and development of the experimental protocol and the methodology, as well as to the data collection, the analysis and interpretation of the results; I also wrote the original draft of the manuscript. Dr. Bourbonnais contributed, with his expertise related to muscle synergies, to the analysis and interpretation of the results. Mr. Goyette contributed mainly to the data processing and to the software development for data extraction and analysis. Professors Gagnon and Duclos contributed to the development of the protocol and methodology and oversaw the analysis and interpretation of the results as well as the writing of the manuscript. All authors contributed significantly to the revision of the intellectual content of the manuscript and approved the final version for publication.

5.3.1. Abstract

Background: Changes in the number of muscle synergies (MSs) and in the weighting of muscles composing each MS are typically altered following an incomplete spinal cord injury (iSCI). Wearable robotic exoskeletons (WRE) represent a promising rehabilitation option, though the effects of various WRE control modes on MSs still remain unknown. **Objective**: This case series characterizes how WRE control modes affect the number of MSs and the weighting of muscles composing each MS in individuals with iSCI. **Setting:** Pathokinesioly laboratory of a rehabilitation research center. **Methods**: Three participants with a chronic iSCI walked at a self-selected

comfortable speed without and with a WRE set in two trajectory-controlled (Total Assistance, TOT; Assistance-as-Needed, ADAPT), and three non-trajectory controlled modes (High Assistance, HASSIST; High Resistance, HRESIST; NEUTRAL). Surface EMG of eight lower extremity (L/E) muscles was recorded and used to extract MSs using a non-negative matrix factorization algorithm. Cosine similarity and weighting relative differences characterized similarities in MSs between individuals with iSCI and able-bodied controls. **Results:** The mode providing movement assistance within a self-selected L/E trajectory (HASSIST) best replicated MSs in able-bodied controls during overground walking. MSs extracted with the trajectory-controlled modes differed to the greatest extent from able-bodied group MSs. **Conclusions:** Most WRE control modes did not replicate the motor control required for typical L/E muscle coordination during stereotypical overground walking. These results highlight the need to gain a better understanding of the effects of the various control modes on L/E motor control for rehabilitation professionals to incorporate research evidence when selecting WRE control mode(s) during WRE locomotor interventions.

Key Words

Coordination; Electromyography; Spinal Cord Injury; Rehabilitation; Technology.

5.3.2 Introduction

Overground locomotor training with Wearable robotic exoskeletons (WRE) represents an emerging and promising neurorehabilitation intervention that aligns with the basic principles of motor learning (e.g., specificity, repetition, and intensity) promoted after a neurological lesion[1]. However, it still remains difficult to pinpoint how this intervention compares with conventional locomotor training interventions in adults with an incomplete spinal cord injury (iSCI) [2-4]. Part of this difficulty relates to the fact that almost all evidence have been gathered using WRE with total lower extremity (L/E) motorized assistance and fixed trajectory guidance during treadmill walking. As a result, after having gained sufficient experience with the WRE, active voluntary participation and stride-to-stride variability, which are essential components in motor learning, becomes regulated and may negatively affect walking recovery[2]. In fact, such an approach may induce a habituation and sensitization phenomenon in which the spinal cord circuits adjust rapidly to repetitive activations of the same sensory pathways[5].

To overcome these obstacles, while also increasing perceived utility and acceptability among rehabilitation professionals, some WRE manufacturers offer L/E control modes providing various levels of assistance or resistance, as well as non-imposed (i.e., non-controlled) trajectory guidance. In the neurorehabilitation context, these L/E control modes allow rehabilitation professionals to personalize WRE-based rehabilitation interventions to maximize locomotion and locomotion-related abilities. However, the effects of the various control modes on L/E muscle coordination underlying locomotion remain unknown, and clinical practice remains predominantly informed by clinical reasoning and accumulated experience.

The L/E muscle coordination can be revealed by characterizing muscle synergies (MSs) using non-negative matrix factorization (NNMF) algorithms. This analysis usually reveals a specific number of MSs (i.e., motor modules) with muscle weightings associated with gait sub-cycles. In adults with iSCI, spinal locomotor control is compromised to various extents and consequently alters how the central nervous system (CNS) coordinates the muscles involved during locomotion. This generally translates into fewer L/E muscle synergies, or an altered weighting of the different muscles involved in a given MS leading to motor impairments during gait[6]. Thus, increasing the number of MSs, or replicating the weighting of muscles similar to those synergies found in able-bodied individuals during overground locomotor training with a WRE, could theoretically translate into improved walking abilities in individuals with iSCI. However, to our knowledge, no study to date has investigated to what extent various WRE control modes may modify the number of MSs and the weighting of muscles composing each MS during overground walking with a WRE in individuals with iSCI who have recovered to various extents their ability to walk.

The aim of this case series is to examine how various WRE trajectory and non-trajectory control modes affect L/E muscle synergies (e.g., number of MSs, weightings of muscle within a given synergy) in individuals with iSCI during overground walking with a WRE. It is hypothesized that the number of MSs and weighting of muscles composing each MS during overground walking without WRE will differ when compared to able-bodied MSs (H1). Moreover, walking with a WRE set in a non-controlled trajectory mode will increase the number of MSs and modify weightings of muscles composing each MS to levels comparable to those extracted in able-bodied individuals (H2). This research represents an initial step to strengthen evidence regarding L/E muscular

coordination that will inform clinical practice on the effects of different control modes when planning personalized WRE locomotor interventions.

5.3.3 Methods

5.3.3.1 Participants

Three participants with traumatic chronic iSCI (ASIA Impairment Scale, AIS = C or D) below the fifth cervical neurological level were recruited for this study. Participants were included if they were able to walk overground for at least 10 meters without or with a walking aid (e.g. , forearm crutches); were able to follow verbal, visual, and auditory commands; and met all WRE manufacturer requirements (e.g., L/E passive range of motion limitations, moderate-to severe L/E spasticity) as verified by a comprehensive physical therapy assessment. Participants were excluded if they presented history of other neurological disorders, including non-traumatic SCI or cognitive impairments. The study was conducted at the Pathokinesiology Laboratory located at the Institut universitaire sur la réadaptation en déficience physique de Montréal. All participants provided written consent to participate. The Research Ethics Committee of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) approved the study (CRIR-1083-0515). All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

5.3.3.2 Clinical Evaluations

Injury severity was evaluated by a certified physiotherapist using the American Spinal Injury Association Impairment Scale (AIS) to categorized participant's neurological injury level and completeness. The L/E muscle strength was assessed and graded according to the Lower Extremity Motor Score (LEMS) of the International Standards for Neurological Classification of SCI (ISNCSCI). The 10-metres walking test was completed at self-selected natural velocity to evaluate walking speed and confirm the participant's ability to walk the test distance.

5.3.3.3 Robotic Exoskeleton

The Ekso GT^{TM} WRE (EKSO Bionics, CA, USA) provides robotic control during overground walking. Specifically during the swing phase, the control modes offered by the Ekso GT^{TM} can be

grouped into trajectory control, including total assistance (TOT) and assistance-as-needed (ADAPT) modes, as well as non-trajectory control, including high assistance (HASSIST), high resistance (HRESIST), and NEUTRAL modes (Table 1). During stance, knee flexion beyond 45 degrees was blocked by the WRE to prevent full knee collapse and falling.

5.3.3.4 Intervention

Participants completed four 45 to 60-minute training sessions over a two-week period. During these sessions, under direct supervision of a certified physiotherapist, participants learned to safely walk with the WRE at a self-selected comfortable speed using forearm crutches and with the WRE set in the five WRE control modes along a 50-metre level tiled corridor.

5.3.3.5 Laboratory Assessment

5.3.3.5.1 Walking Conditions

Participants walked without the WRE at a self-selected natural speed (NAT) on a leveled tiled corridor over a 10-m distance. Thereafter, participants walked with the WRE at a self-selected comfortable speed with all WRE control modes tested in a random order (i.e., participant 1: HASSIST-ADAPT-NEUTRAL-HRESIST-TOT; participant 2: NEUTRAL-ADAPT-HRESIST-TOT-HASSIST; participant 3: HRESIST-HASSIST-ADAPT-NEUTRAL-TOT). Immediately after testing each control mode, the participant's rate of perceived exertion (RPE) was collected using a modified 0 to 10 Borg Scale. Between modes, participants performed lateral weight shift transfers while standing for one minute to minimize any potential carryover effects of the previously tested WRE mode (i.e., wash out).

5.3.3.5.2 Surface Electromyography

Using a Delsys Trigno wireless EMG system (Delsys Inc., Boston, MA, USA), the EMG activity was recorded from eight L/E muscles bilaterally: gluteus medius (GM), rectus femoris (RF), vastus medialis (VM), semitendinosus (ST), biceps femoris (BF), tibialis anterior (TA), medial gastrocnemius (MG), and soleus (SO). After proper skin preparation, all wireless hybrid sensors were positioned in accordance with recommendations of the Surface ElectroMyoGraphy for the

Non-Invasive Assessment of Muscles (SENIAM) (www.seniam.org) to enable surface EMG (1926 Hz) and 3D acceleration data (148 Hz) recording.

Raw EMG data were filtered (Butterworth bandpass 20-400 Hz, 4th order no lag) and processed with a continuous Root Mean Square (RMS) using a centered 250 msec moving window. Each gait cycle was delimited between consecutive foot contacts, which were determined from integrated acceleration peaks from the SO sensors using a Teager-Kaiser Energy Operator (TKEO), and then visually inspected and manually adjusted if needed. All gait cycles were time normalized to 100% with 1% increments from which the stance (0 to 59%) and swing (60 to 100%) phases were depicted. For each walking condition, the best three consecutive cycles, based on the lowest mean coefficient of variation computed for all EMG envelopes over each temporal data point embedded within each time normalized cycles, were automatically selected using a custom-made Labview software before being averaged and amplitude-normalized (i.e., the RMS from each muscle was divided by its own maximum peak value prior to initiating the MSs analysis).

5.3.3.6 Muscle Synergies

An experimental EMG data matrix was calculated for each participant, consisting of the mean of three consecutive gait cycles of each recorded muscle, prior to being submitted to a Non-Negative Matrix Factorization (NNMF) algorithm. The number of muscle synergies was determined by the least number of synergies that could explain the variance accounted for (VAF) in each muscle (VAF_m), with VAF_m greater than 0.9 (90%) and the product of all VAF_m (global VAF, VAF_g) greater than 0.8 (80%). Muscle synergies were grouped based on the Cosine Similarity (CS) of the weight matrices (W) [7, 8]. To analyze the resemblance between the obtained MSs of each walking condition against reference MSs computed among an able-bodied control, CS was calculated between each participant MSs (Wr) against those obtained from a reference participant[9]. The reference MSs were extracted from an able-bodied participant (i.e., control) who was assessed during overground walking without the exoskeleton using the same experimental protocol (i.e., equipment, recorded muscles and experimental conditions) [10]. For this analysis, the inner product of the obtained MSs on each walking trial was calculated and the cosine angle between those synergies and the reference MSs was measured.

According to the reference able-bodied control, the muscles composing each MS were established as: Synergy #1, GM, VM and, to a lesser extent, RF; Synergy #2, SO and MG; Synergy #3, TA and RF; Synergy #4, ST and BF. The CS values closer to 1 indicated greater similarities in the directions of the two compared vectors. When the CS between Wr and Wt was greater than 0.868 and statistically significant ($p < 0.05$) [11], MSs were considered similar. Whenever two distinct MSs in the same walking trial were classified into the same group, these two synergies were considered to have merged together. The synergy with the lowest correlation of the two was deemed to be merged to the synergy presenting the highest correlation value. Synergies not corresponding to any of the reference MSs extracted in able-bodied control were defined as "undefined".

To further visualize how each recorded muscle weighting contributing to a specific synergy was similar to those found in able-bodied reference, the weighting differences (Wd = Wt-Wr) for each muscle and walking trial, were calculated for each participant (Figure 1). In order to calculate Wd, muscles belonging to a specific synergy were weighted by multiplying each muscle in the weight matrix by its maximum peak value found to obtained normalized values to 1 within each synergy and allow weighting matrices subtractions.

5.3.3.7 Statistical Analyses and Interpretation

Differences in MS weightings (Wd) equal to 0 represented perfect matches while values closer to 1 indicated larger divergences in MS weighting, with values ranging between 0 and 0.3 [12] considered to closely reproduce MSs weightings from the able-bodied control. The RPE values were calculated and interpreted according to the American College of Sports Medicine (ACSM) guidelines for exercise testing and prescription to determine the exercise intensity achieved while walking with the WRE [13, 14]. According to these guidelines, an RPE of 1-2 corresponds to very light to light intensity, 3-4 corresponds to a moderate intensity, 5-6 corresponds to a high intensity, and 7 to 10 corresponds to a very high intensity.

5.3.4 Results

5.3.4.1. Participants and Walking Speed

All demographic, clinical characteristics, and walking speed during each experimental trial are summarized in Table 2. Overall, compared to overground walking without WRE (i.e., NAT), walking with the WRE reduced speed between -63.2 and -78.2% for participant 2 and between -55.6 and -66.7% for participant 3, across all WRE control modes. Participant 1 predominantly walked faster than NAT by up to 42.1%.

5.3.4.2. Number of Muscle Synergies

Three to four MSs were found across walking conditions (VAF > 0.8 for all conditions). Synergy #4 was absent in all participants with iSCI during NAT condition but present during all WRE control modes, except for participant 1 who had three synergies in TOT mode. Merging of MSs were observed and mostly found between synergies #1 and #4. Interestingly, only HASSIST mode consistently had all four synergies in able-bodied reference with relatively high CS values and no merged synergies. Undefined MSs were also found in most WRE control modes, except for HASSIST, which presented only one undefined synergy across all participants (Table 3).

5.3.4.3. Muscles Synergy Weightings

Table 3 illustrates similarities between weight matrices for each synergy and for each participant compared to an able-bodied reference using CS values. MS weightings during NAT varied widely across participants, particularly between the left and right L/E. The Wd analysis showed that TOT and ADAPT modes had very different patterns from the reference muscle weightings, illustrated by the scattered data point patterns of muscle weighting relative differences across participants and across MSs presented in Figure 2.

Although some MSs weighting relative differences approached the 0.3 value threshold across the WRE control modes, only HASSIST consistently presented a clustering of point values around the 30% threshold on all participants and on both L/E. This confirms strong similarities between the HASSIST mode and the typical weight of muscles composing each MS found in the able-bodied reference.

5.3.4.4 Rate Perception of Effort (RPE)

The RPE across the different walking conditions are summarized in Figure 3. Participants perceived effort levels ranging from light to moderate, with the greatest effort in HRESIST mode.

5.3.5 Discussion

The present study investigated the effects of different WRE control modes on MSs during walking in individuals with a chronic iSCI. To our knowledge, this is the first study investigating differences in MSs across a range of WRE modes. The three participants presented different degrees of sensorimotor impairment and functional disabilities resulting from their iSCI. The high variability across MSs attributes found across participants highlight the heterogeneity of muscle coordination challenges in adults with iSCI. Reduction in the number of MSs has been associated with an increased muscle co-contraction, poor muscle strength, or restricted joint range of motion because the CNS cannot independently and efficiently access and activate MSs during walking[6, 15, 16]. Clinically, these MSs deficits typically translate into abnormal motor outputs, decreased walking speeds, and increased gait asymmetry [6]. Thus, the reductions in the number of MSs and altered muscle weighting within each MS were expected and fully support the first hypothesis (H1), that the number and weighting of muscles composing each MS during overground walking without WRE will be different than able-bodied MSs.

Synergy #4 emerged while walking with the WRE in all control modes, with varying muscle weightings across participants and L/E sides. Although more MSs reflects improved motor function [17], the results prove otherwise since the more synergies during walking with the WRE did not necessarily match the typical weighting of muscles composing each MS. Indeed, most MSs weightings across control modes were different from those found in able-bodied controls during overground self-selected natural speeds. These findings indicate that, even during TOT and ADAPT control modes during which the L/E trajectory remains totally guided through typical, strict and repetitive kinematics patterns[1], adaptations to these modes did not lead to a typical muscle activation pattern in adults with a chronic iSCI. This is of great relevance because TOT or ADAPT control modes, which are the most commonly used modes in the literature to explore superiority effects of robotic exoskeleton over other conventional locomotor training

interventions in adults with iSCI [2], might not reinforce an adequate neural locomotor pattern for locomotion.

A key finding of this study, which partially supports the second hypothesis, is that only HASSIST mode consistently replicated the number of MSs and weight of muscles composing each MS in the reference able-bodied individual. These findings were observed in both L/Es among all participants and in all main and secondary muscles composing each MS. This is demonstrated by the relative difference values below the 30% threshold set to establish similarities with able-bodied controls. Such effect of the HASSIST mode may result from an increased step variability triggered by the free/non-imposed L/E trajectory while allowing voluntary motor control, providing the assistance that may reduce the need of compensation or activation from other muscles that normally would not participate in a typical synergy. These elements might facilitate the recruitment of MSs similar to those found during overground walking in healthy individuals. Concerning NEUTRAL and HRESIST modes, this MSs weighting "normalization" was not achieved since the lack of assistance and increased limb motion resistance, alongside potential under-optimal compensations for the dynamics of the WRE, might have increased the probability of recruiting additional secondary/compensatory muscles to adapt to the new demands, which translated into different muscle weightings found in able-bodied individuals.

This study provided new evidence that has the potential to impact clinical practice. First, although not all WRE control modes induced motor control adaptations closer to the able-bodied reference, the results showed that typical MS characteristics found in abled-bodied individuals during overground walking without a WRE could be reproduced when individuals with iSCI ambulate with WRE. These aspects might have important implications when selecting WRE control modes before engaging on locomotor training programs using this technology. Second, when exploring the level of effort required to walk during all WRE non-trajectory-controlled modes, the HASSIST mode required a light to moderate effort from all participants to accomplish the walking task. Thus, this control mode could be used to facilitate the swing phase during prolonged periods of walking (i.e., massed practice) and, ultimately, induce beneficial neural plasticity and potentiate locomotor recovery[18].

This study had several limitations. First, the small sample of adults with a chronic iSCI does not allow generalization of the results. In fact, other individuals may benefit from other WRE control modes. Second, since no kinematic analysis was completed in the present study, it remains difficult to determine to what extent WRE movement strategies were similar to those established for overground walking. Lastly, the actual absolute level of assistance or resistance provided remains unknown and is not provided by the WRE manufacturer.

5.3.6. Conclusion

Walking with a WRE in control modes allowing step variability (i.e., self-selected trajectory), and assisting L/E swing phase (i.e. HASSIST), best replicated MSs observed in able-bodied individuals during overground walking, while requiring light to moderate effort. This control mode may allow adults with iSCI to engage in a high-repetition task-specific walking program (i.e., activity-based therapy) needed to induce neuroplastic adaptations and potentiate walking ability. Additional studies with more robust experimental designs and larger sample sizes are needed to strengthen evidence and further support clinical decision-making processes when aiming to improve L/E motor control during walking. Nonetheless, the results of the present study are a first step towards a better understanding of the effects of various control modes on L/E muscular coordination, which can be evaluated through MSs when individuals with iSCI walk with a WRE.

5.3.7 Acknowledgements

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Disclosure of interest

The authors have no conflicts of interest to report.

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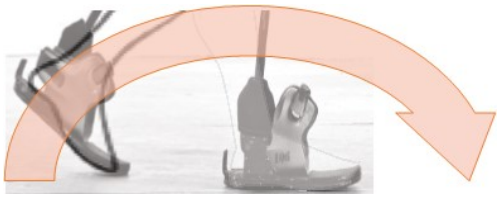
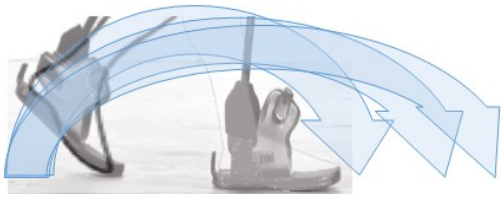
Table 1. – Description of the different control modes investigated during the swing phase when walking with the wearable robotic exoskeleton.

1. Trajectory controlled: The wearable exoskeleton (WRE) automatically initiates steps when the participant reaches both pre-determined lateral and forward body shift thresholds. Once the step is initiated, the exoskeleton swings and controls the hip and knee kinematics for the foot to follow a specific pathway.



1.a. TOT	Provides total motorized assistance continuously to move the hip and knee joints according to a predefined planned hip and knee kinematics configured to drive foot position during the swing phase.
1.b. ADAPT	Provides adaptable motorized assistance to continuously adjust hip and knee joint movements to comply with a predefined planned hip and knee kinematics configured to drive foot position during swing phase.

2. Non-trajectory controlled (i.e., 'free legs'): The participant initiates swing and control freely his L/E kinematics (amplitude, velocity, and acceleration) within the sagittal plane (i.e., no predefined trajectory) during the swing phase of each step.



2.a. NEUTRAL	Provides no assistance and no resistance at the hip and knee joints during swing phase.
2.b. HASSIST	Provides high assistance to facilitate hip flexion and knee extension during swing phase.
2.c. HRESIST	Provides high resistance to augment hip flexor and knee extensor muscular efforts during swing phase.

Table 2. – Demographic and clinical information of participants

	Participants		1		2		3	
Demographic characteristics	**Gender**		M		F		M	
	Age (years)		42		51		60	
	Height (m)		1.80		1.62		1.60	
	Weight (Kg)		65.7		52.1		56.6	
Clinical Information	**Time since injury (years)**		18		1.1		40.7	
	Neurological level of injury		T6-T7		C5		T4	
	American Spinal Injury Association Impairment Scale (AIS)		D (Trauma)		D (Trauma)		D (Trauma)	
	Sensory level and score /224		T7 197/224		C6 132/224		T4 156/224	
	Total Lower Extremity Motor Score (LEMS)		36/50		41/50		46/50	
			R	**L**	**R**	**L**	**R**	**L**
	Hip flexors		4	3	5	5	3	5
	Knee extensors		2	3	5	5	5	5
	Ankle dorsiflexiors		4	4	4	4	5	5
	Long toe extensors		4	4	4	4	3	5
	Ankle plantar flexors		4	4	2	3	5	5
Walking speeds (m/s)	**Walking conditions**							
	Without exoskeleton	**NAT**	0.19		0.87		0.54	
		Control modes						
	With Exoskeleton	**TOT**	0.18		0.19		0.21	
		ADAPT	0.20		0.25		0.24	
		NEUTRAL	0.27		0.28		0.23	
		HASSIST	0.25		0.26		0.23	
		HRESIST	0.23		0.32		0.18	

R= right; L= left

Table 3. – Cosine similarities for all participants and walking trials.

Notice that HASSIST mode presented four synergies with relatively high cosine similarities values, no merged and only one undefined synergy (green dashed square).

		Walking conditions											
		Without exoskeleton		With exoskeleton									
				Control modes									
	Participants	NAT		TOT		ADAPT		NEUTRAL		HASSIST		HRESIST	
		R	L	R	L	R	L	R	L	R	L	R	L
Synergy 1	P1	0,71	0,68	0,88	0,78	0,91	~ #4	0,78	~ #4	0,94	0,92	0,78	~ #4
	P2	0,76	0,81	0,73	~ #3	0,63	~ #3	0,75	~ #4	0,85	0,81	0,8	0,69
	P3	0,83	0,76	~ #4	~ #4	~ #4	0,56	0,63	0,64	0,83	0,82	0,76	0,63
Synergy 2	P1	0,69	0,81	0,81		0,79	0,8	0,74	0,83	0,75	0,83	0,74	0,92
	P2	0,85	0,75	0,82	0,78	0,81	~ #4	0,8	0,92	0,9	0,91	0,94	0,85
	P3	0,82	0,86	0,97	0,74	0,91	0,75	0,94	~ #4	0,84	0,81	0,92	0,83
Synergy 3	P1	0,87	0,67	~ #2	0,67	~ #1	0,82	~ #4	0,79	0,78	0,77	~ #1	0,8
	P2	0,91	0,92	0,96	0,92	0,94	0,87	0,9	0,91	0,95	0,95	0,88	0,93
	P3	0,84	0,86	0,85	0,92	0,94	0,87	0,84	0,91	0,89	0,88	0,83	0,87
Synergy 4	P1			0,94	0,82	0,91	0,8	0,81	0,8	0,9	0,87	0,8	0,68
	P2			0,69	0,86	0,68	0,7	0,87	0,87	0,92	0,93	0,89	0,88
	P3			0,86	0,84	0,88	0,85	0,78	0,71	0,87	0,78	0,77	0,84
UD Synergy	P1			X		X	X	X	X			X	X
	P2				X		XX		X				X
	P3			X	X	X	X		X		X	X	X

Absent synergy *Merged synergy* **UD synergy**= *undefined synergy* X = *undefined synergy*

~ #X = *synergy merged with synergy number X*

Figure legends

Figure 1. – Example of the procedure to calculate muscle synergies weighting differences.

Normal weighting matrix obtained on healthy individuals were subtracted to the obtained experimental tasks. The vertical grey boxes represent main muscles composing a specific muscle synergy while horizontal grey boxes represent the threshold range, i.e., ≤0.3 for a value to be considered similar or close-to normal compared to a healthy reference. In this example, notice that synergy #1, mainly composed by VM, RF and GM muscles, presented almost perfect similarities with the HASSIST mode for participant 1.

Figure 2. – Right and left muscle synergies weightings relative differences for all experimental trials and for each participant.

The vertical gray boxes highlight the muscles defining a specific muscle synergy (i.e., the muscles that contribute the most on a synergy in heathy individuals). The gray horizontal bar represents the limits of 30% from which differences were considered similar to the synergies found in healthy individuals. Notice that for all synergies, the HASSIST mode consistently tended to bring the muscle weightings closer to 30% in all participants. TA = Tibialis Anterior, SO = Soleus, MG = Medial Gastrocnemius, VM = Vastus Medialis, RF = Rectus Femoris, ST = Semitendinosus, BF = Biceps Femoris, GM = Gluteus Medius.

Figure 3. – Ratings of perceived effort during all walking trials for each participant.

Areas highlighted in various shades of gray represent different exercise intensities (i.e., very light, light, moderate, vigorous, near maximum intensity, maximal, and sub-maximal effort) according to the ACSM's guidelines.

Figure 1

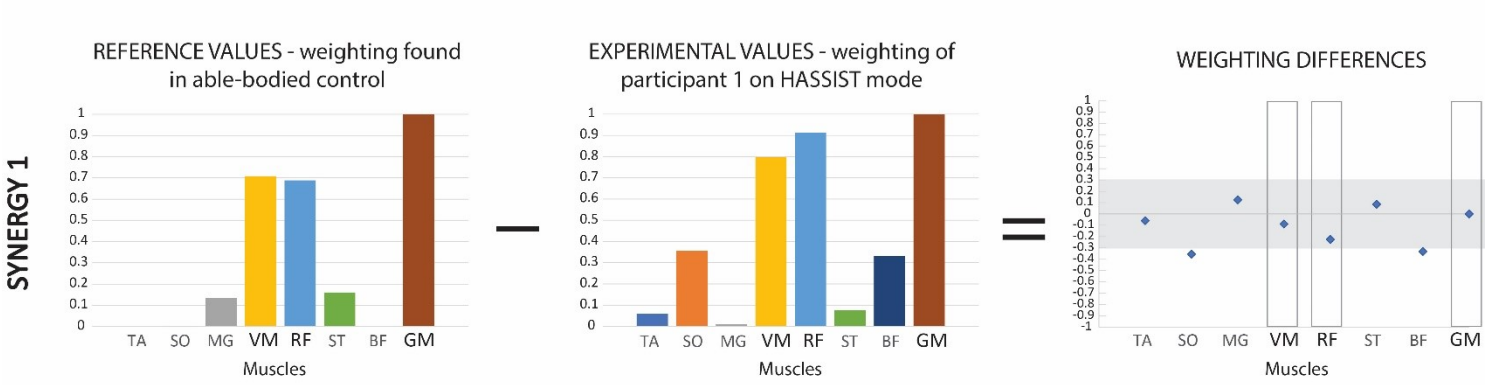

SYNERGY 1
REFERENCE VALUES - weighting found in able-bodied control
EXPERIMENTAL VALUES - weighting of participant 1 on HASSIST mode
WEIGHTING DIFFERENCES
TA SO MG VM RF ST BF GM
Muscles

Figure 2

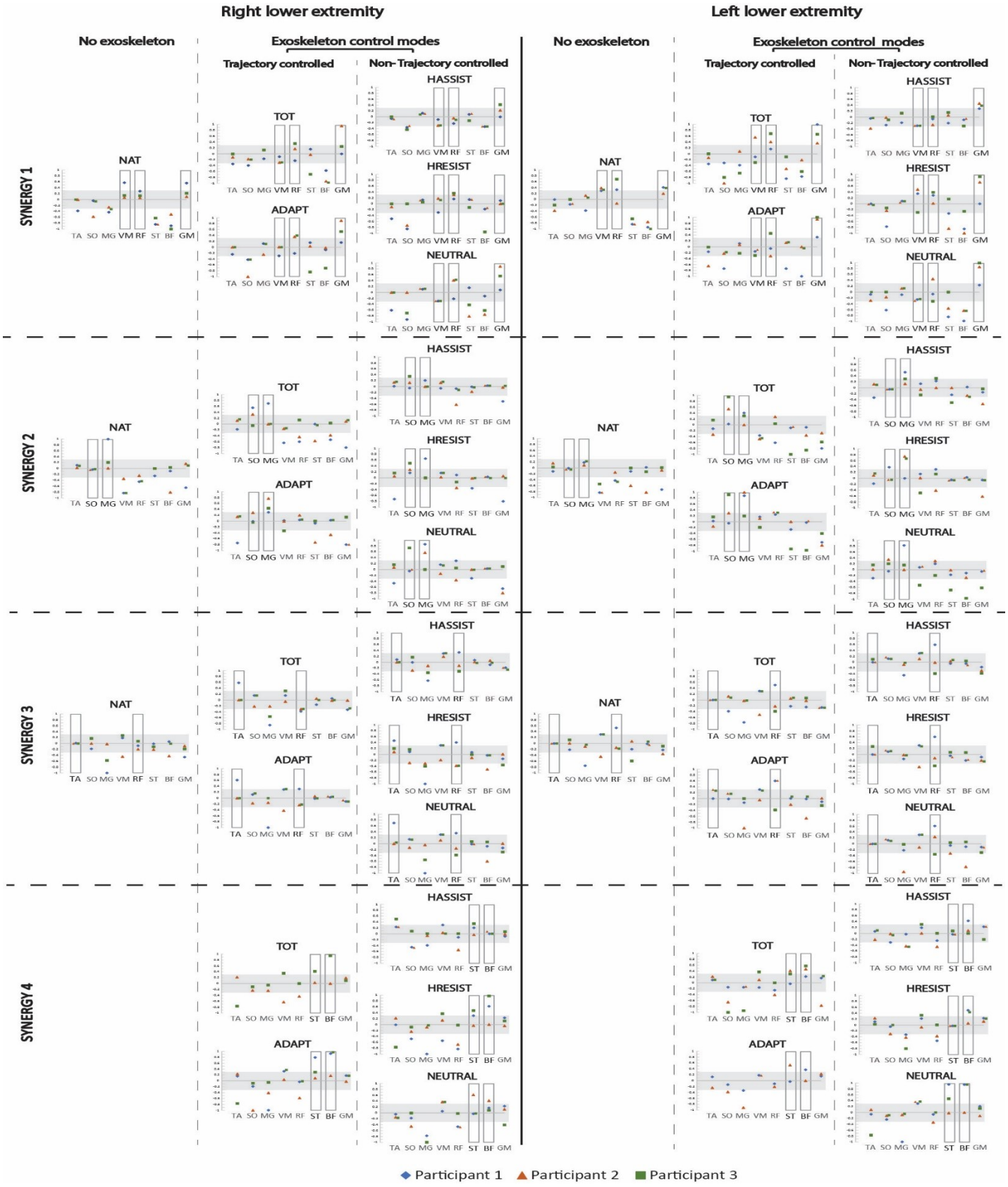
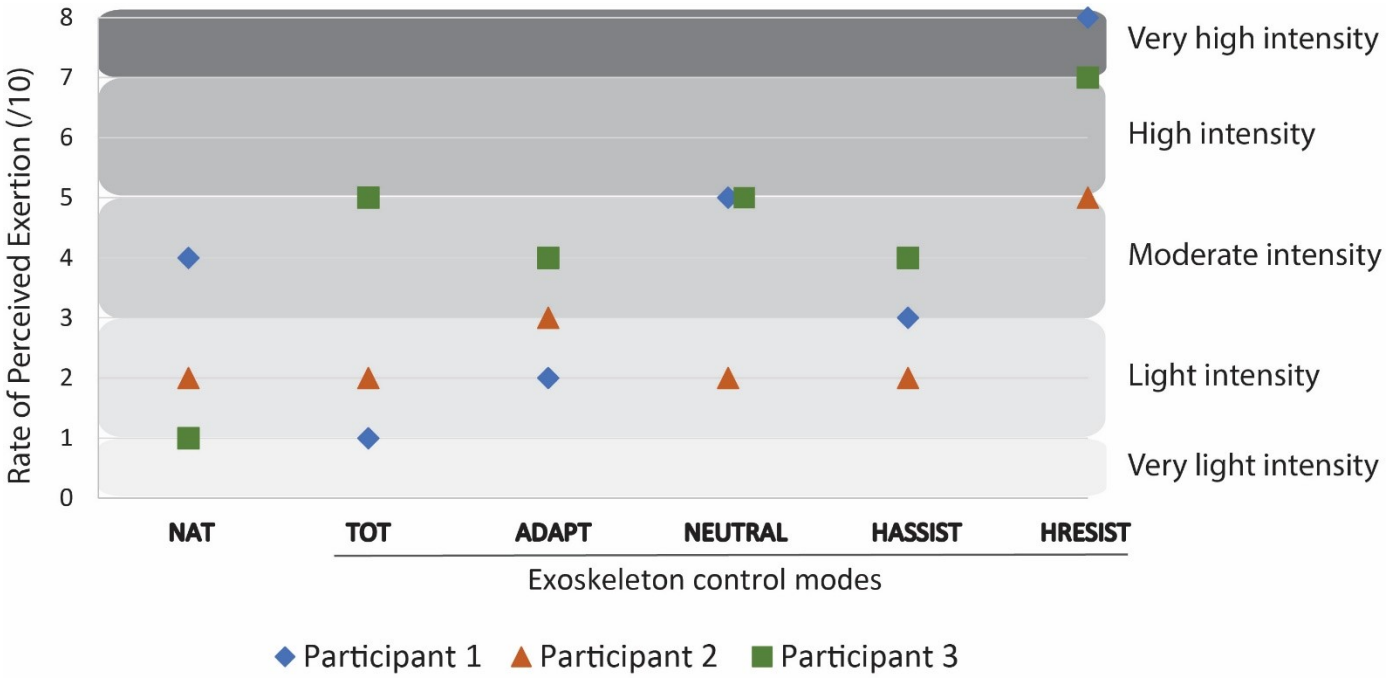

Right lower extremity
Left lower extremity
No exoskeleton
Exoskeleton control modes
Trajectory controlled
Non-Trajectory controlled
SYNERGY 1
SYNERGY 2
SYNERGY 3
SYNERGY 4
NAT
TOT
ADAPT
HASSIST
HRESIST
NEUTRAL
TA SO MG VM RF ST BF GM
Participant 1
Participant 2
Participant 3

Figure 3


Rate of Perceived Exertion (/10)
8
7
6
5
4
3
2
1
0
Very high intensity
High intensity
Moderate intensity
Light intensity
Very light intensity
NAT
TOT
ADAPT
NEUTRAL
HASSIST
HRESIST
Exoskeleton control modes
Participant 1
Participant 2
Participant 3

5.3.8 References

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CHAPTER 6 – DISCUSSION

Locomotor training principles to optimize walking-related rehabilitation outcomes are well documented. However, the effects of second generation WRE offering new control modes features on locomotor training are not well understood. Indeed, it is unclear how to prioritize features of these WRE when developing a WRE-based locomotor rehabilitation training program. As such, the scientific evidence informing clinical practice utilizing these recent features needs to be reported and strengthened. In fact, most decisions in locomotor rehabilitation practices for SCIare supported by out-of-date evidence that was derived when WRE only provided full L/E swing trajectory control or assisted control over an imposed trajectory to replicate a typical gait cycle (Morawietz & Moffat, 2013). Such an approach was novel for the time and allowed long-term manual wheelchair users, who were unable to stand and walk, to do so. However, the potential beneficial effects of WRE training for individuals with sensorimotor impairment and limited locomotor abilities continues to be questioned as this first generation of WRE could not adapt to individuals' abilities and specific therapeutic needs. Based on feedback from rehabilitation professionals and to overcome this problem, manufacturers are developing and commercializing updated WRE with numerous control options (e.g., to assist or resist a non-imposed L/E swing trajectory), however these changes have been implemented without research to prove the effects of these updates to locomotor training programs.

The primary objective of this thesis was to assess the effects of various control modes on L/E muscle coordination during WRE walking in able-bodied individuals and those with iSCI. The three main scientific articles composing the thesis showed CNS neuromuscular adaptations to changes in walking speed and to different control modes during WRE walking in both able-bodied individuals and individuals with iSCI. The evidence from this thesis is based on the use of MSs to evaluate muscle coordination patterns and access the neural control of locomotion in both populations while walking. Based on each individual's neuromuscular output and by exploring aspects related to adaptation to walking with a WRE, the findings of this thesis open up future perspectives for further understanding of the potential beneficial effects of locomotor training programs integrating WRE during neurorehabilitation.

Since a detailed discussion of the results of this thesis has been presented within each scientific article, this discussion expands on the key aspects of the results: speed-related changes, interpretation of the number of MSs, and the effects of WRE on MSs. Thereafter, the discussion elaborates on the main limitations of the measurement tools and data processing, and the potential impacts of the thesis on clinical practice and avenues for future research.

6.1 Speed-related changes and number of muscle synergies

Reductions in walking speed have been well documented during WRE walking (Louie, Eng, & Lam, 2015). Thus, a detailed analysis of the effect of different overground speeds on muscle coordination is necessary to characterize the observed changes in MSs during WRE walking for SLOW, matching those found during NAT, and FAST speeds in able-bodied individuals (Article #1). Furthermore, assessing MSs during overground walking without WRE in able-bodied individuals was required to establish comparators for WRE walking on MSs in Articles #2 and #3 in order to provide accurate and reliable comparisons.

Contrary to what most studies have reported, different walking speeds recruited a different number of MSs, different weighted muscle composition, and a different muscle activation profile. In able-bodied individuals, SLOW walking speeds had well-defined MSs compared to NAT and FAST speeds, where MSs tended to merge as speed increased. As discussed in Article #1, a common biomechanical adaptation to the gait cycle may explain the consistency in the number of MSs at SLOW walking speed compared to other speeds. To this end, the preservation of MSs characteristics during SLOW walking were primarily due to a prolonged double support period and reduced L/E acceleration-deceleration during swing phase. However, at SLOW speed, the use of a metronome to match the stepping cadence during WRE walking may have influenced the walking pattern differently than NAT and FAST speed conditions. Thus, the increased number of MSs during SLOW compared to NAT and FAST might have been influenced by a combination of both biomechanical adaptations to SLOW walking (Article #1) and by reduced step timing variability, since foot strikes matched the metronome's auditory cues, an approach known as auditory-motor anchoring (Wright, Bevins, Pratt, Sackley, & Wing, 2016). Indeed, research exploring metronomic cueing as an approach to reduce fall risk found that, in individuals

with sensorimotor impairments following a cerebellar stroke (Wright et al., 2016) or with Parkinson's disease (Hausdorff et al., 2007), auditory-motor anchoring reduces step time, stance time, double support time, swing time, and joint kinematics variability. The beneficial effects of auditory cueing on motor control are thought to occur via the facilitation of muscle activation through a combination of motor commands from different cortical areas, especially audio-motor pathways at the reticulospinal levels, cerebellum, and basal ganglia structures (Chen, Penhune, & Zatorre, 2009; Molinari, Leggio, De Martin, Cerasa, & Thaut, 2003).

The study did not set out to investigate the activation of CNS structures and spatio-temporal aspects that underlie decreased step time, stance time, and joint kinematics variability during gait. Nonetheless, the results presented in Article #1 provide, for the first time, additional information about the effects of metronomic cueing on the number and characteristics of MSs recruited during gait. It is plausible that auditory cueing increased the need for sensory-motor inputs and therefore increased accessibility of specific motor modules (i.e., MSs) in the spinal cord and leads to a typical and more controlled muscle activation pattern. This finding may have important implications on the way speed changes could be modulated during locomotor neurorehabilitation. Indeed, neurorehabilitation interventions for individuals with a CNS lesion often focus on increasing walking speeds without a thorough understanding of the impact of modifying speeds on L/E muscle coordination.

As walking speed increased, changes to the number of MSs recruited in able-bodied individuals were predominantly explained by MSs merging together. However, a decrease MSs recruitment is commonly associated with inappropriate muscle coordination (Clark et al., 2010). More specifically, fewer MSs are often explained by a lack of accessibility to spinal circuits that control locomotion, reflecting the neuromuscular constraints that result in a reduced ability for overground walking (Clark et al., 2010; Singh, Iqbal, White, & Hutchinson, 2018). From a rehabilitation point of view, maintaining the four well-defined typical MSs for walking may translate into improved locomotor control as the CNS is accessing and combining a wider range of MSs to adapt to the environment. Indeed, a positive correlation between the number of synergies recruited and walking speed has been observed, with fewer MSs associated with slower

walking speeds and increased gait asymmetry in individuals with sensorimotor impairments, compared to able-bodied individuals (Clark et al., 2010; Rodriguez et al., 2013).

Two key findings of this thesis demonstrate problems with drawing conclusions solely based on the number of MSs recruited and may be misleading in a neurorehabilitation context. First, a reduced number of MSs, or merged MSs, were associated with increased walking speed in able-bodied individuals walking at natural self-selected (1.4 m/s) and fast speeds (1.9 m/s) (Article #1). These differences were not due to walking-related impairments but rather to biomechanical constraints of increased walking speeds. Second, despite all tested control modes increasing the number of MSs (from three to four synergies) during WRE walking in all three participants with iSCI (Article #3), these increases were not similar to the typical muscle weighting compositions of able-bodied individuals. Thus, solely aiming to increase the number of MSs recruited during a rehabilitation intervention may not be adequate to induce proper muscle coordination during walking. These two findings align with previous work in which the number of MSs alone did not predict natural self-selected walking speed and were not correlated with L/E muscle strength improvements (Hayes, Chvatal, French, Ting, & Trumbower, 2014). Hence, research on rehabilitation interventions should explore not only the number but, more importantly, the selection of the muscles making up each MS during walking.

6.2 Walking with WRE and muscle synergies composition

As previously stated, first generation WRE with fully motorized control of L/E trajectory-have been studied extensively, with many studies comparing the first generation robot-assisted training with traditional rehabilitation approaches (Swinnen, Duerinck, Baeyens, Meeusen, & Kerckhofs, 2010; Tefertiller, Pharo, Evans, & Winchester, 2011). Since motorized control of L/E trajectory theoretically best replicate the typical gait cycle, the typical MSs found during overground walking at self-selected natural speed are expected to emerge. Surprisingly, three of the trajectory-controlled modes that were tested (i.e., TOT, FIXED0, ADAPT) had the most MS variability, for both able-bodied (Article #2) and iSCI groups (Article #3). MSs may not be affected by the biomechanical constraints of walking because MSs were not properly accessed despite the use of a controlled L/E trajectory to reproduce a typical L/E gait cycle.

To refine the interpretation of MS recruitment during walking, the weighting of MSs (i.e., muscle composition) is of greater importance than the number of MSs recruited. Analyzing muscle composition in MSs provides an understanding of whether MSs are bring properly modulated by the CNS and whether these MSs are required for key walking-related motor subtasks. When using a WRE for overground walking using a trajectory controlled mode equivalent to TOT, differences in the weighted composition of MSs were observed in most control modes (Li et al. 2018). These differences were hypothesized to be produced, in part, by differences between the human- and exoskeleton-generated joint torques that require MS weighting adaptations to the WRE movements (Li, Liu, Yin, & Chen, 2018). Thus, based on the results of this thesis, controlled L/E trajectories during WRE walking do not duplicate the typical gait patterns requirements to allow for the close-to-normal muscle coordination found during overground walking. From these observations, the evidence gathered from walking with WRE with fully motorized control of L/E trajectory may lack applicability to neurorehabilitation practices, but continue to be incorrectly valid for the second generation of WRE which can partially assist the user's L/E motion.

The results of this thesis support the idea that the recent features offered by the second generation of WRE (i.e., freeing L/E swing trajectories from a predetermined and fixed trajectory pattern) facilitates the emergence of MS characteristics comparable to those observed during overground walking in able-bodied individuals. Due to the decreased capability of the CNS to explore possible outcomes for optimal stepping patterns, the repetitive and fixed movement of the trajectory controlled mode may lead to habituation of the neural circuits and reduced motor learning effects (Cai et al., 2006; Shea & Kohl, 1990). Conversely, during non trajectory-controlled modes, the CNS demonstrates improved adaptation to both natural stepping variability and applying proper corrections when an error occurs. The non-trajectory-controlled modes allow for near-natural stepping variability, an intrinsic characteristic of neural circuits, which naturally exist in order to adapt locomotion to specific environmental constraints, despite stepping variability not being directly measured by the WRE. Measuring step variability in real-time and determining the desirable amount of variability needed to optimize locomotor recovery remains a continuing rehabilitation challenge (Cai et al., 2006). For instance, how much variability is required to induce

functional changes? How much variability would lead to aberrant patterns of muscle activation and motor deficits? These aspects have not been investigated. The degree of step variability and self-guided L/E swing trajectory assistance provided by HASSIST were not measured in this thesis, however the HASSIST L/E assistance configuration had close-to-able-bodied muscle weighting composition. This is consistent with previous research where allowing step variability during locomotor training of robotic walking enhanced stepping recovery, compared to locomotor training periods with fixed trajectory paradigms (Cai et al., 2006; Lotze, Braun, Birbaumer, Anders, & Cohen, 2003).

Similar muscle activity outcomes were expected for both NEUTRAL and HRESIST conditions. These non-trajectory-controlled modes were anticipated to allow for the same amount of step variability, however, this was not the case. For instance, L/E muscle strengthening is increasingly becoming a popular approach in clinical practice for adults with SCI. Indeed, research has found that applying resistance to the L/E during the swing phase in individuals with iSCI created a weaker modulation of the TA and biceps femoris muscles, leading to reduced knee flexion (Lam, Wirz, Lünenburger, & Dietz, 2008). In addition, there was a reduction in step length with different levels of resistance in individuals with iSCI. This weaker modulation in response to the different levels of resistance may reflect an impaired modulation in response to an increase in voluntary muscle contraction, or the use of different MSs. Moreover, the removal of resistance to the L/E led to enhanced knee flexion (i.e., post-adaptation effects), showing that the knee flexor activity can be enhanced with this approach (Lam, Wirz, Lünenburger, & Dietz, 2008).

In the context of the control modes investigated in this thesis, muscle strengthening might be made possible via the control option that offers resistance to specific motorized movements (i.e., HRESIST, resisted flexion and extension of the knee and hip) during WRE walking. However, there were inconsistencies in muscle weighting within recruited MSs among individuals with an iSCI compared to MSs of abled-bodied individuals. Despite abnormal weighting of MSs recruited using HRESIST control mode, the clinical utility of this approach during locomotor training, and potential muscle strengthening after-effects require further study (Kim, Eng, & Whittaker, 2004). Nonetheless, it is important to address that even if some individuals with iSCI present clinically with normal or near-to-normal L/E muscle strength grades, their locomotor pattern may differ

from other individuals with iSCI and/or from abled-bodied individuals. This is primarily due to disruptions and limited accessibility of the CNS to the functional modular organization responsible for muscle coordination (Gorassini, Norton, Nevett-Duchcherer, Roy, & Yang, 2009). Thus, assessing both muscle strength and their coordination, as explored by the MS approach, is of critical importance to better understand recovery. For example, synergies related to swing initiation are often found to be absent, contributing to clinical deficits such as foot drop, and necessitating the contribution of other muscles to compensate during this particular phase. Thus, the additional activation of secondary muscles to a specific synergy, such as swing initiation, results in MSs with unspecific muscle weighting composition (Hayes et al., 2014).

Overall, the present research confirms that typical MS number, muscle weighted composition, and profiles found in abled-bodied individuals during overground walking without a WRE could be reproduced when individuals with iSCI ambulate with WRE. This indicates that even after an iSCI, typical MSs are still encoded in the spinal cord and can be accessed by the CNS when proper L/E assistive strategies, such as HASSIST mode, are used. Moreover, the importance of exploring each MSs in detail, is key to the understanding of WRE control modes on muscle coordination during walking and its potential implications in clinical practice.

6.3 Study limitations

Despite the effort and rigor devoted to the development of these thesis projects, there are limitations relate to the sample of the population tested, the choice of measurement tools, and the data processing that have not been fully examined within the three manuscripts. These are discussed in the following sections.

6.3.1 Limitations related to the sample size of the population

The small sample size (n=3) in article # 3 presented must be considered when interpreting the study's results. In fact, the small sample size was, in part, justified by the complexity of grouping individuals with iSCI, given the heterogeneity of sensorimotor impairments and walking abilities characterizing this population. Moreover, there was a very large amount of data collected, and a thorough investigation of each MS extracted, especially of their muscle

composition, across all control modes investigated. Therefore, to present each case in the most detailed manner possible, each participant in Article #3 was treated as a case series, instead of a group, which could have resulted in a misinterpretation of the results. As such, although this small sample size has strengthened currently available evidence, the key finding of Article # 3 needs to be interpreted meticulously and generalization of the results should be avoided. In fact, it is plausible that for other individuals with iSCI, who experience more severe L/E sensorimotor impairments and functional disabilities, the use of different control modes may be required to reach similar or improved effects than the HASSIST mode.

6.3.2 Limitations related to measurement tools and data processing

The EMG equipment (Delsys Trigno^{TM} wireless EMG system) used in the present thesis has the capability to record a maximum of 16 channels. Since EMG was recorded bilaterally in individuals with an iSCI (Article #3), a maximum of eight sensors per side were available for EMG recording of L/E muscles, limiting the recording of additional muscles, such as trunk muscles that would be required to perform lateral shifts during the WRE walking.

The limited number of channels also reduced the capability of using foot switches to precisely identify heel strike and toe-off events required to extract spatio-temporal gait parameters of the gait cycle, particularly the duration of stance and swing phases. This challenge constitutes one of the main limitations of the present work and most likely affected the interpretation of temporal patterns of MSs. Within this context, the EMG sensors fixed to the distal aspect of the L/E (i.e., tibialis anterior and soleus muscles) also contained a three-axis accelerometer (i.e., hybrid sensor). This accelerometer provided the L/E kinematics needed to determine event markers and isolate consecutive heel strikes to identify each gait cycle. These heel strike events, that were essential for the extraction of MSs, were identified using the accelerometer-deceleration spikes from the EMG sensor that were fixed over the soleus muscle. These spikes were validated by fixing an accelerometer on the external malleoli on a sample of able-bodied individuals. Unfortunately, this approach made it challenging to accurately determine the timing of the toe/foot off events to isolate the stance and swing phases,

particularly when walking without a WRE at a FAST speed (Article #1). Hence, the duration of the stance and swing phases were deemed invalid in the context of this work.

Due to the difficulty in accurately identifying toe-off events in the accelerometer signal data, standardized relative times were applied for the stance (i.e., 60% of the gait cycle) and the swing phases (i.e., 40% of the gait cycle) (Winter, 2009). The proportions of stance and swing varied slightly between individuals and across experimental conditions (i.e., walking speeds, WRE control modes), therefore, using a fixed relative time for all gait cycles may not have perfectly reflect how these spatial parameters were altered. Although this could partially explain the observed phase shifts in MSs, especially during the slow walking speed, (Article #1), the results are comparable to previous studies that also report phase shifts, even with accurately identified gait cycle events (Den Otter, Geurts, Mulder, & Duysens, 2004; Kibushi, Hagio, Moritani, & Kouzaki, 2018).

Although increased stepping variability was suggested as a possible mechanism for the obtained results, detailed spatio-temporal characteristics and kinematic and kinetic characteristics of the gait cycle were not investigated in this thesis. Exploration of these outcomes was limited as data collection occurred along a 30-m long corridor that was not equipped with force plates or a 3D motion capture system. However, this increased stepping variability was clearly evident, especially when walking with the WRE in the free-trajectory modes, highlighted by the standard deviations from several consecutive steps in each of the 20 abled-bodied individuals. Such an increased stepping variability justifies, in part, why the three consecutive steps with the smallest variation were selected for the MSs analysis to attribute the observed changes to specific WRE control modes, rather than stepping variability.

Limitations related to the extraction of MSs (i.e., NNMF) impeded the inclusion of two additional participants who completed training in Article #3. The extraction and interpretation of the MSs was not feasible in the two excluded participants, who presented with very severe paresis or paralysis of key L/E muscles, warranting future methodological development. The inactive L/E EMG signals, resulting from severely paretic or paralyzed muscles (i.e., presenting raw EMG signal lower than 10 mV), were extracted by the NNMF algorithm as additional and functional MSs that

contained these inactive muscles. These MSs were then grouped as falsely presenting the same temporal activation profile represented by the physiological EMG signal noise. This phenomenon might limit the generalization of this technique over a larger and heterogeneous population of individuals with iSCI. Caution is advised when collecting surface EMG, since it is plausible that inactive L/E muscles, presenting very weak or aberrant signals, might interfere with the extraction and interpretation of the MSs.

6.4 Clinical implications for clinical practice

The clinical implications of the work presented in this thesis are discussed according to two separate aspects, MSs and WRE control modes.

6.4.1 Muscle synergies to assess the effectiveness of a rehabilitation intervention

Assessing characteristics and patterns of MSs may provide an important tool to the rehabilitation field to help understand why, for example, a particular intervention works for one patient and not for another. It may also help to track changes over time during a particular intervention by evaluating how plasticity in control of movement develops at the neural level.

The necessity of assessing the effects of a specific rehabilitation intervention is of high importance in individuals with iSCI. As previously mentioned, this population is characterized by a wide range of impairments and disabilities that make the task of exploring and interpreting muscle coordination patterns during walking difficult. However, gaining insights into L/E muscle coordination is key to informing the creation of personalized rehabilitation interventions. In this thesis, MSs were used to understand adaptations to motor coordination with the ultimate goal of guiding therapeutic decision-making processes. This work was also completed with consideration to the best WRE control modes that could be applied based on the participant's individual neural output.

However, the methodological complexity linked to the extraction of MSs and their analyses slows its implementation in clinical practice. For instance, although MSs are considered to be constant across locomotor tasks (e.g., running, balancing, and walking), there are reported

variations on the characteristics of the MSs (i.e., number, weighting composition, temporal profile) that may depend, among other factors, on the number of recorded muscles, electrode placement, EMG data processing protocols, and algorithms for extracting MSs. Thus, it is crucial to overcome these potential methodological biases by means of standardized data collection protocols, and better sharing of data collection and analysis methodologies between research groups. This standardization is also important is the training and qualifications of the professionals, postdoctoral fellows or graduate students who could eventually oversee the implementation of MSs analysis in clinical practice. Once accurate muscle signals are recorded, one of the main limitations of this approach is the EMG data processing (i.e., filter, rectification, and removal of artifacts signals) that can alter the characteristics of the extracted MSs and its interpretation. For example, if a movement artifact is not removed from an individual EMG signal, the MSs weighting composition will appear dominated by a particular muscle, masking the contribution of other muscles within a given synergy. This bias can be later misinterpreted as an aberrant MSs. All of these aspects were meticulously analyzed and taken into consideration in this thesis and should not represent an important source of bias.

6.4.2 Individualized selection of exoskeleton control modes to best meet client needs

In this thesis, the extraction of MSs from EMG signals of key L/E muscles was presented as a way to determine whether or not a WRE can positively affect muscle coordination towards those used during overground walking in abled-bodied individuals. The fact that the most commonly used control modes (i.e., trajectory-controlled passive and active modes) tested during walking with a WRE have failed to do so needs to be very carefully interpreted. In fact, the lack of evidence confirming the superior effects of locomotor training programs with a WRE over conventional rehabilitation interventions may be explained in part by the control mode used in these studies. Nonetheless, this remains debatable based on the current state of knowledge and justifies the need for more research in this field.

According to the MS characteristics investigated (i.e., number and weighting muscle composition) the non-trajectory-controlled mode HASSIST best recreated L/E muscle

coordination typical of overground walking. However, this highlights only one of the many clinical utilities of the WRE. In fact, other control modes may better address certain rehabilitation objectives. As an example, if the objective was to strengthen the hip flexors and extensors via an activity-based rehabilitation intervention, it is possible that the HRESIST control mode may better allow therapists to reach this objective. Thus, there are several research opportunities for therapists to gain a better understanding of the pros and cons of each control mode, including how the control modes could be used sequentially during a rehabilitation intervention to optimize walking abilities.

6.5 Future research opportunities

6.5.1 Short term

Over the last decade, extensive effort has been made to provide evidence that MSs reflect the CNS substrate for muscle coordination and their potential for the evaluation of the neural control of different functional tasks. The results of this thesis support the relevance of using MSs to evaluate movement control. Analysis of MS recruitment has demonstrated that altered muscle coordination patterns after an iSCI can be modified and approach those patterns found in able-bodied individuals. These findings lead to investigating the neurophysiological and clinical impact of such changes to muscle coordination.

6.5.1.1 Clinical effects of “normalizing” muscle synergies

Based on the findings of this thesis, a key step could be to investigate the effects of long-term locomotor training protocols, using specific WRE control modes that normalize MSs weightings and adhering to the basic locomotor rehabilitation principles. First, data collection techniques and analysis methods should be refined to overcome some of the limitations of this thesis, such as precisely defining the stance and swing phases during WRE walking (e.g. using Instrumented pressure insoles) and advancing analysis methods to better account for paralysed muscle(s). Second, a better understanding of how WRE control modes affect muscle synergies during walking should be investigated by testing a subset of WRE control modes that have the

best potential for beneficial effects on MSs within a larger sample of individuals with an iSCI, while also adopting a more robust research design.

Testing and comparing WRE-based interventions aiming to "*normalize*" muscle synergies represents another key step to enabling the creation of an evidence-based WRE locomotor training program. When testing intervention effects among individuals with chronic iSCI, it has been suggested that such a program should include at least 45 sessions (Khan et al., 2019). Previous work investigating the safety and feasibility of locomotor training with the Ekso GT WRE (i.e., the WRE used in this thesis) among individuals with iSCI undergoing acute rehabilitation (i.e., less than 6 months after injury) have shown that completing 25 training sessions was safe in terms of cardiovascular stability, effort, skin integrity, pain and falls (Manns, Hurd, & Yang, 2019). Thus, locomotor training protocols with a WRE could be performed in acute and chronic SCI to explore rehabilitation using locomotor training. Such locomotor training should include comprehensive clinical, biomechanical (kinematics, kinetics, and EMG), and neurophysiological (spinal and cortical) assessments to monitor neurological and musculoskeletal adaptations and their effects on performance during walking and walking-related tasks. The endpoint of such a specific locomotor training could translate into reduced compensatory mechanisms that, after an iSCI, induce common maladaptive plasticity in movement control over the long-term.

It would also be interesting to investigate whether or not locomotor training that uses specific WRE control modes (i.e. those that bring MS patterns closer to the typical patterns found in able-bodied individuals) would translate into better adaptation to challenging environmental conditions (i.e., walking around obstacles, over uneven terrain, or on stairs). It is plausible that training locomotor circuits to access proper MS activity would lead to an improved accessibility of normal MS configurations by the CNS. This could allow a flexible combination of spinal motor modules that translate into better adaptations to different walking and environmental conditions. In the long-term, the characterization of the effects of specific WRE control modes normalizing muscle coordination could be used to formulate the first evidence-based recommendations to inform selection of the '*best*' WRE control mode in clinical practice.

6.5.1.2 Exploring spinal and supraspinal changes after MS modifications

In human subjects, direct assessment of changes at the spinal level remain challenging. Spinal reflexes participate in the regulation of EMG amplitudes of various muscles during different phases of gait (Rossignol, Dubuc, & Gossard, 2006). Clinically, these reflexes can inform the therapist about three important factors: 1) the efficacy of sensory afferents to depolarized motoneurons; 2) the functional state of spinal circuits; and 3) the spinal integrations of sensory afferent feedbacks (Smith & Knikou, 2016). Thus, one interesting approach to evaluate such changes in relation to improvements in muscle coordination, is the assessment of heteronymous spinal pathways. This approach can shed light on motoneuron activity across various joints and providing insight to the different spinal levels that are related to muscle coordination deficits (Dyer, Maupas, de Andrade Melo, Bourbonnais, & Forget, 2011). Clinically, changes in heteronymous modulation translate into muscle co-contraction or muscle incoordination. These changes are relate to merged or altered muscle weighting composition, which are also present when exploring MSs that contribute to reduced walking abilities (Hayes et al., 2014). Thus, it is plausible that this approach could investigate spinal changes that are linked to facilitatory or inhibitory aspects of a particular muscle group. In turn, this would aid in understanding how training that is aimed at normalizing muscle coordination could modify interneural spinal circuits. Moreover, understanding these spinal changes is key to future applications of the evidence that has emerged from the WRE control modes explored in this thesis.

Since the recovery of voluntary movement must involve supraspinal control in individuals with iSCI, it would be relevant to assess how WRE control modes that are free from an imposed L/E trajectory would affect voluntary movement recovery. In previous studies, the supraspinal and cortical changes after a SCI have been explored by combining electrical stimulation of the median nerves with recordings of somatosensory evoked potentials (SEP) to explore cortical representation of motor evoked potentials (Sczesny-Kaiser et al., 2015). The use of neuroimaging techniques or of transcranial magnetic stimulation (TMS) to evaluate neuroplasticity of the corticospinal pathways may also represent promising techniques to explore supraspinal changes after locomotor training using a WRE to determine which control modes have the best potential to have beneficial effects on MSs.

6.5.2 Mid and Long term

6.5.2.1 Exoskeleton implementation on the clinical field

Although several health centers in the United States are already using WRE devices as part of the rehabilitation process, the empirical application of the control modes chosen for locomotor training protocols among individuals with iSCI reduces the possibility of implementing such robotic devices on a larger scale. Locomotor training programs utilizing a WRE can personalize settings to achieve close-to-normal muscle coordination patterns, and these individual patterns may be key to confirming the utility and probable superiority of WRE-based training in the rehabilitation field.

However, WRE research and the implementation process of WRE-related rehabilitation are mainly hindered by the high cost of these devices and the need of highly skilled rehabilitation professionals. It is possible that expensive WREs containing a vast quantity of features do not induce meaningful and functional neuromuscular changes, as demonstrated by the trajectory-controlled modes for the iSCI population. As such, instead of focusing on their clinical implementation, specific control modes (e.g., HASSIST) could be used as a reference to develop new robotic devices. This would avoid expensive and complex materials and irrelevant features. In turn, this could lead to the development of more affordable devices containing only essential features to optimize neurorecovery, eventually facilitating its clinical implementation.

6.5.2.2 Muscle synergies as a clinical tool

In the future, MSs may prove to be an essential tool for decision making and for individualizing walking-related rehabilitation interventions. However, further development or improvements of certain aspects of the WRE are needed. These include user-friendly interfaces for EMG recording and the development of advanced analysis methods to account for paralysed muscle(s) when extracting MSs. These techniques would, in turn, streamline the MS extraction process. With the accelerated rate of scientific and technological developments, these streamlined data collection and analysis methods should soon become feasible and may accelerate the implementation of the MS approach in clinical and research settings. As the use of MSs to characterize L/E motor control during walking continues to increase, MSs may prove to be

useful in creating distinct participant groups, based on motor control criteria, and design for them specific locomotor therapeutic interventions, including locomotor training with a WRE set in a specific control mode.

CHAPTER 7 – CONCLUSION

Robotic neurorehabilitation still constitutes an emerging field, requiring further research to investigate the implications of locomotor training and its superior effects over other conventional rehabilitation approaches. By exploring MSs in an effort to assess the integrity of the underlying neural strategies supporting muscle activity during walking, this research has deepened the understanding and interpretation of external elements that might modify MSs, heading towards a more patient-centered approach when using WRE devices.

By evaluating L/E muscle coordination through MSs, this thesis has shown that: (1) reducing walking speed maintains the number and composition of four well-identified MSs, whereas increasing walking speed tends to merge some of these synergies during overground walking; (2) compared to passively- or actively-controlled L/E swing trajectories, a WRE without L/E swing trajectory control best duplicates the typical MSs found during overground walking in both able-bodied individuals and those with iSCI; and (3) of all the non-trajectory controlled modes explored in individuals with iSCI, only the HASSIST best replicates MSs observed in healthy individuals during overground walking.

Additional studies enrolling larger samples of participants with iSCI are needed to strengthen this evidence, inform the development of upcoming research projects, and further support clinical practice. Nonetheless, the work presented in this thesis represents the first step in informing the decision-making process regarding the interpretation of MSs during overground walking and the use of additional WRE L/E control options to rehabilitate the natural modular organization of walking.

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ANNEXES

I. Ethics certificates

I.I Scientific article #1 and #2

Comité d'éthique de la recherche
des établissements du CRIR

Montréal, le 11 avril 2017 — **PAR COURRIER ÉLECTRONIQUE**

Monsieur Dany Gagnon, Ph.D.
CRIR - site de l'IRGLM du CCSMTL

Centre de réadaptation Constance-Lethbridge
Centre de réadaptation Lucie-Bruneau
Hôpital juif de réadaptation
Institut de réadaptation Gingras-Lindsay-de-Montréal
Institut Nazareth et Louis-Braille
Institut Raymond-Dewar

Partenaires
Centre de réadaptation en déficience physique Le Bouclier
Centre de réadaptation Estrie
Centre de réadaptation MAB-Mackay

Objet : Émission de votre certificat d'éthique
Notre dossier : CRIR-1225-0317

Monsieur,

Veuillez trouver, ci-joint, une copie du certificat d'éthique qui a été décerné pour votre projet de recherche intitulé « Comparaison de la performance locomotrice lors de marche au sol avec et sans l'exosquelette robotisé: Une étude exploratoire chez des personnes en bonne santé ». Ce certificat, ainsi que les documents approuvés, sont également disponibles sur la plateforme de soumission des projets de recherche.

Accès : http://ethique.crir.ca/acceschercheur/

Ce certificat est valable pour un an. Le CÉR demande à être informé de toute modification qui pourrait être apportée au projet de recherche mentionné ci-dessus (Formulaire M à compléter via la plateforme).

Nous vous invitons à communiquer avec la personne suivante afin de l'aviser du début de votre projet de recherche :

- Institut de réadaptation Gingras-Lindsay-de-Montréal
  Madame Marie-Thérèse Laramée

Nous vous souhaitons bonne chance dans la réalisation de votre projet. Veuillez recevoir, Monsieur Gagnon, mes cordiales salutations.

Me Anik Nolet
Coordonnatrice à l'éthique de la recherche
des établissements du CRIR

AN/cl

Pièces jointes : certificat d'éthique et copie des documents approuvés

c.c. : Marie-Thérèse Laramée, IRGLM du CIUSSS du Centre-Sud-de-l'Île-de-Montréal

Comité désigné en vertu de l'article 21 du Code civil du Québec

Comité d'éthique de la recherche
des établissements du CRIR

Certificat d'éthique

Par la présente, le comité d'éthique de la recherche des établissements du CRIR (CÉR) atteste qu'il a évalué, par voie accélérée, le projet de recherche **CRIR-1225-0317** intitulé :

« Comparaison de la performance locomotrice lors de marche au sol avec et sans l'exosquelette robotisé ».

Présenté par : **Dany Gagnon, Ph.D**
Cyril Duclos, Ph.D.
Jérémy Da Cunha, étudiant à la maîtrise
Mael Boyer, étudiant à la maîtrise

Le présent projet répond aux exigences éthiques de notre CÉR. Le Comité autorise donc sa mise en œuvre sur la foi des documents suivants :

- **Lettre de présentation datée du 7 mars 2017 ;**
- **Formulaire A ;**
- **Formulaire de l'Institut de réadaptation Gingras-Lindsay de Montréal, daté du 14 mars 2017, attestant que l'établissement accueille favorablement le projet sur le plan de la convenance institutionnelle ;**
- **Formulaire du Comité d'évaluation scientifique du CRIR, daté du 29 mars 2017, attestant de la validité scientifique du projet ;**
- **Protocole de recherche ;**
- **Formulaire de consentement (version française du 11 avril 2017).**

Ce projet se déroulera dans le site du CRIR suivant :

- **Institut de réadaptation Gingras-Lindsay de Montréal du CIUSSS du Centre-Sud-de-l'Île-de-Montréal**

Ce certificat est valable pour un an. En acceptant le présent certificat d'éthique, le chercheur s'engage à :

1. Informer, dès que possible, le CÉR de tout changement qui pourrait être apporté à la présente recherche ou aux documents qui en découlent (Formulaire M) ;
2. Notifier, dès que possible, le CÉR de tout incident ou accident lié à la procédure du projet ;

3. Notifier, dès que possible, le CÉR de tout nouveau renseignement susceptible d'affecter l'intégrité ou l'éthicité du projet de recherche, ou encore, d'influer sur la décision d'un sujet de recherche quant à sa participation au projet ;
4. Notifier, dès que possible, le CÉR de toute suspension ou annulation d'autorisation relative au projet qu'aura formulée un organisme de subvention ou de réglementation ;
5. Notifier, dès que possible, le CÉR de tout problème constaté par un tiers au cours d'une activité de surveillance ou de vérification, interne ou externe, qui est susceptible de remettre en question l'intégrité ou l'éthicité du projet ainsi que la décision du CÉR ;
6. Notifier, dès que possible, le CÉR de l'interruption prématurée, temporaire ou définitive du projet. Cette modification doit être accompagnée d'un rapport faisant état des motifs à la base de cette interruption et des répercussions sur celles-ci sur les sujets de recherche ;
7. Fournir annuellement au CÉR un rapport d'étape l'informant de l'avancement des travaux de recherche (formulaire R) ;
8. Demander le renouvellement annuel de son certificat d'éthique ;
9. Tenir et conserver, selon la procédure prévue dans la *Politique portant sur la conservation d'une liste des sujets de recherche*, incluse dans le cadre réglementaire des établissements du CRIR, une liste des personnes qui ont accepté de prendre part à la présente étude ;
10. Envoyer au CÉR une copie de son rapport de fin de projet / publication.
11. En vertu de l'article 19.2 de la *Loi sur les services de santé et les services sociaux*, obtenir l'autorisation du Directeur des services professionnels de l'établissement sollicité pour prendre part avant d'aller consulter les dossiers des usagers de cet établissement.

Me Michel T. Giroux
Président du CÉR

Date d'émission
11 avril 2017

I.II Scientific article #3

Comité d'éthique de la recherche
des établissements du CRIR

Montréal, le 23 juin 2016

Monsieur Dany Gagnon, Ph.D.
CRIR - site de l'IRGLM

- Centre de réadaptation Constance-Lethbridge
- Centre de réadaptation Lucie-Bruneau
- Hôpital juif de réadaptation
- Institut de réadaptation Gingras-Lindsay-de-Montréal
- Institut Nazareth et Louis-Braille
- Institut Raymond-Dewar

Partenaires

- Centre de réadaptation en déficience physique Le Bouclier
- Centre de réadaptation Estrie
- Centre de réadaptation MAB-Mackay

Objet : Émission de votre certificat d'éthique
Notre dossier : CRIR-1029-0115

Monsieur,

Veuillez trouver, ci-joint, une copie du certificat d'éthique qui a été décerné pour votre projet de recherche intitulé « L'effet d'un programme d'entraînement locomoteur avec un exosquelette robotisé sur les capacités locomotrices des personnes ayant subi une lésion médullaire incomplète ». Ce certificat, ainsi que les documents approuvés, sont également disponibles sur la plateforme de soumission des projets de recherche.

Accès : http://ethique.crir.ca/acceschercheur/

Ce certificat est valable pour un an. Le CÉR demande à être informé de toute modification qui pourrait être apportée au projet de recherche mentionné ci-dessus (Formulaire M à compléter via la plateforme).

Nous vous invitons à contacter les personnes suivantes afin de les aviser du début de votre projet de recherche :

- Centre de réadaptation Lucie-Bruneau
  Madame Geneviève Baril
- Institut de réadaptation Gingras-Lindsay-de-Montreal
  Madame Marie-Thérèse Laramée
- Institut de réadaptation en déficience physique du Québec
  Madame Lyne Martel

À noter que vous pourrez débuter votre projet à l'IRDPQ uniquement lorsque vous recevrez l'autorisation de la personne dûment mandatée par le CIUSSS de la Capitale-Nationale.

.../2

Nous vous souhaitons la meilleure des chances dans la réalisation de votre projet.

Veuillez recevoir, Monsieur Gagnon, mes cordiales salutations.

Me Anik Nolet
Coordonnatrice à l'éthique de la recherche
des établissements du CRIR

AN/cl

Pièces jointes : certificat d'éthique et copie des documents approuvés

c.c. : Geneviève Baril, CRLB du Centre-Sud-de-l'Île-de-Montréal
Marie-Thérèse Laramée, IRGLM du CIUSSS du Centre-Sud-de-l'Île-de-Montréal
Lyne Martel, IRDPQ du CIUSSS de la Capitale-Nationale

Comité d'éthique de la recherche
des établissements du CRIR

Certificat d'éthique

Par la présente, le comité d'éthique de la recherche des établissements du CRIR (CÉR) atteste qu'il a évalué le projet de recherche **CRIR-1029-0115** intitulé :

«L'effet d'un programme d'entraînement locomoteur avec un exosquelette robotisé sur les capacités locomotrices des personnes ayant subi une lésion médullaire incomplète »

Présenté par: **Dany Gagnon, Ph.D.**
Sylvie Nadeau, Ph.D.
Cyril Duclos, Ph.D.
Laurent Bouyer, Ph.D.
François Routhier, Ph.D.

Le présent projet répond aux exigences éthiques de notre CÉR. Le Comité autorise donc sa mise en œuvre sur la foi des documents suivants :

- **Lettre d'introduction datée du 6 janvier 2015;**
- **Formulaire A;**
- **Formulaire d'évaluation du Centre de réadaptation Lucie-Bruneau, daté du 23 janvier 2015, mentionnant que le projet est acceptable sur le plan de la convenance institutionnelle;**
- **Formulaire d'évaluation de l'Institut de réadaptation Gingras-Lindsay de Montréal, daté du 20 janvier 2015, mentionnant que le projet est acceptable sur le plan de la convenance institutionnelle;**
- **Évaluation scientifique du 1er août 2014 réalisée par l'Institut Rick Hansen;**
- **Preuve d'octroi d'une subvention de 100 000 $ de l'Institut Rick Hansen;**
- **Preuve d'octroi d'une subvention de 30 000 $ et don d'un exosquelette par la compagnie « Bionik Laboratories»;**
- **Budget;**
- **Résumé sommaire du projet;**
- **Protocole de recherche;**
- **Contrat avec l'Institut Rick Hansen;**
- **Formulaire de consentement destiné aux participants ayant subi une lésion médullaire (version du 23 juin 2016);**
- **Affiche de recrutement (23 juin 2016);**
- **Cahier d'évaluation clinique : T1;**
- **Cahier d'évaluation clinique : T2;**
- **Cahier d'évaluation clinique : T3**
- **Licence d'établissement pour les instruments médicaux 5213 décernée Ekso Bionics en date du 31 janvier 2013 ;**
- **Courriel de Dany Gagnon daté du 18 mai 2016.**

Ce projet se déroulera dans les sites du CRIR suivants :

- **Centre de réadaptation Lucie-Bruneau du CIUSSS du Centre-Sud-de-l'Île-de-Montréal**
- **Institut de réadaptation Gingras-Lindsay de Montréal du CIUSSS du Centre-Sud-de-l'Île-de-Montréal**

Ce certificat est valable pour un an. En acceptant le présent certificat d'éthique, le chercheur s'engage à :

1. Informer, dès que possible, le CÉR de tout changement qui pourrait être apporté à la présente recherche ou aux documents qui en découlent (Formulaire M) ;
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3. Notifier, dès que possible, le CÉR de tout nouveau renseignement susceptible d'affecter l'intégrité ou l'éthicité du projet de recherche, ou encore, d'influer sur la décision d'un sujet de recherche quant à sa participation au projet ;
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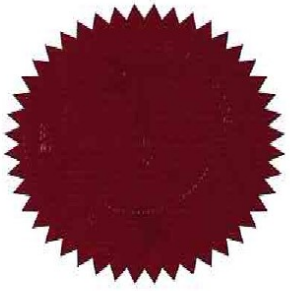
6. Notifier, dès que possible, le CÉR de l'interruption prématurée, temporaire ou définitive du projet. Cette modification doit être accompagnée d'un rapport faisant état des motifs à la base de cette interruption et des répercussions sur celles-ci sur les sujets de recherche ;
7. Fournir annuellement au CÉR un rapport d'étape l'informant de l'avancement des travaux de recherche (formulaire R) ;
8. Demander le renouvellement annuel de son certificat d'éthique ;
9. Tenir et conserver, selon la procédure prévue dans la *Politique portant sur la conservation d'une liste des sujets de recherche*, incluse dans le cadre réglementaire des établissements du CRIR, une liste des personnes qui ont accepté de prendre part à la présente étude ;
10. Envoyer au CÉR une copie de son rapport de fin de projet / publication ;
11. En vertu de l'article 19.2 de la *Loi sur les services de santé et les services sociaux*, obtenir l'autorisation du Directeur des services professionnels de l'établissement sollicité avant d'aller consulter les dossiers des usagers de cet établissement, le cas échéant.



Me Michel T. Giroux
Président du CÉR

Date d'émission
23 juin 2013

Composition du comité d'éthique de la recherche des établissements du CRIR

M. Simon Coulombe / Mme Delphine Labbé (membre substitut)	Une personne possédant une vaste connaissance du domaine psychosocial en réadaptation
Dre Céline Lamarre / Mme Imen Khelia (membre substitut)	Une personne possédant une vaste connaissance du domaine biomédical en réadaptation
Mme Saïda El Haïli / Mme Isabelle Fournier (membre substitut)	Clinicien détenant une vaste connaissance des déficits sensoriel visuels ou auditifs
Mme Mariama Touré / M. Dany Gagnon (membre substitut)	Clinicienne détenant une vaste connaissance des déficits moteurs ou neurologiques
M. Yanick Farmer / Me Delphine Roigt (membre substitut)/	Une personne spécialisée en éthique
Me Michel T. Giroux / Me Nathalie Lecoq (membre substitut)	Une personne spécialisée en droit
Mme Monique Provost / Mme Marie-Claude Lavigne (membre substitut)	Une personne non affiliée à l'établissement et provenant de la clientèle des personnes adultes et aptes
Mme Diane L. Gaumond / Mme Dominique Labrèche (membre substitut)	Une personne non affiliée à l'établissement et provenant de la clientèle des personnes mineures ou inaptes
M. Michel Sinotte /	Une personne siégeant à titre de représentante du public
Mme Suzette McMaster Clément	Une personne siégeant à titre de représentante du public
À déterminer	Représentant de l'Université du Québec à Montréal
M. Cyril Duclos	Représentant de l'Université de Montréal
Mme Patricia McKinley	Représentante de l'Université McGill
Me Anik Nolet	Secrétaire du CER et membre non-votant

II. Consent forms

II.I Scientific articles #1 and #2

FORMULAIRE D'INFORMATION ET DE CONSENTEMENT

1. TITRE DU PROJET

Analyse de l'activité et des synergies musculaires aux membres inférieurs lors de la marche au sol sans et avec un exosquelette robotisé de marche: Une étude exploratoire auprès de personnes en bonne santé.

2. RESPONSABLE DU PROJET

Dany Gagnon, pht, PhD
Professeur agrégé
École de réadaptation, Université de Montréal
Chercheur régulier
Laboratoire de pathokinésiologie, Centre de recherche interdisciplinaire en réadaptation du Montréal métropolitain (CRIR)
Institut de réadaptation Gingras-Lindsay de Montréal (IRGLM) | CIUSSS Centre-Sud-de-l'Île-de-

3. COLLABORATEURS

Manuel J. Escalona Castillo, MSc
Candidat au Doctorat en Sciences de la réadaptation
École de réadaptation, Université de Montréal
Laboratoire de pathokinésiologie, CRIR site IRGLM

Damien Le Flem, TRP
Étudiant à la M. Sc. physiothérapie, stagiaire de recherche sous la direction de Dany Gagnon
École de réadaptation, Université de Montréal
Laboratoire de pathokinésiologie, CRIR site IRGLM

Martin Vermette, pht, MSc
Professionnel de recherche en réadaptation
Laboratoire de pathokinésiologie, CRIR site IRGLM

4. ORGANISME SUBVENTIONNAIRE

Ce projet est financé en grande partie via l'Initiative pour le développement de nouvelles technologies et pratiques en réadaptation (INSPIRE; 2015-2020) financée par la Fondation LRH détenue par D. Gagnon. De plus, le projet s'insère dans les travaux prévus suite à l'obtention récente d'une subvention d'infrastructure 'Fonds des leaders' du Fond canadien pour l'Innovation (FCI ; 2017-2022) : Infrastructure de recherche pour permettre de nouvelles avancées scientifiques en lien avec les exosquelettes robotisés portables utilisés pour la marche au sol.

5. PRÉAMBULE

Nous vous invitons à participer à un projet de recherche visant à mieux comprendre la performance locomotrice lors de la marche au sol avec et sans un exosquelette robotisé de marche au sol (EXORM). Avant d'accepter de participer à ce projet de recherche, veuillez prendre le temps de lire, de comprendre et de considérer attentivement les renseignements présentés dans ce formulaire.

Le présent formulaire de consentement vous explique les buts, les procédures, les avantages, les risques et inconvénients de cette étude, de même que les personnes avec qui communiquer au besoin.

Le présent formulaire de consentement peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles aux chercheurs et aux autres membres du personnel affectés au projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

6. DESCRIPTION DU PROJET ET DE SES OBJECTIFS

La capacité locomotrice est fréquemment diminuée chez les personnes aux prises avec des déficiences sensorimotrices, notamment en termes de vitesse, d'endurance à la marche mais aussi d'indépendance fonctionnelle. Avec un patron locomoteur souvent affecté et modifié par plusieurs mouvements compensatoires, ces individus sont également plus susceptibles de perdre l'équilibre voire de chuter. Il est donc essentiel de tenter d'améliorer leur capacité ambulatoire via un entraînement locomoteur spécifique, intensif et répétitif, particulièrement lors de la réadaptation fonctionnelle intensive.

Plusieurs principes d'assistance à la mobilité ont été développés ces dernières années dans le but de favoriser et de faciliter l'entraînement locomoteur des personnes atteintes de déficiences sensorimotrices. Les exosquelettes robotisés de marche au sol (EXORM) représentent l'une de ces technologies émergentes en réadaptation et en activité physique adaptée. Les EXORM produisent une assistance ou une résistance motorisée aux hanches et aux genoux pour faciliter ou résister les mouvements spécifiques de marche. Un EXORM pèse généralement plus de 25 kg, supporte une masse corporelle maximale de 100 kg et accommode une gamme de largeurs de bassin (30 - 46 cm) et de tailles (1,52 - 1,93 m). Des capteurs de pression et des accéléromètres permettent à l'EXORM de détecter en temps réel les mouvements du corps et le déplacement du centre de gravité par rapport à la base de sustentation. Ces afférences sont prises en compte via des algorithmes d'intelligence artificielle

complexes permettant de produire en synergie les mouvements aux hanches, genoux et chevilles nécessaires aux transitions assis-debout et à une marche sécuritaire et fluide.

Indépendamment de la capacité locomotrice intrinsèque de l'EXORM (c.-à-d. une vitesse maximale de 1,6 m/s), le niveau de performance locomotrice attendu d'une personne avec des déficiences sensorimotrices lors de la marche au sol avec un EXORM demeure méconnu. De plus, on ne sait pas si la marche au sol sans et avec l'EXORM est similaire ou non chez une personne en bonne santé, particulièrement en termes de vitesse, de distance et de recrutement musculaire aux membres inférieurs lors de la marche. Enfin, les effets de l'utilisation d'un EXORM sur l'activité et les synergies musculaires aux membres inférieurs lors de la marche n'ont pratiquement pas été étudiés. C'est pourquoi nous croyons qu'il est nécessaire d'approfondir les connaissances en lien avec cette technologie novatrice.

L'**objectif principal** de cette étude exploratoire est donc de comparer l'activité électromyographique (EMG) des principaux muscles du membre inférieur, les différentes synergies musculaires en jeu ainsi que les paramètres spatiotemporaux qui caractérisent la marche avec et sans EXORM chez des personnes en bonne santé.
Ces nouvelles preuves scientifiques guideront le développement d'un nouveau programme d'entrainement locomoteur qui sera testé auprès de personnes ayant une lésion incomplète de la moelle épinière.

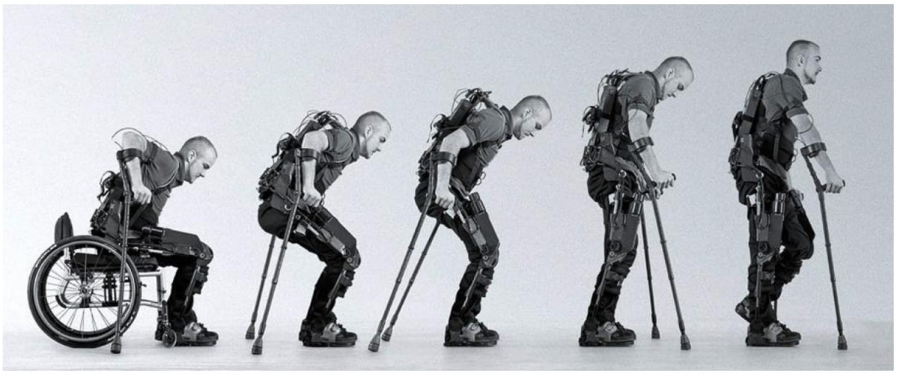


Figure 1 : Aperçu d'un exosquelette robotisé de marche au sol

7. NATURE DE LA PARTICIPATION

Votre participation à ce projet s'articule autour d'**une évaluation clinique initiale**, de **quatre séances d'entraînement** et d'**une évaluation finale** qui auront lieu au Laboratoire de pathokinésiologie du Centre de recherche en réadaptation du Montréal métropolitain situé à l'Institut de réadaptation Gingras-Lindsay-de-Montréal (4ème étage).

■ ***Évaluation clinique initiale***
Une évaluation clinique initiale sera complétée avant le programme d'entraînement. Elle durera un maximum de 20 minutes et permettra de confirmer l'éligibilité de chaque participant pour la marche avec l'exosquelette robotisé en plus de mesurer différents paramètres anthropométriques nécessaires à l'ajustement de l'EXORM

■ ***Séances d'entraînement***

Suite à la séance d'évaluation clinique, le programme d'entraînement locomoteur avec l'EXORM débutera. Ce programme inclura quatre séances d'entraînement réparties sur une période de deux semaines. Chaque séance durera 45 minutes. Au début de l'entraînement, vous vous familiariserez progressivement avec l'EXORM en pratiquant des tâches de passage assis-debout, d'équilibre en position debout et de marche dans un corridor avec une marchette. Au cours des séances, vous apprendrez progressivement à marcher en toute sécurité avec l'EXORM en modes passif (c.-à-d. aucun mouvement volontaire aux membres inférieurs), actif (c.-à-d. mouvements actifs aux membres inférieurs) et actif résisté (c.-à-d. mouvements actifs aux membres inférieurs avec résistance appliquée via l'exosquelette) en utilisant des béquilles canadiennes à des vitesses confortable et rapide ainsi qu'avec l'assistance humaine requise. En tout temps, vous serez accompagné minimalement par un physiothérapeute et/ou un thérapeute en réadaptation physique ainsi qu'un collaborateur de recherche.

■ **Évaluation finale**

L'évaluation finale, qui durera environ deux heures, comportera une évaluation de la marche : Vous devrez marcher dans un corridor une distance d'environ 20 mètres pour 9 conditions différentes:

- *Sans EXORM à vitesse naturelle*
- *Sans EXORM à vitesse rapide*
- *Sans EXORM à vitesse équivalente à celle avec EXORM en mode trajectoire libre, abduction déverrouillée et sans assistance (cadence rythmée par métronome)*
- *Avec EXORM en mode trajectoire contrôlée et assistance maximum*
- *Avec EXORM en mode trajectoire contrôlée et 0% assistance*
- *Avec EXORM en mode trajectoire libre et assistance maximum*
- *Avec EXORM en mode trajectoire libre et sans assistance*
- *Avec EXORM en mode trajectoire libre et résistance maximum*
- *Avec EXORM en mode trajectoire libre, abduction déverrouillée et sans assistance*

Avant l'évaluation de la marche, nous collerons des boitiers sans fil sur votre membre inférieur droit à l'aide de ruban adhésif après avoir nettoyé la peau. Ces boitiers permettront d'enregistrer l'EMG de plusieurs muscles importants pour la marche ainsi que les déplacements des différents segments impliqués lors de la locomotion.

8. AVANTAGES POUVANT DÉCOULER DE VOTRE PARTICIPATION

Vous ne retirerez personnellement pas d'avantage à participer à cette étude. Toutefois, vous contribuerez à l'avancement des connaissances en lien avec la performance locomotrice lors de la marche au sol avec un exosquelette robotisé.

9. RISQUES ET INCONVÉNIENTS POUVANT DÉCOULER DE VOTRE PARTICIPATION

■ ***Risques***

Le risque de perte d'équilibre ou de chute lors de l'exécution des transferts assis-debout et de la marche au sol avec l'EXORM ne peut être complètement éliminé. Afin de limiter ce risque, une personne expérimentée sera toujours à vos côtés afin d'assurer votre sécurité pendant les séances d'entraînement et les évaluations.

■ ***Inconvénients***

Les efforts demandés lors de l'évaluation clinique initiale, des séances d'entraînement et de l'évaluation finale pourraient entraîner tout au plus une certaine fatigue musculaire localisée et temporaire aux membres supérieurs ou inférieurs. À cet effet, des pauses pourront vous être accordées afin d'éviter l'installation de la fatigue qui devrait rapidement s'estomper une fois la séance d'entraînement ou l'évaluation terminée.
La pose de boitiers sans fil sur votre membre inférieur droit pourrait nécessiter le rasage de poils sur les surfaces où ils seront placés. Dans ce cas, soyez assurés que les règles d'hygiène les plus strictes seront mises en place à cet effet. En parallèle, il se pourrait que la peau en contact avec les boitiers sans fil devienne irritée suite à l'usage de produits adhésifs. Dans un tel cas, une lotion calmante sera appliquée sur votre peau à la fin du projet. Si l'irritation persiste au-delà de 36 heures, vous devrez aviser le responsable du projet.

10. Accès aux résultats à la fin de la recherche

À votre demande, une fois la présente étude terminée, vous aurez la possibilité d'obtenir un sommaire des résultats généraux découlant de ce projet.

Je souhaite recevoir un sommaire des résultats :

Non ☐ **Oui** ☐ courriel : _____

11. Confidentialité

Tous les renseignements personnels recueillis à votre sujet au cours de l'étude seront codifiés afin d'assurer leur confidentialité. Seuls les membres de l'équipe de recherche y auront accès. Cependant, à des fins de contrôle du projet de recherche, votre dossier de recherche pourrait être consulté par une personne mandatée par le Comité d'éthique de la recherche des établissements du CRIR ou par la Direction de l'éthique et de la qualité du Ministère de la santé et des services sociaux du Québec, qui adhère à une politique de stricte confidentialité. Les données de recherche colligées sur papier seront conservées sous clé dans une filière du Laboratoire de pathokinésiologie de l'IRGLM par le responsable de l'étude pour une période de cinq ans suivant la fin du projet. Les données de recherche colligées via informatique seront archivées sur une section protégée et à accès limitée pour la recherche sur le serveur informatique de l'IRGLM pour une période de cinq ans suivant la fin du projet. L'ensemble des données sera détruit cinq ans après la fin du projet. En cas de présentation de résultats ou de publication liée à cette recherche, rien ne pourra permettre de vous identifier.

12. Participation volontaire et droit de retrait

Vous êtes libre d'accepter ou de refuser de participer à ce projet de recherche. Vous pouvez vous retirer de cette étude à n'importe quel moment, sans avoir à donner de raison, ni à subir de préjudice de quelque nature que ce soit. Vous avez simplement à aviser la personne ressource de l'équipe de recherche, et ce, par simple avis verbal. En cas de retrait de votre part, les documents écrits vous concernant seront détruits, à votre demande.

13. ÉTUDES ULTÉRIEURES

Il se peut que les résultats obtenus à la suite de cette étude donnent lieu à une autre recherche. Dans cette éventualité, autorisez-vous le responsable de ce projet à vous contacter à nouveau et à vous demander si vous souhaitez participer à cette nouvelle recherche ?

- ☐ Non
- ☐ Oui pour une durée d'un an *
- ☐ Oui pour une durée de deux ans *
- ☐ Oui pour une durée de trois ans *

* *Notez que si vous cochez l'une des trois dernières cases, vos coordonnées personnelles seront conservées par le chercheur principal pour la période à laquelle vous avez consenti.*

14. RESPONSABILITÉ DE L'ÉQUIPE DE RECHERCHE

En acceptant de participer à cette étude, vous ne renoncez à aucun de vos droits ni ne libérez les chercheurs ou l'établissement de leurs responsabilités civiles et professionnelles.

15. INDEMNITÉ COMPENSATOIRE

Aucune indemnité compensatoire n'est prévue pour votre participation à l'évaluation initiale et aux séances d'entraînement. Pour l'évaluation finale, un montant de 25.00$ vous sera remis en contrepartie des contraintes et des inconvénients découlant de votre participation.
Notez que le stationnement vous sera remboursé lors des évaluations et des séances d'entraînement si vous utilisez celui situé devant le Pavillon Gingras de l'IRGLM.

16. PERSONNES-RESSOURCES

Si vous avez des questions concernant le projet de recherche, si vous souhaitez vous retirer de l'étude ou si vous voulez faire part à l'équipe de recherche d'un incident, vous pouvez contacter : Monsieur Dany Gagnon, pht, Ph.D., responsable du projet, Laboratoire de pathokinésiologie du CRIR situé à l'installation IRGLM du Centre-Sud-de-l'Île-de-Montréal, au

Si vous avez des questions sur vos droits et recours ou sur votre participation à ce projet de recherche, vous pouvez communiquer avec Me Anik Nolet, coordonnatrice à l'éthique de la recherche des établissements du CRIR

Pour ces questions, vous pouvez aussi contacter Madame Céline Roy, commissaire locale aux plaintes et à la qualité des services CIUSSS du Centre-Sud-de-l'Île-de-Montréal

17. CONSENTEMENT

Je déclare avoir lu et compris le présent projet, la nature et l'ampleur de ma participation, ainsi que les risques et les inconvénients auxquels je m'expose tel qu'expliqué dans le présent formulaire. J'ai eu l'occasion de poser toutes les questions concernant les différents aspects de l'étude et de recevoir des réponses à mes questions. Une copie signée de ce formulaire d'information et de consentement doit m'être remise.

Je, soussigné(e), accepte volontairement de participer à cette étude. Je peux me retirer en tout temps sans préjudice d'aucune sorte. Je certifie qu'on m'a laissé le temps voulu pour prendre ma décision.

NOM DU PARTICIPANT **SIGNATURE DU PARTICIPANT**

_____ _____

Fait à Montréal, le _____, 20_____

18. ENGAGEMENT DU CHERCHEUR OU DE SON REPRÉSENTANT

Je, soussigné (e), _____, certifie

(a) avoir expliqué au signataire les termes du présent formulaire;
(b) avoir répondu aux questions qu'il m'a posées à cet égard;
(c) lui avoir clairement indiqué qu'il reste, à tout moment, libre de mettre un terme à sa participation au projet de recherche décrit ci-dessus;
(d) que je lui remettrai une copie signée et datée du présent formulaire.

_____

Signature du responsable du projet ou de son représentant

Fait à Montréal, le _____, 20_____

II.II. Scientific article #3

FORMULAIRE D'INFORMATION ET DE CONSENTEMENT

1. TITRE DU PROJET

Analyse de l'activité et des synergies musculaires aux membres inférieurs lors de la marche au sol sans et avec un exosquelette robotisé de marche chez les personnes ayant une lésion médullaire incomplète.

2. RESPONSABLE DU PROJET

Dany Gagnon, pht, PhD
Professeur agrégé
École de réadaptation, Université de Montréal
Chercheur régulier
Laboratoire de pathokinésiologie, Centre de recherche interdisciplinaire en réadaptation du Montréal métropolitain (CRIR)
Institut de réadaptation Gingras-Lindsay de Montréal (IRGLM) | CIUSSS Centre-Sud-de-l'Île-de-Montréal

3. COLLABORATEURS

Manuel Escalona Castillo, MSc
Candidat au Doctorat en Sciences de la réadaptation
École de réadaptation, Université de Montréal
Laboratoire de pathokinésiologie, CRIR site IRGLM

Martin Vermette, pht, MSc
Professionnel de recherche en réadaptation
Laboratoire de pathokinésiologie, CRIR site IRGLM

4. ORGANISME SUBVENTIONNAIRE

Ce projet est financé en grande partie via l'Initiative pour le développement de nouvelles technologies et pratiques en réadaptation (INSPIRE; 2015-2020) financée par la Fondation LRH détenue par D. Gagnon. De plus, le projet s'insère dans les travaux prévus suite à l'obtention récente d'une subvention d'infrastructure 'Fonds des leaders' du Fond canadien pour l'Innovation (FCI ; 2017-2022) : Infrastructure de recherche pour permettre de nouvelles

avancées scientifiques en lien avec les exosquelettes robotisés portables utilisés pour la marche au sol.

5. PRÉAMBULE

Nous vous invitons à participer à un projet de recherche visant à mieux comprendre la performance locomotrice lors de la marche au sol avec et sans un exosquelette robotisé de marche au sol (EXORM). Avant d'accepter de participer à ce projet de recherche, veuillez prendre le temps de lire, de comprendre et de considérer attentivement les renseignements présentés dans ce formulaire.

Le présent formulaire de consentement vous explique les buts, les procédures, les avantages, les risques et inconvénients de cette étude, de même que les personnes avec qui communiquer au besoin.

Le présent formulaire de consentement peut contenir des mots que vous ne comprenez pas. Nous vous invitons à poser toutes les questions que vous jugerez utiles aux chercheurs et aux autres membres du personnel affectés au projet de recherche et à leur demander de vous expliquer tout mot ou renseignement qui n'est pas clair.

6. DESCRIPTION DU PROJET ET DE SES OBJECTIFS

La capacité locomotrice est fréquemment diminuée chez les personnes aux prises avec des déficiences sensorimotrices, notamment en termes de vitesse, d'endurance à la marche mais aussi d'indépendance fonctionnelle. Avec un patron locomoteur souvent affecté et modifié par plusieurs mouvements compensatoires, ces individus sont également plus susceptibles de perdre l'équilibre voire de chuter. Il est donc essentiel de tenter d'améliorer leur capacité ambulatoire via un entraînement locomoteur spécifique, intensif et répétitif, particulièrement lors de la réadaptation fonctionnelle intensive.

Plusieurs principes d'assistance à la mobilité ont été développés ces dernières années dans le but de favoriser et de faciliter l'entraînement locomoteur des personnes atteintes de déficiences sensorimotrices. Les exosquelettes robotisés de marche au sol (EXORM) représentent l'une de ces technologies émergentes en réadaptation et en activité physique adaptée. Les EXORM produisent une assistance ou une résistance motorisée aux hanches et aux genoux pour faciliter ou résister les mouvements spécifiques de marche. Un EXORM pèse généralement plus de 25 kg, supporte une masse corporelle maximale de 100 kg et accommode une gamme de largeurs de bassin (30 - 46 cm) et de tailles (1,52 - 1,93 m). Des capteurs de pression et des accéléromètres permettent à l'EXORM de détecter en temps réel les mouvements du corps et le déplacement du centre de gravité par rapport à la base de sustentation. Ces afférences sont prises en compte via des algorithmes d'intelligence artificielle complexes permettant de produire en synergie les mouvements aux hanches, genoux et chevilles nécessaires aux transitions assis-debout et à une marche sécuritaire et fluide.

Indépendamment de la capacité locomotrice intrinsèque de l'EXORM (c.-à-d. une vitesse maximale de 1,6 m/s), le niveau de performance locomotrice attendu d'une personne avec des déficiences sensorimotrices lors de la marche au sol avec un EXORM demeure méconnu. De plus, on ne sait pas si la marche au sol sans et avec l'EXORM est similaire ou non chez une personne en bonne santé, particulièrement en termes de vitesse, de distance et de recrutement musculaire aux membres inférieurs lors de la marche. Enfin, les effets de l'utilisation d'un EXORM sur l'activité et les synergies musculaires aux membres inférieurs lors de la marche n'ont pratiquement pas été étudiés. C'est pourquoi nous croyons qu'il est nécessaire d'approfondir les connaissances en lien avec cette technologie novatrice.

L'**objectif principal** de cette étude exploratoire est donc de comparer l'activité électromyographique (EMG) des principaux muscles du membre inférieur, les différentes synergies musculaires en jeu ainsi que les paramètres spatiotemporaux qui caractérisent la marche avec et sans EXORM chez des personnes ayant une lésion médullaire incomplète (LMi).
Ces nouvelles preuves scientifiques guideront le développement d'un nouveau programme d'entrainement locomoteur qui sera testé auprès de personnes ayant une LMi de la moelle épinière.

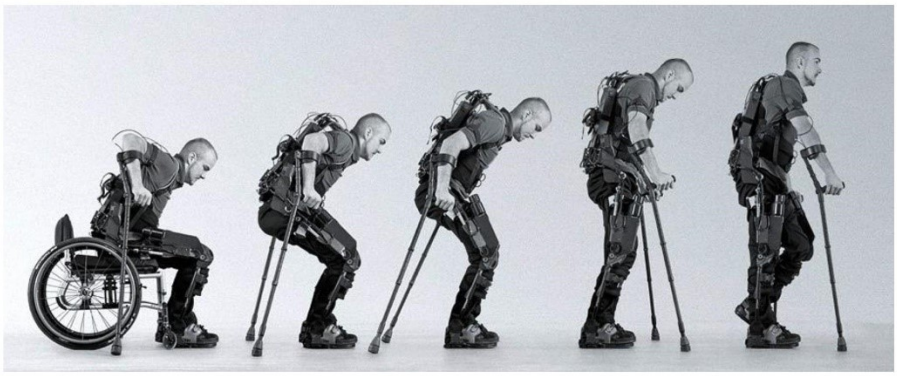


Figure 1 : Aperçu d'un exosquelette robotisé de marche au sol

7. NATURE DE LA PARTICIPATION

Votre participation à ce projet s'articule autour d'**une évaluation clinique initiale**, de **quatre séances d'entraînement** et d'**une évaluation finale** qui auront lieu au Laboratoire de pathokinésiologie du Centre de recherche en réadaptation du Montréal métropolitain situé à l'Institut de réadaptation Gingras-Lindsay-de-Montréal (4ème étage).

■ ***Évaluation clinique initiale***
Une évaluation clinique initiale sera complétée avant le programme d'entraînement. Elle durera un maximum de 20 minutes et permettra de confirmer l'éligibilité de chaque participant pour la marche avec l'exosquelette robotisé en plus de mesurer différents paramètres anthropométriques nécessaires à l'ajustement de l'EXORM

■ ***Séances d'entraînement***
Suite à la séance d'évaluation clinique, le programme d'entraînement locomoteur avec l'EXORM débutera. Ce programme inclura quatre séances d'entraînement réparties sur une période de deux semaines. Chaque séance durera 45 minutes. Au début de l'entraînement, vous vous familiariserez progressivement avec l'EXORM en pratiquant des tâches de passage assis-debout, d'équilibre en position debout et de marche dans un corridor avec une marchette. Au cours des séances, vous apprendrez progressivement à marcher en toute sécurité avec l'EXORM en modes passif (c.-à-d. aucun mouvement volontaire aux membres inférieurs), actif (c.-à-d. mouvements actifs aux membres inférieurs) et actif résisté (c.-à-d. mouvements actifs aux membres inférieurs avec résistance appliquée via l'exosquelette) en utilisant des béquilles canadiennes à des

vitesses confortable et rapide ainsi qu'avec l'assistance humaine requise. En tout temps, vous serez accompagné minimalement par un physiothérapeute et/ou un thérapeute en réadaptation physique ainsi qu'un collaborateur de recherche.

■ **Évaluation finale**
L'évaluation finale, qui durera environ deux heures, comportera une évaluation de la marche : Vous devrez marcher dans un corridor une distance d'environ 10 mètres pour 10 conditions différentes dans l'ordre suivant :

- *Sans EXORM à vitesse naturelle avec aide technique*
- *Sans EXORM à vitesse équivalente à celle avec EXORM en mode trajectoire libre, et sans assistance (cadence rythmée par métronome)*
- *Avec EXORM en mode trajectoire contrôlée et assistance maximale*
- *Avec EXORM en mode trajectoire contrôlée et assistance au besoin par le EXORM*
- *Avec EXORM en mode trajectoire libre et assistance maximale*
- *Avec EXORM en mode trajectoire libre et assistance minimale*
- *Avec EXORM en mode trajectoire libre et sans assistance*
- *Avec EXORM en mode trajectoire libre et résistance minimale*
- *Avec EXORM en mode trajectoire libre et résistance maximale*

Avant l'évaluation de la marche, nous collerons des boitiers sans fil sur vos membres inférieurs à l'aide de ruban adhésif après avoir nettoyé la peau. Ces boitiers permettront d'enregistrer l'EMG de plusieurs muscles importants pour la marche ainsi que les déplacements des différents segments impliqués lors de la locomotion.

8. AVANTAGES POUVANT DÉCOULER DE VOTRE PARTICIPATION

Vous ne retirerez personnellement pas d'avantage à participer à cette étude. Toutefois, vous contribuerez à l'avancement des connaissances en lien avec la performance locomotrice lors de la marche au sol avec un exosquelette robotisé.

9. RISQUES ET INCONVÉNIENTS POUVANT DÉCOULER DE VOTRE PARTICIPATION

■ ***Risques***
Le risque de perte d'équilibre ou de chute lors de l'exécution des transferts assis-debout et de la marche au sol avec l'EXORM ne peut être complètement éliminé. Afin de limiter ce risque, une personne expérimentée sera toujours à vos côtés afin d'assurer votre sécurité pendant les séances d'entraînement et les évaluations.

■ ***Inconvénients***
Les efforts demandés lors de l'évaluation clinique initiale, des séances d'entraînement et de l'évaluation finale pourraient entraîner tout au plus une certaine fatigue musculaire localisée et temporaire aux membres supérieurs ou inférieurs. À cet effet, des pauses pourront vous être accordées afin d'éviter l'installation de la fatigue qui devrait rapidement s'estomper une fois la séance d'entraînement ou l'évaluation terminée.
La pose de boitiers sans fil sur vos membres inférieurs pourrait nécessiter le rasage de poils sur les surfaces où ils seront placés. Dans ce cas, soyez assurés que les règles d'hygiène les plus strictes seront mises en place à cet effet. En parallèle, il se pourrait que la peau en contact avec les boitiers sans fil devienne irritée suite à l'usage de produits adhésifs. Dans un tel cas,

une lotion calmante sera appliquée sur votre peau à la fin du projet. Si l'irritation persiste au-delà de 36 heures, vous devrez aviser le responsable du projet.

10. Accès aux résultats à la fin de la recherche

À votre demande, une fois la présente étude terminée, vous aurez la possibilité d'obtenir un sommaire des résultats généraux découlant de ce projet.

Je souhaite recevoir un sommaire des résultats :

Non ☐ **Oui** ☐ courriel : _____

11. Confidentialité

Tous les renseignements personnels recueillis à votre sujet au cours de l'étude seront codifiés afin d'assurer leur confidentialité. Seuls les membres de l'équipe de recherche y auront accès. Cependant, à des fins de contrôle du projet de recherche, votre dossier de recherche pourrait être consulté par une personne mandatée par le Comité d'éthique de la recherche des établissements du CRIR ou par la Direction de l'éthique et de la qualité du Ministère de la santé et des services sociaux du Québec, qui adhère à une politique de stricte confidentialité. Les données de recherche colligées sur papier seront conservées sous clé dans une filière du Laboratoire de pathokinésiologie de l'IRGLM par le responsable de l'étude pour une période de cinq ans suivant la fin du projet. Les données de recherche colligées via informatique seront archivées sur une section protégée et à accès limitée pour la recherche sur le serveur informatique de l'IRGLM pour une période de cinq ans suivant la fin du projet. L'ensemble des données sera détruit cinq ans après la fin du projet. En cas de présentation de résultats ou de publication liée à cette recherche, rien ne pourra permettre de vous identifier.

12. Participation volontaire et droit de retrait

Vous êtes libre d'accepter ou de refuser de participer à ce projet de recherche. Vous pouvez vous retirer de cette étude à n'importe quel moment, sans avoir à donner de raison, ni à subir de préjudice de quelque nature que ce soit. Vous avez simplement à aviser la personne ressource de l'équipe de recherche, et ce, par simple avis verbal. En cas de retrait de votre part, les documents écrits vous concernant seront détruits, à votre demande.

13. Études ultérieures

Il se peut que les résultats obtenus à la suite de cette étude donnent lieu à une autre recherche. Dans cette éventualité, autorisez-vous le responsable de ce projet à vous contacter à nouveau et à vous demander si vous souhaitez participer à cette nouvelle recherche ?

☐ Non
☐ Oui pour une durée d'un an *
☐ Oui pour une durée de deux ans *
☐ Oui pour une durée de trois ans *

* *Notez que si vous cochez l'une des trois dernières cases, vos coordonnées personnelles seront conservées par le chercheur principal pour la période à laquelle vous avez consenti.*

14. Responsabilité de l'équipe de recherche

En acceptant de participer à cette étude, vous ne renoncez à aucun de vos droits ni ne libérez les chercheurs ou l'établissement de leurs responsabilités civiles et professionnelles.

15. Indemnité compensatoire

Aucune indemnité compensatoire n'est prévue pour votre participation à l'évaluation initiale et aux séances d'entraînement. Pour l'évaluation finale, un montant de 25.00$ vous sera remis en contrepartie des contraintes et des inconvénients découlant de votre participation.
Notez que le stationnement vous sera remboursé lors des évaluations et des séances d'entraînement si vous utilisez celui situé devant le Pavillon Gingras de l'IRGLM.

16. Personnes-ressources

Si vous avez des questions concernant le projet de recherche, si vous souhaitez vous retirer de l'étude ou si vous voulez faire part à l'équipe de recherche d'un incident, vous pouvez contacter : Monsieur Dany Gagnon, pht, Ph.D., responsable du projet, Laboratoire de pathokinésiologie du CRIR situé à l'installation IRGLM du Centre-Sud-de-l'Île-de-Montréal, au

Si vous avez des questions sur vos droits et recours ou sur votre participation à ce projet de recherche, vous pouvez communiquer avec Me Anik Nolet, coordonnatrice à l'éthique de la recherche des établissements du CRIR
suivante:

Pour ces questions, vous pouvez aussi contacter Madame Céline Roy, commissaire locale aux plaintes et à la qualité des services CIUSSS du Centre-Sud-de-l'Île-de-Montréal

17. Consentement

Je déclare avoir lu et compris le présent projet, la nature et l'ampleur de ma participation, ainsi que les risques et les inconvénients auxquels je m'expose tel qu'expliqué dans le présent formulaire. J'ai eu l'occasion de poser toutes les questions concernant les différents aspects de l'étude et de recevoir des réponses à mes questions. Une copie signée de ce formulaire d'information et de consentement doit m'être remise.

Je, soussigné(e), accepte volontairement de participer à cette étude. Je peux me retirer en tout temps sans préjudice d'aucune sorte. Je certifie qu'on m'a laissé le temps voulu pour prendre ma décision.

NOM DU PARTICIPANT **SIGNATURE DU PARTICIPANT**

_____ _____

Fait à Montréal, le _____, 20____

18. ENGAGEMENT DU CHERCHEUR OU DE SON REPRÉSENTANT

Je, soussigné (e), _____, certifie

(a) avoir expliqué au signataire les termes du présent formulaire;
(b) avoir répondu aux questions qu'il m'a posées à cet égard;
(c) lui avoir clairement indiqué qu'il reste, à tout moment, libre de mettre un terme à sa participation au projet de recherche décrit ci-dessus;
(d) que je lui remettrai une copie signée et datée du présent formulaire.

_____

Signature du responsable du projet ou de son représentant

Fait à Montréal, le _____, 20_____

III. Summary of the doctoral trajectory

The development of the projects integrated into my doctoral studies, which started in the winter 2016 semester, are summarized in figure 16. The original project of my Ph.D. consisted in assessing the effects of 18-session locomotor training program using the WRE offered over a 6-8 week period to individuals with iSCI using a comprehensive biomechanical laboratory-based assessments (kinematic, kinetics and EMG) and clinical evaluations. The WRE provided "assistance-as-needed" during the locomotor training program that was completed by a total of 5 participants specifically recruited for this study. The project started in February 2016 and was completed in December 2017. Unfortunately, inconsistency and heterogeneity of the final data due most likely to measurement errors during clinical assessments as well as poor EMG signal quality during the pre and post-training evaluations did not allows the research team to reach any conclusion with regards to the effects of the locomotor training program, and this initial project was left aside. Parallel to my original main project, between 2016 and 2017, a feasibility study regarding critical aspects for locomotor training programs in terms of recruitment, attendance, learnability, performance and safety in individuals with complete SCI was completed (Gagnon et al., 2018); a quasi-experimental study investigating the effects of a locomotor training program among individuals with a complete SCI on bone mineral density and body composition (Karelis, Carvalho, Castillo, Gagnon, & Aubertin-Leheudre, 2017) was also completed; this last study was performed in collaboration with the Université du Quebec à Montréal (UQAM). Over the course of this locomotor training program, I also performed a transversal study to assess the cardiorespiratory demands on 13 individuals with a complete spinal cord injury walking with the WRE. The results of this study were later published in 2018 (See appendix IV). The data collected during each locomotor training among both individuals with a cSCI or iSCI lead to the publication, on early 2018, of another article evaluating the feasibility, recruitment, attendance, learnability, performance and safety aspects of the locomotor trainings performed using the robotic exoskeleton.

On early 2018, we had the opportunity of acquiring a newer model (Ekso^{TM} GT) from the WRE used in all the studies mentioned above (Ekso^{TM}). This newer WRE model presented new control modes that confronted us with a wide range of options for locomotor training programs. However, before engaging into another locomotor training program, even with all the knowledge collected from all our previous work, we had no knowledge into how to accurately choose among all available options in order to explored locomotor training effects over a group or over specific individuals with iSCI. From these questions, the work that constitutes this thesis was divided into three parts resulting in the three scientific articles (See Figure X).

Muscle synergies from 26 L/E were analyzed (20 unilateral L/E recording for able-bodied participants and bilateral recording for the three participants with iSCI). Thus, each of the able-bodied participants performed three overground walking trials (article #1) and six exoskeleton control modes trials (article #2); also one overground trial and five exoskeleton control modes trials in participants with iSCI were performed (article #3). Overall, a total of 216 MSs were meticulously analyzed in the research presented in this thesis.

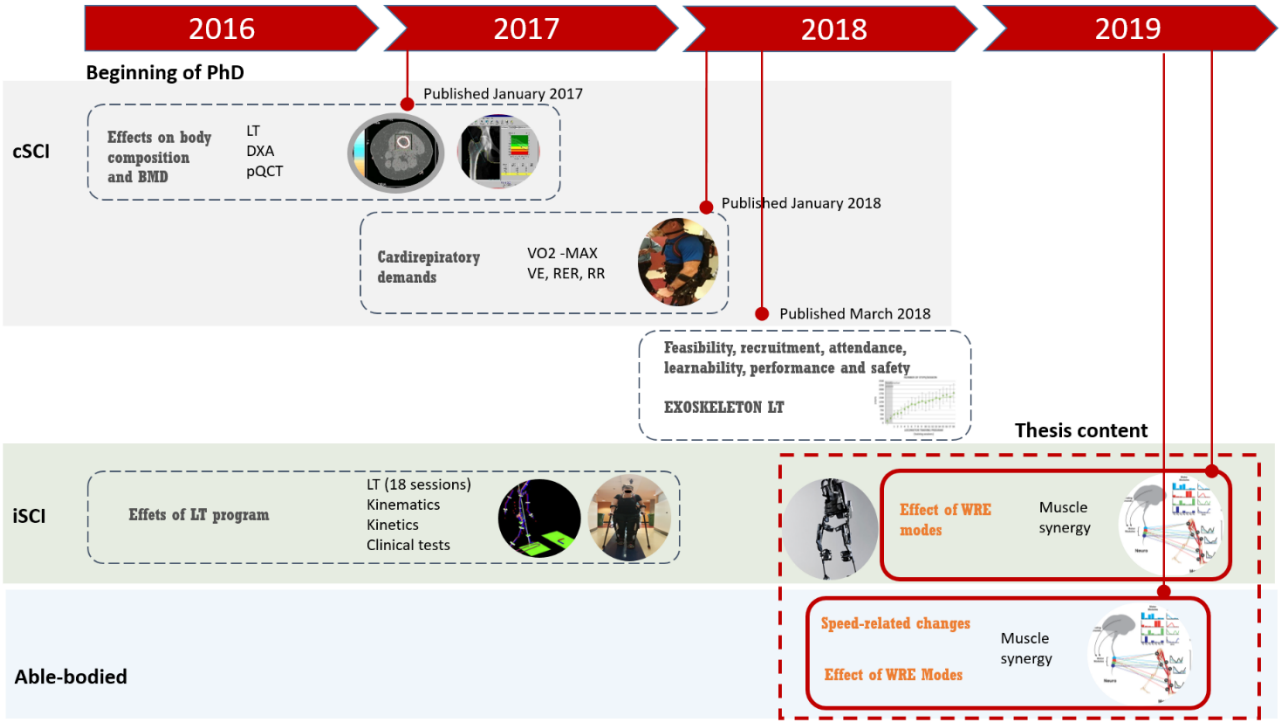


Figure 1. – Chronology and development of projects, as well as the scientific articles that constitutes this thesis.

IV. Article #4: Cardiorespiratory demand during overground walking with a robotic exoskeleton *

* Published article: Escalona MJ, Brosseau R, Vermette M, Comtois AS, Duclos C, Aubertin-Leheudre M, Gagnon DH. Cardiorespiratory demand and rate of perceived exertion during overground walking with a robotic exoskeleton in long-term manual wheelchair users with chronic spinal cord injury: A cross-sectional study. Ann Phys Rehabil Med. 2018 Jul;61(4):215-223. doi: 10.1016/j.rehab.2017.12.008. Epub 2018 Jan 31.

Manuel J. Escalona [a,b], Rachel Brosseau [a,c], Martin Vermette[b], Alain Steve Comtois [d], Mylène Aubertin-Leheudre [d], Cyril Duclos [a,b], Dany H. Gagnon [a,b]

[a] École de réadaptation, Université de Montréal, Montreal, QC, Canada

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[c] Institut de cardiologie de Montréal, QC, Canada

[d] Faculté des sciences, Département des sciences de l'exercice, Université du Québec à Montréal, QC, Canada

Corresponding author: Dany H. Gagnon, Pathokinesiology Laboratory, Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal, Centre intégré universitaire de santé et services sociaux du Centre-Sud-de-l'Île-de-Montréal–Institut de réadaptation Gingras-Lindsay-de-Montréal, 6300 Avenue Darlington, Montreal, QC, H3S 2J4 Canada

Abstract

Introduction: Many long-term wheelchair users adopt a sedentary lifestyle resulting in progressive physical deconditioning with an increased risk of musculoskeletal, cardiovascular and endocrine/metabolic morbidity and mortality. Engaging in a walking program with an overground robotic exoskeleton may be an effective strategy for mitigating these potential negative health consequences and optimizing fitness in this population. However, additional research is warranted to inform the development of adapted physical activity programs incorporating walking with an overground robotic exoskeleton. **Objectives:** To determine cardiorespiratory demands during sitting, standing and overground walking with a robotic exoskeleton, and to verify if overground walking with a robotic exoskeleton results in at least a moderate intensity level of physical exercise. **Methods:** Thirteen long-term wheelchair users who sustained a complete motor spinal cord injury enrolled into a walking program with an overground robotic exoskeleton. Cardiorespiratory measures and the rate of perceived exertion (RPE) were recorded using a portable gas analyzer system during sitting, standing, and four 10-meter walking tasks with the robotic exoskeleton. Each user also performed an arm crank ergometer test to determine maximal cardiorespiratory ability. **Results:** Cardiorespiratory measures increased by a range of 9% to 35% from sitting to standing, and further increased by 22% to 52% from standing to walking with the robotic exoskeleton. During walking, median relative heart rate (%HR_{max}), relative oxygen consumption (%VO_{2max}), and respiratory exchange ratio (RER) values reached 82.9%, 41.8%, and 0.9, respectively, whereas the median RPE reached 3.2/10. **Conclusion:** Overground walking with the robotic exoskeleton on a short distance allowed users to achieve a moderate intensity level of exercise. Hence, overground locomotor training program with a robotic exoskeleton may lead to cardiorespiratory health benefits.

Key words: Spinal cord injuries, exercise, rehabilitation, technology, physical fitness, oxygen consumption.

1. Introduction

Most long-term wheelchair users with a complete motor spinal cord injury (SCI) adopt a sedentary lifestyle with prolonged non-active sitting and limited opportunities to engage in physical activities (12). As a result, many individuals with a SCI experience progressive physical deconditioning as they age, leading to secondary negative health consequences. The myriad of complex multifactorial health consequences, especially those linked to endocrine and metabolic disorders (e.g., diabetes mellitus, dyslipidemia, obesity) have risen drastically over the past few years and are known to increase the risk of cardiovascular morbidity and mortality among individuals with a SCI (6, 12, 14, 17). In fact, cardiovascular disease is now considered as the leading cause of mortality among individuals with a chronic SCI living in the community (6). Moreover, individuals with paraplegia present 70% greater risk of developing cardiovascular disease compared to gender- and age-matched able-bodied individuals (3, 8).

Engaging in regular physical activity is a strategy for mitigating secondary negative health consequences and for optimizing fitness in persons with SCI (Washburn et al., 1998; Jacobs et al., 2004). It is now recommended for persons with a SCI to perform prolonged moderate-intensity level exercise (minimum of 20 minutes) two times per week, in conjunction with strengthening exercises to preserve physical fitness (7). For long-term manual wheelchair users with paresis or paralysis of the trunk and lower extremity muscles, arm crank or wheelchair ergometry is typically recommended to achieve prolonged moderate intensity exercise. However, there has been a growing interest over the past few years for overground walking with a robotic exoskeleton. Robotic exoskeletons typically provide maximal external support that allows overground walking among wheelchair users with very limited or no ambulatory ability because these exoskeletons reproduce movement strategies and weight-bearing patterns at the lower extremities similar to those documented during typical gait in able-bodied individuals. The upper extremities and trunk muscles greatly contribute to body weight shifts required to initiate steps and to the control of dynamic balance during overground walking with the robotic exoskeleton. This represents a promising new approach given that previous exploratory studies suggested that moderate cardiorespiratory demand could be anticipated during overground walking with a robotic exoskeleton based only on a few objective measures (1, 5). Moreover, potential beneficial

musculoskeletal adaptations (e.g., increased lean body mass, increased bone mineral density at the lower extremities) were also recently documented (10). Hence, overground walking with a robotic exoskeleton, performed in a standing position, may mitigate secondary negative health consequences to a greater extent than arm crank or wheelchair ergometry. Nevertheless, compelling evidence is needed to inform the development of adapted physical activity programs. One of the steps involved in this process is gaining additional insight into the cardiorespiratory and metabolic requirements of overground walking with a robotic exoskeleton.

The first objective of this study was to compare cardiorespiratory demand between sitting, standing and overground walking with a robotic exoskeleton in long-term manual wheelchair users with a chronic SCI. The secondary objective was to investigate if cardiorespiratory exertion measured and perceived during overground walking with a robotic exoskeleton achieves at least a moderate level of intensity to anticipate cardiorespiratory health benefits in this population. It was hypothesized that 1) cardiorespiratory demand would progressively increase when transitioning from sitting, standing and walking tasks with a robotic exoskeleton (1), and that 2) a moderate level of physical activity would be achieved during overground walking with a robotic exoskeleton (5).

2. Methods

2.1. Participants

A non-probabilistic convenience sample was recruited for this study. This sample included 13 individuals who sustained a non-progressive complete motor SCI below the 6^{th} cervical vertebra (American Spinal Injury Association Impairment Scale (AIS) = A or B), had no voluntary ambulatory ability, used a manual wheelchair as their primary mode of mobility and previously qualified for overground walking with a robotic exoskeleton following a comprehensive physical therapy assessment. Participants had also completed two familiarization sessions, and were participating in an 18-session overground locomotor training program (2-3 sessions/week) with a wearable robotic exoskeleton (i.e., parent intervention trial). Exclusion criteria included history of other neurological disorders, injuries to the skin in areas of contact with the exoskeleton, psychiatric or cognitive impairments that could interfere with the tasks and/or poorly controlled

spasticity of the lower extremities. The present sample represents a sub-sample of participants who had initiated this parent intervention trial, had completed at least 4 training sessions with the robotic exoskeleton and had acquired the ability to ambulate at least 50 meters with the robotic exoskeleton with proper rhythm and balance strategies with minimal or contact guard assistance. Additional recruitment information, including details about the inclusion and exclusion criteria for overground walking with the robotic exoskeleton, is further described elsewhere (**). The study was conducted at the Pathokinesiology Laboratory of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) located at the CIUSSS du Centre-Sud-de-l'Île-de-Montréal–Site: Institut de réadaptation Gingras-Lindsay-de-Montréal. All participants gave their written consent to participate in the study after being informed of the objectives and nature of their participation in the study. The Research Ethics Committee of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal approved the present study (CRIR-1083-0515).

2.2. Robotic exoskeleton

The Ekso^{TM} GT overground robotic exoskeleton (EKSO Bionics, CA, USA) was used in this study. This system provides maximal external support and generates flexion and extension movements at the hips and knees via motors in a sequence that replicates walking. The ankles were supported with a non-motorized dynamic orthosis. When walking, steps were initiated by shifting body weight laterally and forward toward the supporting lower extremity (L/E) before the oscillating L/E could start moving (i.e., ProStep mode). These body weight shifts were generated through active trunk and U/E movements and facilitated using an extra wide Rollator walker or forearm crutches to ensure contact points with the ground.

2.3. Experimental tasks

2.3.1. Sitting, standing, and walking

Cardiorespiratory parameters were assessed while sitting, standing and walking with the robotic exoskeleton during a single session (i.e., single-group repeated measure design). In the sitting and standing positions, cardiorespiratory parameters were recorded for 1 minute respectively. Participants were asked to adopt a resting position during the sitting task recordings

and a static position during the standing task recordings using assistive devices (Rollator walker or forearm crutches) for support in order to maintain balance and allow total support by the Ekso^{TM} GT. Participants were also asked not to talk during the recording periods to avoid bias in measured respiratory variables. During the walking trials, participants were asked to walk a 10-meter distance at a natural self-selected velocity down a corridor. A total of four trials were completed. Rest periods were allowed between trials to avoid fatigue. Walking speed was calculated by dividing the 10-meter distance of each trial by the total time taken to complete it. After each trial, participants were also asked to report their rate of perceived exertion (RPE) on a 10-point modified Borg scale.

2.3.2. Maximal cardiorespiratory ability

Participants completed an incremental peak exercise test on an arm crank ergometer (Biodex Upper Body Cycle, 950-164; Biodex Medical Systems, Shirley, NY) during a separate session that was completed 1-week before or after the experimental tasks. After a 2-minute warm-up without resistance, the initial resistance was set at 10 W and progressively increased by 10W every minute. Participants were asked to arm-crank at a cadence of 50 revolutions/minute (13). At the end of each increased resistance period, participants rated their perceived exertion (RPE) on a 10-point modified Borg scale. Participants were encouraged to exercise to exhaustion. Exertion was considered to be maximal if a respiratory exchange ratio (RER) > 1.1 was reached, if a plateau in VO_2 was reached (change < 2.1 mL/kg/min) with an increase in exercise intensity (4) and/or when a cadence of at least 40 revolutions per minute could not be maintained. After the test, participants performed a 2-minute cool-down period and after five minutes of rest and observation, they were allowed to leave the laboratory.

2.4. Cardiorespiratory assessment

During the above-mentioned experimental tasks, participants were equipped with a breath-by-breath COSMED K4b^2 portable gas analyzer system comprised of a turbine, gas analyzer unit and a battery pack. This system has been shown to be valid and reliable (9, 16). Both the turbine and gas analyzer unit were calibrated prior to the experiment using a known ventilation volume (i.e., 3 L syringe) and standard gas mixture, respectively. The turbine collected

exhaled gases via a sealed face mask placed over the nose and mouth to prevent air loss at a sampling frequency of 20 Hz. The gas analyzer unit was secured on the anterior part of the thorax, whereas the battery pack was held by a research associate standing and walking at the participant's side. In addition to the COSMED K4b^2 system, heart rate was monitored using the Polar® Soft Strap heart rate monitor (Polar FT4; Polar, Lachine, Canada) placed around the chest. During all experimental tasks, cardiorespiratory outcome measures were recorded, including oxygen consumption (VO_2 in mL/kg/min), carbon dioxide production (VCO_2 in mL/min), ventilation (VE in L/min), tidal volume (VT in L), respiratory exchange ratio (RER), respiratory rate (RR in cycles/min^{-1}) and heart rate (HR in beats/min).

2.5. Data conditioning and analysis

All recorded data were first visually inspected and aberrant values (±3 SD of the mean) were excluded. Then all cardiorespiratory outcome measures recorded for the sitting and standing tasks were averaged over 1 minute for each participant before computing a group average. All cardiorespiratory outcome measures recorded during the walking tasks were averaged over the time it took to walk each 10-meter distance and the participant's average was computed before computing a group average. Moreover, the relative cardiorespiratory demand for the walking task only was computed for maximal HR and VO_{2max} and expressed as a percentage. The $\%HR_{max}$ and $\%VO_{2max}$ measures computed during the overground walking task with the robotic exoskeleton (i.e., numerator) were normalized against those obtained during the arm crank ergometer test (i.e., denominator; maximal cardiorespiratory ability). During this latter test, maximal HR and VO_{2max} measures were calculated using a basic 10-second moving average applied to the last minute before the end of each trial.

2.6. Statistics and data interpretation

Non-parametric descriptive statistics (i.e., median and interquartile range) were calculated for demographics and clinical characteristics as well as for all outcome measures. To verify the first hypothesis, Friedman tests were used to verify if differences existed between the absolute cardiorespiratory outcome measures recorded for the sitting, standing, and walking tasks. Whenever statistically significant differences were identified ($p < 0.05$), post hoc analyses

using a Wilcoxon signed-rank test (i.e., non-parametric pairwise comparisons) were applied to identify the difference(s). Because a total of 3 pairwise comparisons were tested, the statistically significant level was adjusted to $p < 0.017$ (i.e., 0.05/3). All statistical analyses were performed using SPSS statistic software version 22.0 (IBM Corporation, Armonk, New York). To verify the second hypothesis, only $\%HR_{max}$, $\%VO_{2max}$, RER and RPE values were used and interpreted according to ACSM guidelines for exercise testing and prescription to determine the exercise intensity achieved while walking with the robotic exoskeleton (15). To reach at least a moderate level of intensity during physical activity, these guidelines suggest that $\%HR_{max}$, $\%VO_{2max}$, RER and RPE should be above 64%, 45%, ≥0.9 and ≥3 on the modified Borg scale, respectively. Participants were deemed to have achieved moderate exercise intensity whenever at least one objective criterion (i.e., $\%HR_{max}$, $\%VO_{2max}$ and/or RER) and RPE reached at least a moderate exercise intensity level.

3. Results

3.1. Participants

All demographic and clinical characteristics as well as walking experience with the robotic exoskeleton are summarized in Table 1. Walking performance during the 10-m walking test is summarized in Table 2.

3.2. Cardiorespiratory demands during experimental tasks

All cardiorespiratory outcome measures recorded during the sitting, standing, and walking tasks are illustrated in Figure 1. Overall, most of the cardiorespiratory outcome measures progressively increased from sitting to standing to walking and reached their greatest values with the walking task (p values between 0.001- 0.013). The only two exceptions found were linked to RER and VT. The only significant difference in RER was found between standing and walking ($p = 0.006$). Similar values were observed for VT across the three experimental tasks ($p > 0.017$).

3.3. Exercise intensity during the walking task

The four cardiorespiratory outcome measures selected to characterize exercise intensity when walking with the robotic exoskeleton are illustrated in Figures 2A and 2B. Moreover, the different exercise intensities (i.e., very light, light, moderate, vigorous, near maximum intensity, maximal and sub maximal effort) defined for these outcome measures are highlighted in various shades of gray. Overall, median relative heart rate (%HR_{max}), relative oxygen consumption (%VO_{2max}), and respiratory exchange ratio (RER) values reached 82.9%, 41.8%, and 0.9, respectively, whereas the median rate of perceived exertion reached 3.2/10. A total of 11of the 13 participants (85%) achieved at least a moderate intensity level when only objective criteria (i.e., %HR_{max}, %VO_{2max} and/or RER) were considered, whereas the remaining two participants only reached a light intensity. In contrast, when a criterion measuring subjective perceptive aspects during exertion (i.e., RPE) was considered, a total of 9 of the 13 participants perceived at least a moderate intensity level when walking with the robotic exoskeleton, whereas the remaining four participants perceived a light intensity. These 4 participants may have underestimated their RPE as they reached objective values (%$VO_{2max,}$ %HR_{max} and/or RER) corresponding to at least a moderate intensity exercise level.

4. Discussion

The main objective of this study was to compare cardiorespiratory demand between sitting, standing and overground walking tasks with a robotic exoskeleton and to investigate if persons with complete SCI can achieve at least a moderate level of intensity during the latter task as measured by cardiorespiratory effort. This study demonstrated that 1) there was an increasing demand between the sitting, standing and walking tasks for most of the cardiorespiratory variables and that 2) walking with the robotic exoskeleton allowed most of the participants (11 out of 13) to reach a moderate-to-vigorous intensity level of exercise.

4.1. Greatest cardiorespiratory demand achieved during walking

The results of the present study support the hypothesis that cardiorespiratory demands increase progressively when transitioning from sitting, standing and walking with the robotic exoskeleton. Overall, key cardiorespiratory measures significantly increased by a range of 9% to 35% from sitting to standing and further increased by an additional range of 22% to 52% from

standing to walking with the robotic exoskeleton. The greatest increase found between the standing and walking tasks may be explained by the active contribution of upper limbs and trunk necessary for weight shifting and balance during assisted-walking (which is discussed in greater detail below). The only exceptions were VT, which was comparable across the three tasks, and RER, for which significant differences were found between the sitting and standing conditions.

These results are mostly consistent with those reported by Asselin et al. who also investigated sitting, standing and walking with a robotic exoskeleton. The latter study revealed similar VO_2 and HR measures between sitting and standing but confirmed significant differences between the latter two tasks and overground walking with a robotic exoskeleton. These authors reported that the HR and $V0_2$ values increased by 31% and 62% between the standing and walking conditions, respectively. These finding support the results of the present study. The fact that the participants in the present study were in a resting seated position for at least 10 minutes after transferring from the wheelchair into the exoskeleton (i.e., a demanding functional activity) may, in part, explain why there was a difference between the sitting and standing tasks. A portion of the discrepancy observed in cardiorespiratory response while walking between the two studies may be explained by factors such as walking speed or number of training sessions completed (i.e., level of experience with the robotic exoskeleton). Compared to the walking speed identified in this study (i.e., a median of 0.17 m/s), Evans et al. found that an increasing walking speed from a comfortable (0.19 ± 0.01 m/s) to a fast (0.27 ± 0.05) walking speed during overground walking with a robotic exoskeleton during a 6-meter walking test did not significantly change the relative intensity of the task, which was considered to be moderate according to ACSM criteria. Moreover, previous studies that have measured cardiovascular capacities at about the 40^{th} training session (Asselin et. 2015) and the 5^{th} training session (5), have found cardiovascular demands to be compatible with a moderate level of physical exercise. Hence, the results of this study have most likely not been influenced by the fact that the cardiorespiratory variables were recorded between the 4^{th} and 14^{th} session. Nonetheless, it is possible that participants learned to significantly increase their walking speed over time (≥40 training sessions), therefore eventually having an impact on cardiorespiratory demand.

Since VT remained comparable across the three tasks given that most participants (9/13) presented with a neurological lesion level higher than the 6th thoracic vertebra, paralysis or paresis of the intercostal muscles may have interfered with thoracic movements. This may be reflected in the lack of change in VT values due to increased compensatory RR values as observed in the present study. Another possible explanation is that limited walking time needed to complete the 10-meter walking test may have precluded a response in VT. Lastly, potential SCI-related autonomic changes and various degrees of remaining sympathetic control across participants may have had an impact on the cardiorespiratory demands during the walking task with the robotic exoskeleton (18).

To our knowledge, no previous study has reported variables such as VCO_2, RR, VT or VE during overground walking with a robotic exoskeleton. These complementary variables strengthen the current level of evidence. Respiratory volume and RER represent key parameters since they could indirectly explain the actual exertion and/or cardiorespiratory changes during overground walking with the robotic exoskeleton. This dynamic exercise, which solicits trunk and U/E muscles differently (further details provided in section 4.2), requires an increased oxygen demand and modified cardiorespiratory system responses.

4.2. Potential cardiorespiratory health benefits

The results of the present study support the hypothesis that a moderate level of physical activity is achieved during overground walking with a robotic exoskeleton. In general, $\%HR_{max}$, $\%VO_{2max}$, RER, or RPE values recorded in this study reached at least a moderate intensity level based on ACMS guidelines for exercise testing and prescription. Hence, the increased upper extremity and trunk workload during overground walking with the robotic exoskeleton, predominantly needed for body weight shifts to initiate steps and for bodyweight support and dynamic standing balance, are sufficient to induce at least moderate exercise intensity. However, these results mask significant variability in the relative intensity level reached across participants. For example, VO_2 and HR varied from light intensity to vigorous – near maximal intensity. The present results strengthen those previously reported (1), which documented that VO_2 reserve values reached 25% to 33% of their maximum estimated value, while HR reserve attained half of

the maximum estimated values, i.e. moderate intensity values. However, the maximal values used to estimate these reserves were estimated using a prediction model based on able-bodied individuals or based on median values computed form individuals with a chronic SCI during an upper arm crank exercise. Finally, a case-series study reported results contradict the findings of the present study (11). In fact, Kressler et al. concluded that walking with an overground exoskeleton only leads to a light exercise intensity based on variables such as VO_2, HR and metabolic equivalent. This low exercise intensity was computed during a one-hour walking training session during which participants were allowed to stop and rest as needed to avoid fatigue. This may partly explain the difference found between this case-series study and the results of other studies.

Objective cardiorespiratory measures used in this study to classify exercise intensity are substantiated by most participants who reported an RPE of at least moderate exercise intensity. Only 4 participants reported light intensity despite presenting objective cardiorespiratory values, i.e., $\%HR_{max}$, $\%VO_{2max}$ and/or RER, resulting in moderate to vigorous exercise intensity. Similar findings were previously reported by Asselin et al. and Baunsgaard et al., who found that participants reported an RPE of very light intensity during overground walking with a robotic exoskeleton despite VO2 and HR values corresponding to at least a moderate intensity level. In fact, it is well acknowledged that RPE does not perfectly correlate with physiological variables. This is explained by the fact that RPE is influenced by many other factors such as psychological factors (e.g., mood state, motivation, and exercise experience) (2). Nonetheless, measuring RPE remains relevant, particularly to evaluate the ability to continue an activity over a determined period of time.

The results of the present study confirm that overground walking with a robotic exoskeleton could potentially lead to cardiorespiratory health benefits in individuals with a complete motor SCI who engage in an adapted physical activity program incorporating overground walking with a robotic exoskeleton. Therefore, based on the relative demand documented in the present study and according to the physical activity guidelines for adults with SCI (7), it is plausible that participating in at least two 20-minute sessions per week of overground walking with the robotic exoskeleton, combined with strength training, may be sufficient to

maintain fitness. Furthermore, although it remains to be thoroughly investigated among a large cohort followed over time, these cardiorespiratory benefits may also translate into cardiovascular and endocrine/metabolic health benefits.

4.3. Limitations

Because the present study included a relatively small and homogeneous group of individuals with a complete motor SCI who were engaged in a supervised adapted physical activity program (n=13), caution is warranted when generalizing the results to a larger group of similar individuals or to other individuals with different sensorimotor impairments. Considering that the maximal VO_2 and HR values were recorded during an arm ergocycle, it is possible that localized upper extremity muscular fatigue was underestimated among some participants. However, such an approach is frequently used and is preferred among long-term manual wheelchair users with a complete motor spinal cord injury over the use of predictions based on values observed during a lower-limb exercise in healthy individuals. Additionally, the fact that cardiorespiratory demand was measured while walking at a self-selected comfortable speed during a 10mWT, that took on average 57 seconds to complete (with minimum and maximal times of 38 and 89 seconds respectively), the observed values may not reflect the total cardiorespiratory demand to expect during a 45- to 60-minute training session during which fatigue develops if no or limited rest periods are allowed. Nonetheless, studies that have measured these demands over a longer period (i.e., 6-minute walk test) have found similar results (Evans et al., 2015).

5. CONCLUSION

Cardiorespiratory demands progressively increased when transitioning from sitting, standing and overground walking tasks with an robotic exoskeleton. Moreover, overground walking with a robotic exoskeleton on a short distance is generally associated with at least a moderate level of physical activity. Consequently, it is plausible that overground gait training with a robotic exoskeleton leads to cardiorespiratory health benefits. Additional research is needed for a better understanding of the cardiorespiratory demands during prolonged overground walking with a robotic exoskeleton with limited rest periods or with different walking speed combinations (e.g., self-selected comfortable and maximal speeds). This is essential to inform the

development of community-based adapted physical activity programs targeting the population investigated in the present study. The impact and effectiveness of such programs will also need to be assessed.

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Table 1. Demographic and clinical characteristics as well as training completed with the exoskeleton previous to the recordings of cardiorespiratory outcomes of all participants

	Demographic characteristics				Clinical information					Experience with exoskeleton		
Participants	**Gender**	**Age (years)**	**Heigth (m)**	**Weight (Kg)**	**Time since injury (years)**	**NLI**	**AIS**	**Motor score /100**	**Sensory score /224**	**Sessions**	**Number of steps taken**	**Total walking time (Hrs)**
EC1	F	26.7	1.61	61.4	2.2	T6	A	50	104	10	10037	4.7
EC2	M	28.4	1.78	73.9	5.1	T6	A	50	108	13	13820	6.4
EC3	M	63.1	1.85	96.0	8.3	T10	A	50	143	7	4620	3.5
EC4	M	32.2	1.92	91.2	8.0	T6	A	50	118	4	3269	2.2
EC5	M	42.9	1.80	66.6	14.4	C6	A	28	48	4	1075	1.0
EC6	M	51.5	1.67	61.9	31.4	T6	B	50	140	14	21246	9.9
EC7	M	43.8	1.75	107.0	3.4	T10	A	50	143	14	16243	8.9
EC9	M	38.1	1.60	64.3	6.9	T9	A	50	115	7	4386	2.3
EC10	M	27.2	1.70	56.2	4.2	T4	A	50	104	14	9739	4.5
EC11	F	31.1	1.60	63.7	1.0	T8	A	55	124	6	5858	3.1
EC12	F	39.4	1.68	75.5	4.7	T3	A	50	80	10	10139	6.8
EC13	F	51.9	1.62	58.5	5.2	T4	A	50	96	13	11412	5.6
EC14	F	30.9	1.63	48.7	0.8	T6	A	50	42	10	14289	6.3
Median	**-**	**38.1**	**1.7**	**64.3**	**5.1**	**-**	**-**			**10**	**10037**	**4.6**
[min-max]	**-**	**26.7-63.1**	**1.6-1.9**	**48.7-107.2**	**0.8-31.4**	**-**	**-**			**4-14**	**1075-21246**	**0.9-9.9**

Kg= kilograms, m=meters, NLI= neurological level of injury

Table 2. Walking performance and walking aid used during the 10-meter walking test with a robotic exoskeleton

Participants	10mWT time (s)	Speed (mps)	Technical aid
EC1	38	0.26	C
EC2	40	0.25	C
EC3	89	0.11	C
EC4	57	0.18	C
EC5	58	0.17	RW
EC6	56	0.18	C
EC7	52	0.19	RW
EC9	69	0.14	C
EC10	54	0.19	RW
EC11	64	0.16	C
EC12	58	0.17	C
EC13	63	0.16	C
EC14	50	0.20	C
Median	**57**	**0.17**	**-**
Min-max	**38-89**	**0.11-0.26**	**-**

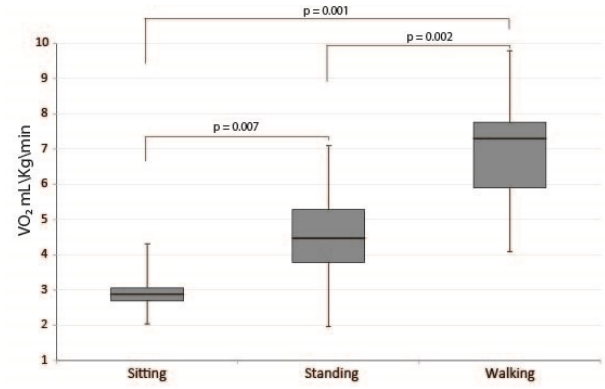
s= seconds, mps= meters per second, C= Canadian crutches, RW= rollator walker.

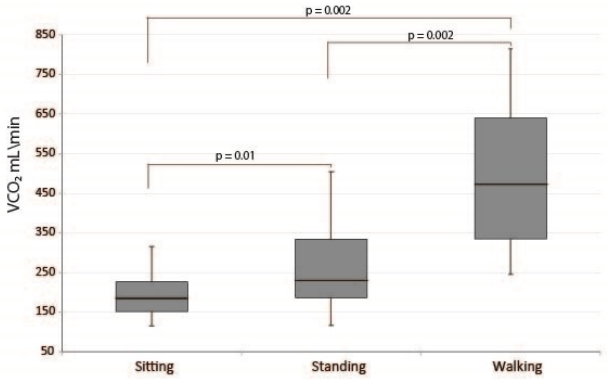
Figure legends

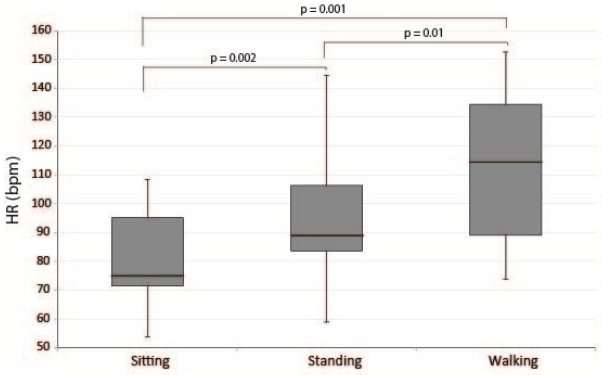
Figure 1. Median values of all cardiorespiratory outcome measures during sitting, standing and walking with the robotic exoskeleton. P values ≤ 0.017 were considered statistically significant.

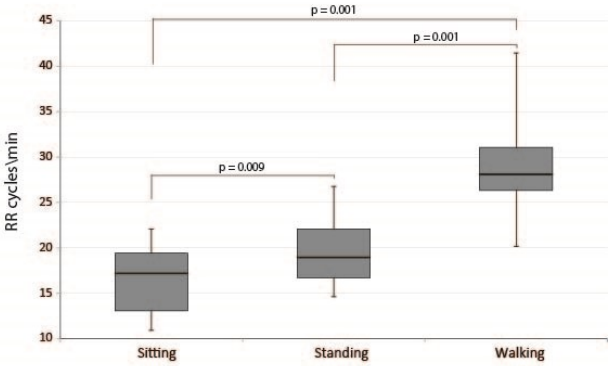
Figure 2. **A**. Median values of the four cardiorespiratory outcome measures characterizing exercise intensity during walking with the robotic exoskeleton. **B**. Individual mean values for all participants. Areas highlighted in various shades of gray represent the different exercise intensities (i.e., very light, light, moderate, vigorous, near maximum intensity, maximal and sub-maximal effort) according to the ACSM guidelines.

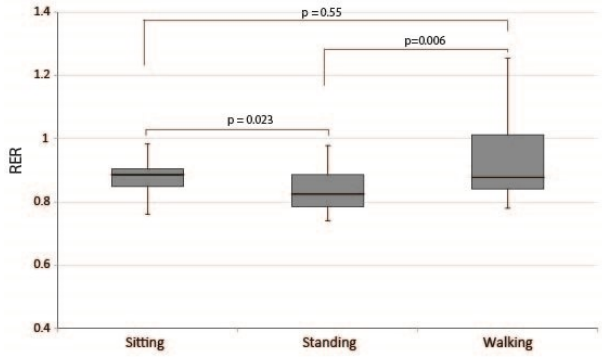
Figure 1

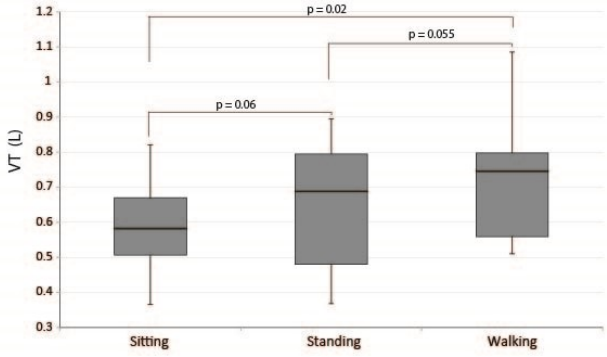

p = 0.001
p = 0.002
p = 0.007
VO2 mL\Kg\min
Sitting
Standing
Walking


p = 0.002
p = 0.002
p = 0.01
VCO2 mL\min
Sitting
Standing
Walking


p = 0.001
p = 0.01
p = 0.002
HR (bpm)
Sitting
Standing
Walking


p = 0.001
p = 0.001
p = 0.009
RR cycles\min
Sitting
Standing
Walking


p = 0.55
p=0.006
p = 0.023
RER
Sitting
Standing
Walking


p = 0.02
p = 0.055
p = 0.06
VT (L)
Sitting
Standing
Walking

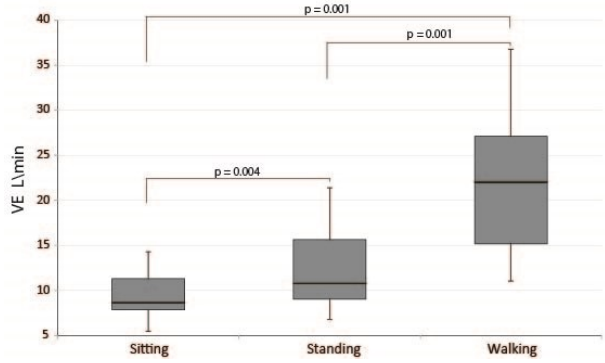
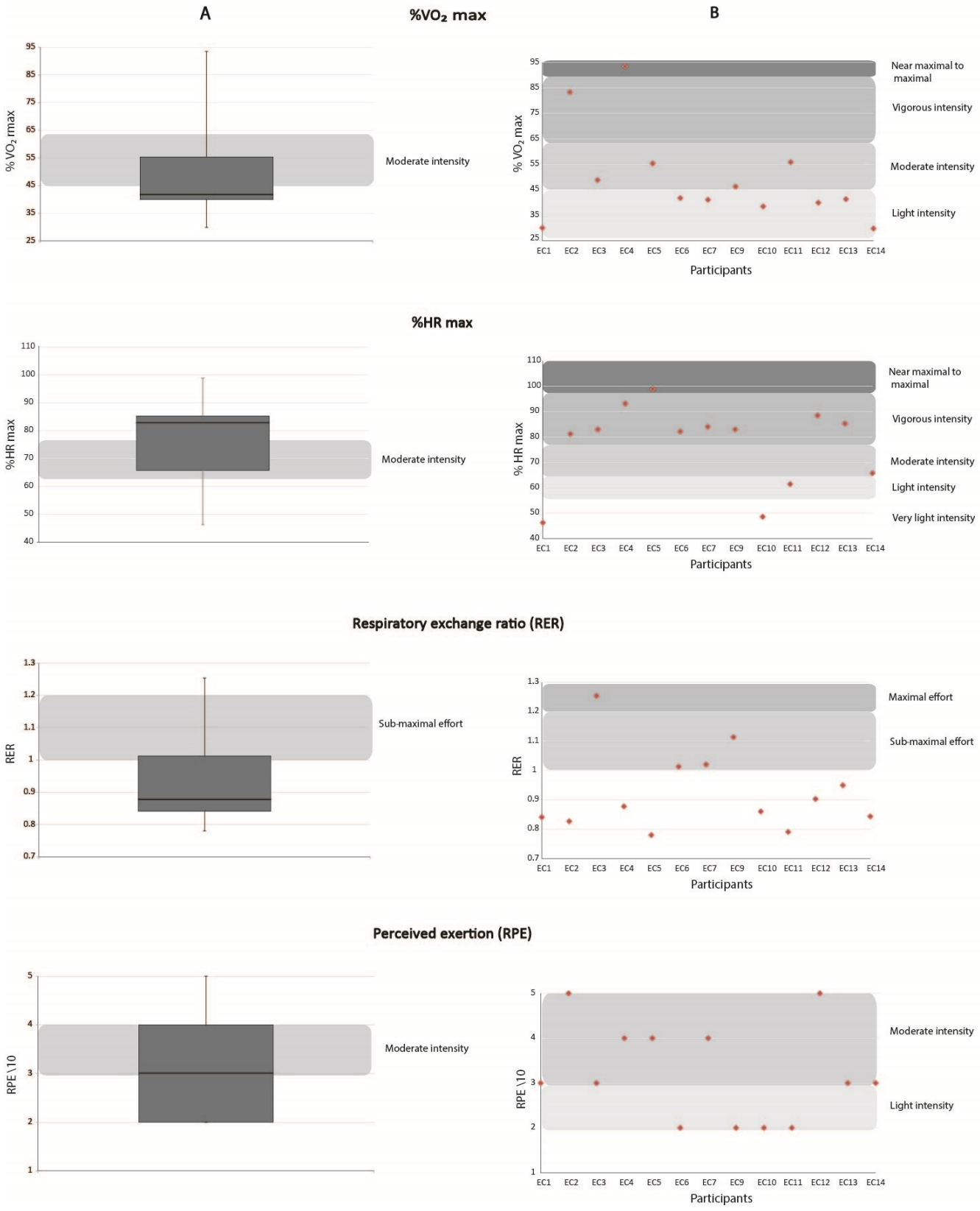

p = 0.001
p = 0.001
p = 0.004
VE L\min
Sitting
Standing
Walking

Figure 2


A
%VO2 max
% VO2 rmax
Moderate intensity
B
% VO2 max
Near maximal to maximal
Vigorous intensity
Moderate intensity
Light intensity
EC1 EC2 EC3 EC4 EC5 EC6 EC7 EC9 EC10 EC11 EC12 EC13 EC14
Participants
%HR max
%HR max
Moderate intensity
% HR max
Near maximal to maximal
Vigorous intensity
Moderate intensity
Light intensity
Very light intensity
Participants
Respiratory exchange ratio (RER)
RER
Sub-maximal effort
Maximal effort
Participants
Perceived exertion (RPE)
RPE \10
Moderate intensity
Light intensity
Participants

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V. Clinical evaluation form for scientific article #3

Centre intégré universitaire de santé et de services sociaux du Centre-Sud-de-l'Île-de-Montréal Québec | CRIR Centre de recherche interdisciplinaire en réadaptation | Université de Montréal | INSPIRE | Laboratoire de Pathokinésiologie Analyse du mouvement et des activités fonctionnelles www.pathokin.ca

Nom:

No de dossier: S

Dr: ---

DDN:

CRIR et Programme ☐ Lésions médullaires ou ☐ Neurologie
Évaluation initiale – Physiothérapie – Entraînement à la marche à l'aide d'un exosquelette robotisé

Évaluateur : _____ Date de la lésion : _____

Diagnostic : _____

Prescription pour entraînement reçue : ☐O ☐N⇨Date probable d'obtention : _____

Dominance : ☐D ☐G Genre : ☐F ☐H Poids : _____ ☐kg ☐lbs Taille : _____ ☐cm ☐pi-po.

La présente évaluation consiste à vérifier si la personne répond aux critères d'utilisation de l'exosquelette robotisé de marche Ekso GT™. Par conséquent, il ne s'agit pas d'une évaluation complète en physiothérapie en vue d'un traitement d'une condition de santé. La structure de l'évaluation respecte les principes reconnus en physiothérapie en présentant une analyse validant l'admissibilité du sujet et un plan de traitement proposant, le cas échéant, des adaptations aux protocoles d'utilisation de l'exosquelette

1.ÉVALUATION SUBJECTIVE

Bilan de la douleur (Type, intensité, fréquence, durée, ⇧ par, ⇩ par) **:**

Paresthésies:

Spasticité:

Faiblesse/Paralysie rapportée: (☑, >, =, <): MSD ☐ _____ MSG ☐ MID ☐ _____ MIG ☐

Autres :

OBJECTIFS DE L'USAGER :

_____

_____

_____

NOM : _____ **Dossier :** _____

2. ÉVALUATION OBJECTIVE

2,1 OBSERVATIONS GÉNÉRALES

Comportement et orientation:

2,2 ASIA (prog. LM) – ☐ Voir annexe

Niveau de sévérité: A ☐ B ☐ C ☐ D ☐ E ☐

Niveau sensitif: D: _____ G: _____

Niveau moteur: D: _____ G: _____

Cotation motrice: MSD: _____ MSG: _____

MID: _____ MIG: _____

Commentaires (réalisée par, date, etc.) :

2,3 CHEDOKE : (prog. Neuro) ☐ Voir formulaire Chedoke-McMaster au dossier ☐ N/A

2,4 FONCTIONS NEUROVÉGÉTATIVES

Hypotension orthostatique:

Verticalisation:

Dysréflexie autonomique:

Œdème:

Bande abdominale: oui ☐ non ☐ **Bas anti-embolie:** non ☐ oui => courts ☐ longs ☐

Coloration / T° des extrémités:

2,5 CONDITION DE LA PEAU

Plaies, cicatrices, lésions cutanées :

NOM : _____ **Dossier :** _____

2,6 AMPLITUES ARTICULAIRES, BILAN MUSCULAIRE MANUEL, SPASTICITÉ

AA's	DROITE	GAUCHE
Épaule - Ext.		
Coude - Ext.		
Poignet - Ext.		
Hanche - Flexion		
Hanche - Ext.		
Hanche – Ext.		
Genou - Flexion		
Genou - Ext.		
Cheville - FP		
Cheville - DF (genou Ext.)		
Genou – Flexion pour atteindre 0° DF		
Remarque – AA's :		

BMM	DROITE	GAUCHE
Épaule – Fl		
Épaule – Ext.		
Coude – Fl		
Coude – Ext.		
Poignet – Ext.		
Préhension (lbs)		
Hanche – Fl		
Hanche – Ext.		
Hanche – ABD		
Genou – Fl		
Genou – Ext.		
Cheville - DF		
Cheville – FP		
Remarque – BBM MI's :		

SPASTICITÉ	DROITE	GAUCHE
Coude – Fl'eurs / Ext'eurs		
Poignet - Fl'eurs / Ext'eurs		
Hanche - Fl'eurs / Ext'eurs		
Hanche – Adducteurs		
Genou - Fl'eurs / Ext'eurs		
Cheville – Fl.-Plantaires		
Cheville - Inverseurs		
Autre :		
Autre :		
Autre :		
Remarque (Spasticité) :		

Échelle Ashworth mod.

0 : Pas d'augmentation du tonus musculaire ;

1 : Légère augmentation du tonus musculaire qui se manifeste par une secousse suivi d'un relâchement ou par une résistance minime à la fin de l'amplitude articulaire lorsque le segment affecté est déplacé ;

1+ : Légère augmentation du tonus musculaire qui se manifeste par une secousse suivie d'une résistance minime à travers le reste (moins que la moitié) de l'amplitude articulaire ;

2 : Augmentation plus marquée du tonus musculaire à travers la presque totalité de l'amplitude articulaire, mais le segment affecté peut être déplacé avec facilité ;

3 : Augmentation considérable du tonus musculaire, le mouvement passif est difficile ;

4 : Le segment affecté est rigide.

NOM : _____ **Dossier :** S

2,7 POSTURE

Assis:

Debout/Décubitus:

2,8 FONCTION: *Spécifier au besoin: (I): Indépendance complète ou modifiée; (S): Supervision; (A): Aide légère (<25%), modérée (25@50%), maximale (50@75%) ou totale (>75%); (NE): Non Évaluée*

Transferts	I	S	A	NE	
FR => Mat. même niveau	☐	☐	☐	☐	
Assis <=> Debout	☐	☐	☐	☐	
Assis <=> Debout dans Ekso	☐	☐	☐	☐	

Déplacements	I	S	A	NE	NA	
FR Manuel	☐	☐	☐	☐	☐	
FR Motorisé	☐	☐	☐	☐	☐	
Marche						
-Marche exercice	☐	☐	☐	☐	☐	
-Dans l'établissement	☐	☐	☐	☐	☐	

Patron de marche/orthèses :

TESTS DE MARCHE		**Commentaires**
Vitesse de marche sur 10m	Naturelle: s	
	Rapide: s	

Aide tech.: ☐ Ø MAR: ☐ Ø-roue ☐ 2-roues; ☐ 4-roues ou déambulateur; ☐ B.A.; ☐ B.C.; ☐ C-Quad; ☐ C.S.
Main(s) utilisée(s) : ☐ D ☐ G ☐ Bilat ☐ N/A
Orthèses : **AFO :** ☐ D ☐ G ☐ Bilat ☐ Ø **KAFO :** ☐ D ☐ G ☐ Bilat ☐ Ø

NOM : _____ **Dossier :** S

3. ANALYSE ET PLAN DE TRAITEMENT

CRITÈRES D'ADMISSIBILITÉ POUR ENTRAÎNEMENT EXOSQUELETTE

3,1 CRITÈRES DU FOURNISSEUR DE L'EXOSQUELETTE	**Rencontré OUI**	**NON**	⇨ **PLAN DE TRAITEMENT / ADAPTATIONS PROPOSÉES**
1. AA's suffisantes des hanches (5° d'extension; 110° de flexion)	☐	☐	
2. AA's suffisantes de genoux (0° d'extension; 110° de flexion)	☐	☐	
3. AA's suffisantes des chevilles (0° DF et 25° FP)	☐	☐	
4. AA's des épaules permettant 50° d'extension	☐	☐	
5. Les mesures anthropologiques entrant dans les limites de la charte de l'exosquelette	☐	☐	
6. Symétrie des MI's	☐	☐	
7. Poids du sujet < 100 kg (220 lbs)	☐	☐	
8. Force de préhension permettant l'usage des A.T.'s	☐	☐	
9. Score Ashworth mod. ≤ 3 aux MI's	☐	☐	
10. Sujet indépendant à l'équilibre assis statique	☐	☐	
11. Sujet indépendant aux transferts FR⇔matelas	☐	☐	
12. Intégrité de la peau permettant l'usage de l'exosquelette	☐	☐	
13. Condition médicale permettant la verticalisation et la marche *(Ø HTO, Ø dysréflexie, Ø risque de Fx, etc)*	☐	☐	
14. Sujet est un candidat pour la marche avec d'autres appareils	☐	☐	
15. Sujet peut suivre les consignes et exprimer la douleur ressentie	☐	☐	

3,2 AUTRES INCAPACITÉS LIÉES À L'USAGE DE L'EXOSQUELETTE OU DU PROTOCOLE DE RECHERCHE	**TRAITEMENTS / ADAPTATIONS PROPOSÉES**

3,3 ANALYSE - Sujet ☐ accepté ou ☐ refusé

Fréquence prévue des traitements : _____ fois/semaine, pour environ _____ semaines

☐ Le plan de traitement et ses modalités, incluant les risques et conséquences possibles, ont été expliqués à l'usager et celui-ci consent au plan de traitement suggéré.

NOM : _____ **Dossier :** _____

ANNEXE - Mesures anthropométriques

Largeur des hanches (DD)		**Segment fémoral (DD)** *(Siège jusqu'au sommet des genoux fléchis)*				**Segment tibial (assis)** *(Semelle du soulier au sommet du genou fléchi)*			
Mesure (cm)	**Valeur Ekso**	**Mesure (cm)**		**Valeur Ekso**		**Mesure (cm)**		**Valeur Ekso**	
		G	D	G	D	G	D	G	D
ABD hanche :		Valeur globale :				Valeur globale :			

Souliers utilisés pour les mesures : _____

Mise en garde du manufacturier Ekso Bionic

If a patient has an **upper leg length discrepancy** greater than a half-inch (>0.5"/ >1.3cm) or a lower leg discrepancy greater than three-quarters of an inch (>.75" / >1.90cm), Ekso use is not recommended and the patient should fail screening. An upper leg length discrepancy of a half-inch (≤0.5"/ ≤1.3cm) or less may be accommodated by averaging the Ekso values of the right and left upper leg (e.g., if the right upper leg Ekso value is 25 and the left upper leg Ekso value is 29; the upper leg value may be averaged to 27).

A **lower leg length discrepancy** of three-quarters of an inch (≤0.75" / ≤1.90cm) or less can be accommodated with a shoe lift, if deemed appropriate by the physical therapist.

Regardless of patient leg length discrepancies, the **Ekso must be set to the same settings on each leg** to operate and balance correctly.

Be aware that the Ekso values provided in Form 3 are recommended starting points and may need to be adjusted based on visual assessments after donning the device.

TABLEAU 3 - RIGIDITÉ RECOMMANDÉE DES CHEVILLES (Utiliser comme guide uniquement) :

Rigidité ⇨	**1**	**2**	**3**	**4**
Présence de force en FP	Force élevé à normale de la cheville	Force de FP modérée à bonne, et sujet pèse moins de 60kg (130lbs)	Force de FP modérée et sujet pèse entre 60-80 kg (130-180lbs)	Force de FP faible à modérée et sujet pèse entre 80-100 kg (180-200lbs)
Absence de force en FP			Absence de force en FP et sujet pèse moins de 64kg (140lbs)	Absence de force en FP et sujet pèse plus de 64kg (140lbs)
	⇧ ⇧ ⇧	⇧ ⇧ ⇧	⇧ ⇧ ⇧	⇧ ⇧ ⇧
Type de sujet correspondant	MI normal, côté non affecté	Force partielle et faible poids	Force partielle et poids plus élevé ou aucune force et faible poids	Force limitée ou absente et sujet plus pesant

RÉGLAGE DE RIGIDITÉ - CHEVILLE GAUCHE :		**RÉGLAGE DE RIGIDITÉ - CHEVILLE DROITE :**	

ANNEXE - CHARTE DE DIMENSIONNEMENT DE L'EXOSQUELETTE EKSO GT™
(Source : Ekso Bionics Unités : Système métrique)

Hip Width - A

PATIENT MEAS.	EKSO VALUE	HIP ABD	PATIENT MEAS.	EKSO VALUE	HIP ABD
<35.8	0		40.8	10	
35.8	0	2	41	11	
36	1	to	41.2	11	
36.2	1	1	41.4	11	
36.4	2		41.6	12	
36.6	2	*Est.	41.8	12	
36.8	2		42	13	0
37	3		42.2	13	to
37.2	3		42.4	13	-1
37.4	4		42.6	14	
37.6	4		42.8	14	*Est.
37.8	4		43	15	
38	5		43.2	15	
38.2	5		43.4	15	
38.4	6	1	43.6	16	
38.6	6	to	43.8	16	
38.8	6	0	44	17	
39	7		44.2	17	
39.2	7	*Est.	44.4	17	-1
39.4	8		44.6	18	to
39.6	8		44.8	18	-2
39.8	8		45	19	
40	9		45.2	19	*Est.
40.2	9		45.4	19	
40.4	10		45.6	20	
40.6	10				

(*Ideal width between feet when walking is ~1 inch/2.5cm)

Upper Leg - B

PATIENT MEAS.	EKSO VALUE	PATIENT MEAS.	EKSO VALUE
51	0	56.4	21
51.2	1	56.6	22
51.4	2	56.8	23
51.6	2	57	23
51.8	3	57.2	24
52	4	57.4	25
52.2	5	57.6	26
52.4	6	57.8	26
52.6	6	58	27
52.8	7	58.2	28
53	8	58.4	29
53.2	9	58.6	30
53.4	9	58.8	30
53.6	10	59	31
53.8	11	59.2	32
54	12	59.4	33
54.2	12	59.6	33
54.4	13	59.8	34
54.6	14	60	35
54.8	15	60.2	36
55	16	60.4	36
55.2	16	60.6	37
55.4	17	60.8	38
55.6	18	61	39
55.8	19	61.2	40
56	19	61.4	40
56.2	20		

Lower Leg - C

PATIENT MEAS.	EKSO VALUE	PATIENT MEAS.	EKSO VALUE
48.0	0	55.8	24
48.2	0	56.0	25
48.4	1	56.2	26
48.6	1	56.4	26
48.8	2	56.6	27
49.0	2	56.8	28
49.2	3	57.0	28
49.4	3	57.2	29
49.6	4	57.4	30
49.8	5	57.6	30
50.0	5	57.8	31
50.2	6	58.0	32
50.4	7	58.2	32
50.6	7	58.4	33
50.8	8	58.6	34
51.0	9	58.8	34
51.2	9	59.0	35
51.4	10	59.2	36
51.6	10	59.4	36
51.8	11	59.6	37
52.0	12	59.8	38
52.2	12	60.0	38
52.4	13	60.2	39
52.6	14	60.4	40
52.8	14	60.6	41
53.0	15	60.8	41
53.2	16	61.0	42
53.4	16	61.2	43
53.6	17	61.4	43
53.8	18	61.6	44
54.0	18	61.8	45
54.2	19	62.0	45
54.4	20	62.2	46
54.6	20	62.4	47
54.8	21	62.6	48
55.0	22	62.8	48
55.2	22	63.0	49
55.4	23	63.2	50
55.6	24	63.4	50

ANNEXE - ÉVALUATION ASIA

ÉVALUATION MOTRICE

MUSCLES CLÉS

	D	G	
C5	☐	☐	Fléchisseurs du coude
C6	☐	☐	Extenseurs du poignet
C7	☐	☐	Extenseurs du coude
C8	☐	☐	Fléchisseurs des doigts (phalange distale du majeur)
D1	☐	☐	Abducteurs des doigt (5e doigt)

TOTAL M.S. ☐ + ☐ = ☐
(25) (25) (50)

Commentaires

Source :

	D	G	
L2	☐	☐	Fléchisseurs de la hanche
L3	☐	☐	Extenseurs du genou
L4	☐	☐	Dorsifléchisseurs de la cheville
L5	☐	☐	Extenseurs du gros orteil
S1	☐	☐	Fléchisseurs plantaires de la cheville

TOTAL M.I. ☐ + ☐ = ☐
(25) (25) (50)

0 = paralysie totale
1 = contraction palpable ou visible
2 = mouv. actif, sans gravité
3 = mouv. actif, contre gravité
4 = mouv. actif, contre une certaine résistance
5 = mouv. actif, contre une pleine résistance
NE = non évaluable

CONTRACTION ANALE VOLONTAIRE : ☐ Oui ☐ Non

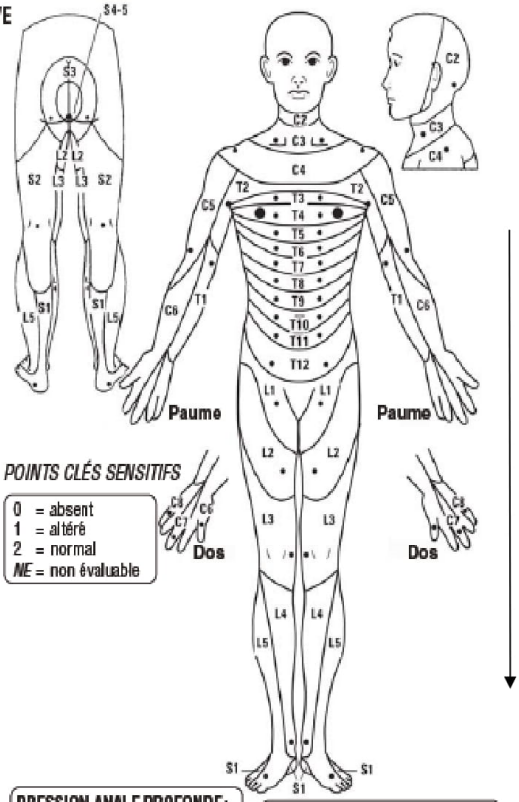
BCR: ☐ Présent ☐ Absent ☐ Inconnu

ÉVALUATION SENSITIVE

	TOUCHER LÉGER D	TOUCHER LÉGER G	PIQÛRE D	PIQÛRE G
C2				
C3				
C4				
C5				
C6				
C7				
C8				
D1				
D2				
D3				
D4				
D5				
D6				
D7				
D8				
D9				
D10				
D11				
D12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				
TOT. max.	☐ (56)	☐ (56)	☐ (56)	☐ (56)

☐ + ☐ = ☐ SCORE PIQÛRE (max : 112)

☐ + ☐ = ☐ SCORE TOUCHER LÉGER (max : 112)



POINTS CLÉS SENSITIFS

0 = absent
1 = altéré
2 = normal
NE = non évaluable

PRESSION ANALE PROFONDE: ☐ Oui ☐ Non

AUTRES DÉFICITS NEUROLOGIQUES

- ☐ Myélopathie
- ☐ Radiculopathie périphérique sans atteinte médullaire
- ☐ Radiculopathie périphérique avec atteinte médullaire
- ☐ Aucun
- ☐ Inconnu

NIVEAU NEUROLOGIQUE	D	G
SENSITIF	☐	☐
MOTEUR	☐	☐

NIVEAU NEUROLOGIQUE GLOBAL ☐

COMPLET OU IMCOMPLET
Incomplet = sensation ou fonction motrice à S4-5 ☐

ÉCHELLE DE SÉVÉRITÉ ASIA (A à E) ☐

À compléter seulement pour ASIA A

ZONE DE PRÉSERVATION PARTIELLE

	D	G
SENSITIF	☐	☐
MOTEUR	☐	☐

_____ _____
Signature Année mois jour Heure