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Ambulatory rehabilitation in patients with spinal cord injury: A clinical perspective

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Ambulatory rehabilitation in patients with spinal cord injury

A clinical perspective

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Ambulatory rehabilitation in patients with spinal cord injury

A clinical perspective

DISSERTATION

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by

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The research presented in this thesis was conducted at the School for Public Health and Primary Care: CAPHRI, Department of Epidemiology, of Maastricht University. CAPHRI participates in the Netherlands School of Primary Care Research CaRe. CAPHRI was classified as 'excellent' by the external evaluation committee of leading international experts that reviewed CAPHRI in December 2010.

CONTENTS

LIST OF ABBREVIATIONS

ACS	Anterior cord syndrome
AIS	American spinal injury association impairment scale
ASIA	American spinal injury association
BSS	Brown-Séquard syndrome
CCS	Central cord syndrome
CNS	Central nervous system
EMG	Electromyography
ISCoS	International spinal cord society
ISNCSCI	International standards for neurological classification of spinal cord injury
LEMS	Lower extremity motor score
MS	Motor score
NLI	Neurological level of injury
PCS	Posterior cord syndrome
RI	Relative improvement
SC	Spinal cord
SCI	Spinal cord injury
SD	Standard deviation
TMW	Ten meter walk test
TUG	Timed up and go test
UEMS	Upper extremity motor score
WISCI	Walking index for spinal cord injury

CHAPTER 1
General introduction

BACKGROUND

Spinal cord injury: "*an ailment not to be treated*." This statement was made about 4,000 years ago by a copyist who commented on what may be the first scientific description of two cases of a cervical spinal injury, which was written 1,000 years earlier [1]. It has now been established that acute treatment of a severe trauma is followed by a multidisciplinary rehabilitation approach. Patients who experience a spinal cord injury (SCI) today have an almost normal life expectancy [2-4]. Regaining the ability to ambulate on one's own legs is, among others, an important rehabilitation goal [5, 6]. Fortunately this is not an unrealistic scenario for numerous patients with incomplete spinal lesions. Spontaneous recovery processes and targeted physical rehabilitation measures help patients achieve this goal.

Nevertheless, the lives of most other people with spinal cord injuries are governed by remaining impairment. Recently, substantial endeavors have been made to relieve their lives, as much as possible, of detrimental sequelae by partial or complete cure of the SCI. These novel interventions will likely comprise a combination of well-shaped agents applied locally at the spinal cord and a goal-oriented rehabilitation intervention [7, 8]. This thesis is intended to help understand the processes underlying the recovery of ambulation during rehabilitation and may contribute to further shaping these interventions in order to optimally support future patients with SCIs.

The thesis focuses on the clinical perspective of the rehabilitation of ambulatory function. Rehabilitation interventions are increasingly based on pre-clinical studies. Furthermore, the thesis addresses the assessment of walking function in adult patients with SCIs. Important anatomical and physiological issues are presented as a basis for understanding the clinical picture of an SCI and the approaches used for rehabilitative training.

Structure and function of the spinal cord

The spinal cord (SC) is the interconnection between the brain and the peripheral nervous system that conducts sensory information and motor commands. In addition, the SC contains its own neural circuitry with the ability to modify reflexes and to control and generate elementary movements strongly involved in the walking function.

Structure of the spinal cord

The SC and the brain make up the central nervous system (CNS). The SC originates at the medulla oblongata of the brain stem and extends down the bony spinal canal to the upper lumbar spine. Notably, an adult's SC is shorter than the spine itself due

to the different growth of the nerves and bony structures (Figure 1.1). The average length of the SC is about 44 cm with a diameter of approximately 0.6 to 1.3 cm. Two regions at the cervical and lumber levels of the SC have a greater diameter; they contain the neurons which connect the CNS to the peripheral nervous system. The SC narrows at the caudal end, forms the conus medullaris and finally passes into the filum terminale, a non-nervous structure that attaches the SC to the coccyx. In the spinal canal below the conus medullaris, spinal nerves form the cauda equina. These nerves belong to the peripheral nervous system while the SC belongs to the CNS [9].

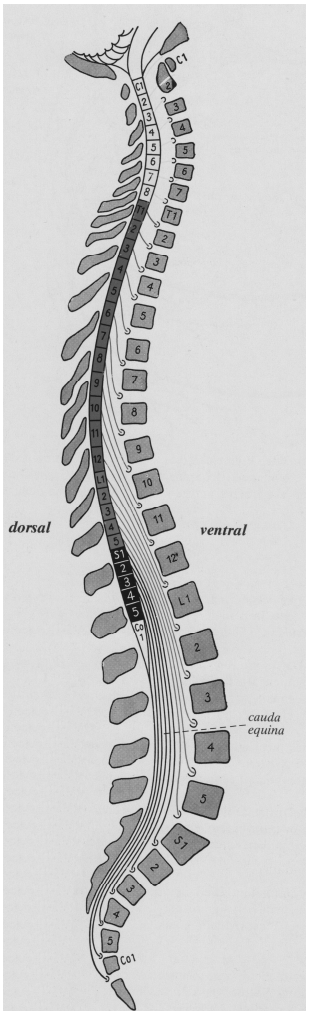


Figure 1.1 Position of the human spinal cord within the spinal canal. The spinal cord segments are numbered and marked with a grey scale: cervical: white; thoracic: dark grey; lumbar: light grey; sacral: black; coccygeal: white. At the caudal end of the spinal column is the cauda equina. Note the relationship between spinal cord segments and the vertebral segments. (from: Sobotta Atlas der Anatomie des Menschen © Elsevier GmbH, Urban & Fischer, München).

Both the brain and the SC are embedded in multilayer meninges and float in the cerebrospinal fluid. The SC is divided into 31 segments (Figure 1.1). A spinal nerve branches out from each segment on both sides (Figure 1.2). These nerves contain

sensory and motor nerve fibers; in the thoracic and lumbar regions, the nerves have vegetative nerve fibers as well. The target organs of these nerves are somatotopically arranged. It is known from which segment a given muscle is innervated (myotome) and which segment corresponds to a given area on the skin (dermatome) [10]. This fact is the basis for the determination of the neurological level of injury (NLI) in the case of a damaged SC. The signs and symptoms pertaining to the autonomic nerve system do not correspond as clearly to a segmental region.

A cross section of the human SC shows two distinct regions. The centrally located grey matter is shaped like an H or a butterfly and contains cell bodies and interneurons. The ventral horns mainly contain the motor neurons which travel via anterior root to the target muscles. The dorsal horns are formed by the cell bodies of the ascending nerves (Figure 1.2).

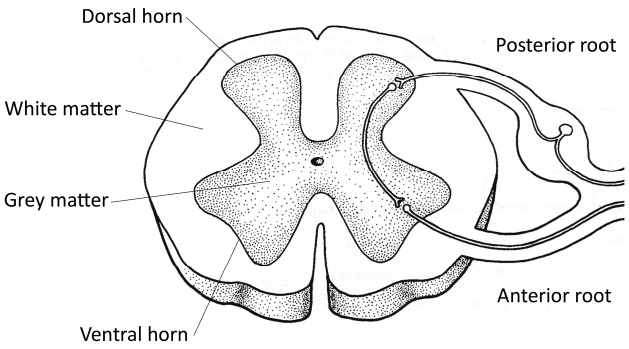


Figure 1.2 Cross-section of the human spinal cord. The H-shaped grey matter is located centrally, surrounded by the white matter. The ventral and dorsal nerve roots are shown for one side (left) only.

Blood supply to the spinal cord

Three main arteries ensure that blood is supplied to the SC. About two-thirds of the anterior portion of the SC is perfused by the anterior spinal artery, a blood vessel which runs alongside anteriorly in the middle of the SC. The posterior portion of the SC is supplied by the two posterior spinal arteries, which are located in a posterior-lateral position alongside the SC.

Pathways

The white matter which surrounds the central grey matter contains ascending and descending axons with multiple pathways. For the clinical work, two afferent and one efferent pathway are most important.

The *dorsal column* pathway conveys light touch, vibration and proprioceptive information essential to the coordination of movements. Nerve fibers enter the SC through the dorsal root and ascend ipsilaterally in the dorsal column to the region of the medulla oblongata, where they are connected to secondary neurons (internal actuate fibers) which decussate to the opposite side and project into the thalamus. Fibers from the lower parts of the body are embedded in the *fasciculus gracilis*; those fibers from the upper parts travel along the more laterally located *fasciculus cuneatus* (Figure 1.3).

The *spinothalamic tract* lies in the anterolateral region and transmits temperature and pain sensation. Afferents from this system enter the SC via the dorsal root and cross to the opposite side either at the level where they entered the SC or in one of the adjacent segments. In the anterolateral portion, the fibers ascend directly to the thalamus (Figure 1.3).

The efferent motor fibers travel caudally from the motor cortex, decussate in the medulla oblongata and descend into the lateral region of the SC as *corticospinal tract* (or pyramidal tract). These fibers largely connect with their target motor neurons in the ventral horn. Part of the tract ends in spinal interneuronal circuits that indirectly mediate signals to the motor neurons. The axons of those neurons project without further synapsing to the respective skeletal muscles (Figure 1.3).

The proximate positioning of the spinothalamic and the corticospinal tracts is clinically significant. A spared function for temperature and pain, indicating a partial integrity of the spinothalamic pathway, is of high prognostic value for motor recovery following an SCI.

The somatotopic organization is discernible in each pathway. Fibers travelling to the upper extremities are located more centrally and those travelling to the legs are located more laterally [11]. This fact is the basis for the clinical presentation of the central cord syndrome.

In addition to the long pathways projecting between the brain, brain stem and the periphery, there are additional connections which begin and end within the SC. These interneurons and propriospinal systems are involved in the processing of afferent input such as the reciprocal inhibition or polysynaptic reflexes.

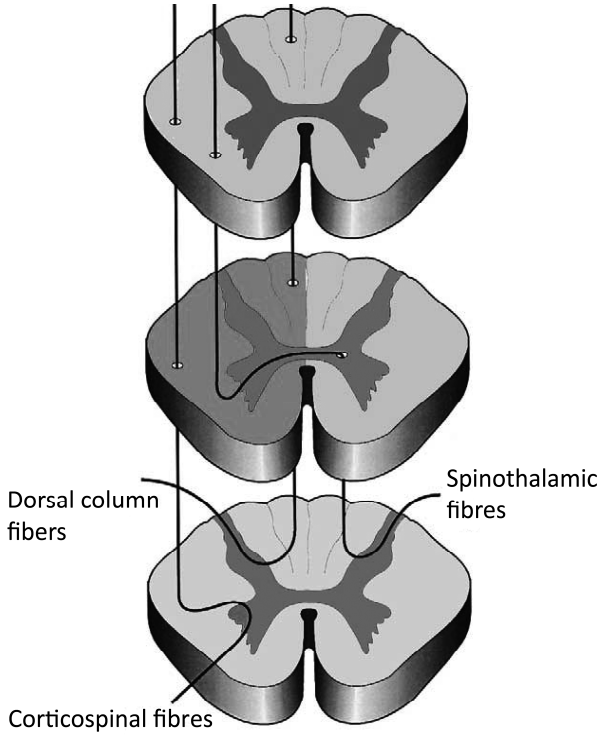


Figure 1.3 Schematic drawing of three clinically important spinal pathways: dorsal column, spinothalamic and corticospinal tracts. Note the decussation of the different tracts on different levels. The grey shaded area on the right side of the middle segment shows the area affected by a lesion leading to a Brown-Séquard syndrome. (from: Tattersall R, Turner B. Brown-Séquard and his syndrome. Lancet. 2000 Jul 1;356(9223): 61-3.).

Central pattern generator, spinal locomotor center

The SC not only transmits information between the brain and the peripheral organs, but neuronal circuitries within the SC are capable of generating and controlling more complex movements. The network that is generally referred to as the central pattern generator (CPG) can generate coordinated rhythmic and synergistic activation of flexor and extensor motor neurons independent of afferent proprioceptive feedback or supraspinal control. This phenomenon has been extensively studied in numerous animal models [12].

The CPG-driven activity is also present in humans with clinically complete SCIs and can be analyzed by means of electromyographic (EMG) recordings [13]. Interestingly, this activity is not a rigid and stereotypical EMG pattern of the leg muscles, but becomes adapted and modulated according to peripheral proprioceptive afferent sensory feedback information [14, 15]. An increase in EMG amplitude and a decrease in inappropriate activity can be observed by providing adequate proprioceptive stimulation during a series of experimental therapy sessions, which indicates that these neural centers can be trained [16]. However, when the training stopped in patients with complete SCIs where voluntary effort did not result in any

muscle activation below the NLI, the EMG amplitude dropped to a level similar to that prior to the training. Patients who regain ambulatory function maintain their level of EMG activity (Chapter 2, [17]). The spinal locomotor pattern generator is both a resource and a target for rehabilitation efforts aimed at improving walking function in those patients who are likely to recover motor function, as is often the case in incomplete SCI.

SPINAL CORD INJURY

Damage to the SC's nervous structure results in a clinical syndrome that is characterized by impaired or lost motor, sensory and autonomic functions. Accordingly the clinical presentation of an SCI involves paralysis, reduced or lost sensations and symptoms associated with autonomic dysfunctions [18].

Motor impairment

The motor impairment which results from an SCI can vary between complete loss of voluntary motor function and mild paresis. The number of affected muscles depends on the location and extent of the SCI. Based on the knowledge of myotomes, the level of SCI can be derived from the paralysis pattern. For this purpose, certain key muscles have been defined which are known to be innervated by a known SC segment.

If the SCI involves the corticospinal tract (which is also referred to as the *upper motor neuron*), a spastic plegia will result. However, the damaged segments will exhibit a flaccid paresis and abolished reflexes due to the Wallerian degeneration of the affected *lower motor neurons*. The same finding is made when the cauda equina is damaged; in such situations, the lesion affects the peripheral nerve system. Although the extent of motor impairment is critical for regaining the ability to perform activities of daily living (ADL), it has been shown that it is not the only determinant (Chapter 3, [19]).

Sensory impairment

A dorsal column lesion results in impaired touch, vibration and proprioception sensation. If only one side of the SC is affected, the sensory loss will affect the ipsilateral side of the body below the NLI. Temperature and pain perception are affected when the anterolateral portion of the SC is damaged. If the damage is restricted to one side, the loss will be found on the contralateral side. By examining the single

dermatomes, the level at which the SC lost its function in response to the injury can be determined.

Autonomic dysfunction

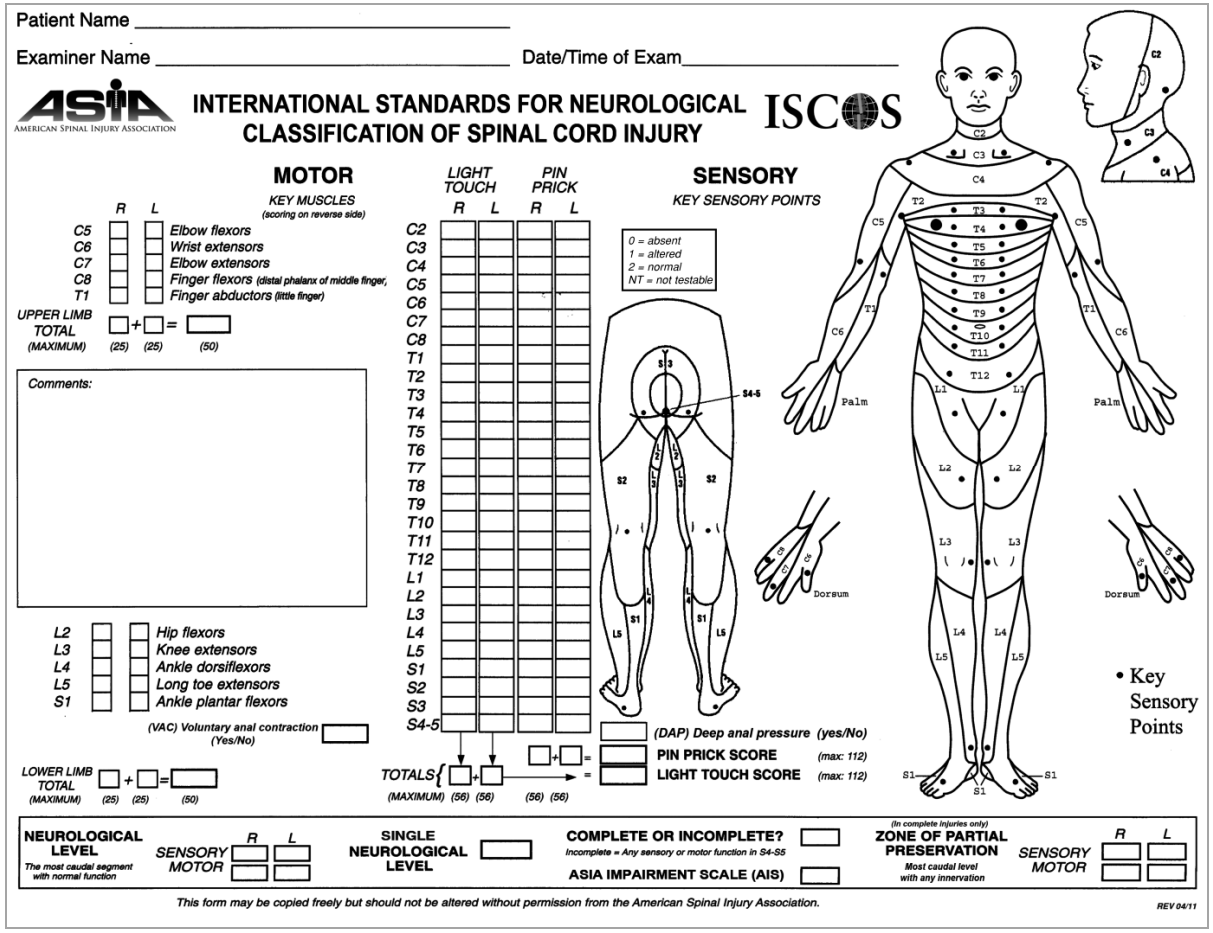
In contrast to the motor and sensory impairments which can be related to a certain segmental level, the autonomic dysfunctions can vary considerably. Most prominent in almost all SCI cases are the loss of voiding function related to bladder and bowel. Typical signs and symptoms in an SCI above the mid-thoracic level are bradycardia, orthostatic hypotension and autonomic dysreflexia due to the disruption of sympathetic pathways. Also notable is the loss of body temperature regulation in patients with a high thoracic or cervical lesion.

Classification of spinal cord injuries

The classification is geared to the leading SCI symptoms: motor and sensory impairment. In 1982, the American Spinal Injury Association (ASIA) developed and published a standardized examination form for patients with SCIs [20]. These international standards for neurological classification of spinal cord injury (ISNCSCI) have been revised repeatedly. In 1992, the standards were also adopted by the International Spinal Cord Society (ISCoS). The most recent version dates to 2011 (Figure 1.4) [21].

Classification is based on a clinical neurological examination for which the patient has to be awake and able to cooperate. This examination comprises motor and sensory tests. The classification follows a defined algorithm to define the neurological level and completeness of the SCI (Figure 1.4B).

Motor testing
The level of paralysis is assessed using a muscle function test that grades the strength of a voluntary muscle contraction in one of six categories (Figure 1.4B, Muscle function grading). Five key muscles from the upper and lower extremities are examined. The respective values of the muscle grading are summed up to the upper extremity motor score (UEMS), the lower extremity motor score (LEMS) or the total motor score (MS). UEMS and LEMS ranges between 0 and 50 (25 for each side) and total MS between 0 and 100. In addition to the muscles on the extremities, the anal sphincter is examined and the presence (or absence) of a voluntary contraction is evaluated.



A

Figure 1.4 The international standards for neurological classification of spinal cord injury comprising motor and sensory testing. The spinal cord injury is classified according to the level of injury and an impairment scale. A indicates the front and B the rear page of the classification. American Spinal Injury Association: International Standards for Neurological Classification of Spinal Cord Injury, revised 2011; Atlanta, GA. Reprinted 2011.

B

Muscle Function Grading

0 = total paralysis

1 = palpable or visible contraction

2 = active movement, full range of motion (ROM) with gravity eliminated

3 = active movement, full ROM against gravity

4 = active movement, full ROM against gravity and moderate resistance in a muscle specific position.

5 = (normal) active movement, full ROM against gravity and full resistance in a muscle specific position expected from an otherwise unimpaired peson.

5* = (normal) active movement, full ROM against gravity and sufficient resistance to be considered normal if identified inhibiting factors (i.e. pain, disuse) were not present.

NT = not testable (i.e. due to immobilization, severe pain such that the patient cannot be graded, amputation of limb, or contracture of >50% of the range of motion).

ASIA Impairment (AIS) Scale

☐ **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 and includes the sacral segments S4-S5 (light touch, pin prick at S4-S5: or deep anal pressure (DAP)), 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 neurological level of injury (NLI) have a muscle grade less than 3 (Grades 0-2).

☐ **D = Motor Incomplete.** Motor function is preserved below the neurological level**, and <u>at least half</u> (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 ISNCSCI are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E. Someone without an initial SCI does not receive an AIS grade.

**For an individual to receive a grade of C or D, i.e. motor incomplete status, they must have either (1) voluntary anal sphincter contraction or (2) sacral sensory sparing <u>with</u> sparing of motor function more than three levels below the motor level for that side of the body. The Standards at this time allows even non-key muscle function more than 3 levels below the motor level to be used in determining motor incomplete status (AIS B versus C).

NOTE: When assessing the extent of motor sparing below the level for distinguishing between AIS B and C, the ***motor level*** on each side is used; whereas to differentiate between AIS C and D (based on proportion of key muscle functions with strength grade 3 or greater) the ***single neurological level*** is used.

Steps in Classification

The following order is recommended in determining the classification of individuals with SCI.

1. Determine sensory levels for right and left sides.
2. Determine motor levels for right and left sides.
   Note: in regions where there is no myotome to test, the motor level is presumed to be the same as the sensory level, if testable motor function above that level is also normal.
3. Determine the single neurological level.
   This is the lowest segment where motor and sensory function is normal on both sides, and is the most cephalad of the sensory and motor levels determined in steps 1 and 2.
4. Determine whether the injury is Complete or Incomplete. (i.e. absence or presence of sacral sparing)
   If voluntary anal contraction = **No** *AND all S4-5 sensory scores =* **0** *AND deep anal pressure =* **No,** *then injury is COMPLETE. Otherwise, injury is incomplete.*
5. Determine ASIA Impairment Scale (AIS) Grade:

Is injury <u>Complete?</u> If **YES,** AIS=A and can record ZPP (lowest dermatome or myotome on each side with some preservation)

NO ↓

Is injury motor <u>Incomplete?</u> If **NO**, AIS=B (Yes=voluntary anal contraction OR motor function more than three levels below the motor level on a given side, if the patient has sensory incomplete classification)

YES ↓

Are <u>at least</u> half of the key muscles below the single <u>neurological</u> level graded 3 or better?

NO ↓ AIS=C YES ↓ AIS=D

If sensation and motor function is normal in all segments, AIS=E

Note: AIS E is used in follow-up testing when an individual with a documented SCI has recovered normal function. If at initial testing no deficits are found, the individual is neurologically intact; the ASIA Impairment Scale does not apply.

Sensory testing
Two sensory modalities are examined: light touch (dorsal column tract) and pin prick (spinothalamic tract). Every segment is given a score between 0 and 2 (Figure 1.4A). The total sensory scores range between 0 and 112 for each of the two modalities. In addition to the examination of the abovementioned dermatomes, the patients are examined to see whether they perceive deep anal pressure (DAP), which is a gentle pressure exerted to the anorectal wall that is innervated by the pudental nerve (S4-S5).

Level of spinal cord injury
The ISNCSCI distinguishes between the motor and sensory levels for both sides and a single neurological level. A level is defined as the lowest segment with normal function. Lesions related to the cervical cord or the first thoracic segment will affect the arms, legs and trunk; this form of SCI is referred to as *tetraplegia* or *quadriplegia*. Lesions in lower regions of the SC that result in symptoms in the legs (and trunk) are labeled *paraplegia*.

Completeness of spinal cord injury/ASIA impairment scale
The sacral sparing is essential for the categorization of an injury as either complete or incomplete. Sacral sparing means that the patients have preserved motor (voluntary anal sphincter contraction) or sensory function (perianal sensation or DAP) in segments S4-S5. A complete injury is categorized as ASIA impairment scale (AIS) A (Figure 1.4B). Incomplete injuries are further subdivided according to preserved motor function into AIS B, C or D. Patients who recover completely from their SCI symptoms are considered to be AIS E.

Spinal cord injury clinical syndromes

In addition to tetraplegia and paraplegia, special forms of clinical presentations can be found depending on the location and extent of the SC lesion [22].

Central cord syndrome
Central cord syndrome (CCS) is characterized by a more pronounced paralysis of the upper extremities compared to the lower extremities, which remain less affected. It is caused by a lesion in the center of the cervical SC involving the grey matter and the axons lying more central projecting to the motor neurons of the upper body. The more laterally located axons that travel to the ventral horns and contain the lower body's motor neurons become less compromised.

CCS frequently occurs in older persons with preexisting myelopathy due to degenerative processes of the cervical spine. An inadequate minor trauma associated with

a trip or a fall then results in CCS. CCS is not restricted to elderly people; it can also occur in younger patients following a trauma. The prognosis for regaining ambulatory function after experiencing CCS is generally good (Chapter 4, [23]).

Brown-Séquard syndrome
Brown-Séquard syndrome (BSS) results from a SC injury that mainly occurs to one side of the SC (Figure 1.3). Clinically, a paresis and loss of touch sensation are present on the ipsilateral side and the perceptions of temperature and pain are impaired on the contralateral side. A pure BSS is rare but lateralized paresis with more or less clear dissociated somatosensory deficits is more frequent. These BSS lesions are referred to as BSS plus syndrome [24]. Like CCS, patients with BSS have a good prognosis for regaining ambulatory function (Chapter 4, [23]).

Anterior cord syndrome
Anterior cord syndrome (ACS) is characterized by damage to about two-thirds of the anterior portion of the SC, resulting in a loss of motor and sensory functions for pain and temperature. The perception of touch is not affected. This type of lesion occurs when the blood supply from the anterior spinal artery is interrupted.

Posterior cord syndrome
In its pure form, this syndrome rarely occurs; typically, those patients present with a loss of touch, vibration and proprioception due to a dorsal column lesion. Since the anterior portion of the SC is unaffected, motor function and sensations of pain and temperature are preserved. Although motor function is not affected, these patients exhibit substantial difficulties performing coordinated movements consistent with a spinal ataxia. People with severe cases may be dependent on a wheelchair for their mobility.

Cauda equina syndrome
When the spinal lesion is below the conus medullaris, the cauda equina is damaged rather than the SC itself. The patients will show a flaccid paresis with abolished reflexes. In these patients, it is not appropriate to activate and train spinal locomotor centers since the reflex arcs have been disrupted. However, this lesion type represents a low SCI and the proximal leg muscles (i.e., hip flexors (L2) and knee extensors (L3)) are normally under voluntary control. With adapted ankle-foot orthoses (AFO) or knee-ankle-foot orthoses (KAFO) these patients may regain ambulatory function even if the SCI is classified as AIS A.

Etiology

Most SC injuries are acquired; these types are presented in the first and second of the following categories. The third category deals with congenital SC injuries, which are not included in this thesis.

Traumatic injury

In most cases, a lesion to the SC is associated with spinal instability due to torn ligaments and/or fractures of one or multiple vertebrae. The main causes of those lesions include motor vehicle accidents and falls [25]. The cervical spine is more exposed than the thoracic and lumbar regions, so a relatively small impact there can result in an SCI. In contrast, stronger forces are required to lesion the SC in the thoracic, lumbar and sacral regions. Often these traumas result not only in a spine fracture but in multiple lesions of surrounding structures (e.g., ribs, lung). The greatest number of lesions is found in the regions which are biomechanically predisposed (i.e., the conjunctions between head and thorax or thorax and pelvis) (Figure 1.5).

Only in rare cases is the SC completely torn apart; more often the anatomical structure remains partially intact. Due to the trauma, the spinal canal narrows and the SC and/or the blood supply is compressed. Zones of lesion severity can be distinguished around the lesion site. Axons and nerves are completely damaged in the center of maximum compression. Nerves around that zone lose some of their function but remain structurally intact. The temporary loss of function is known as neurapraxia and the recovery of a patient after SCI can partially be attributed to the resolution of the neurapraxia [18].

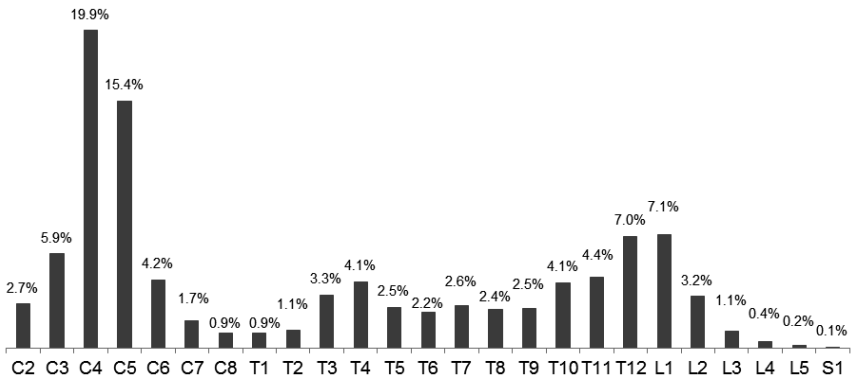


Figure 1.5 Frequency distribution of traumatic SCI in relation to neurological level of injury. Data originate from the European Multicenter Study about Spinal Cord Injury (EMSCI). Numbers are percentages; n=2054.

Non-traumatic

Non-traumatic SCIs are caused by vascular, inflammatory, immunological or neoplastic conditions. Because of the variety of etiologies, the group of non-traumatic SCIs is more heterogenous than the group of traumatic injuries. A non-traumatic SCI can emerge acutely (e.g., due to an acute hemorrhage) or develop over several months (e.g., myelopathy due to a degenerative narrowing of the spinal canal). Non-traumatic SCIs are often incomplete although complete loss of function is not uncommon. The clinical pathway of the German Society for Neurology (Deutsche Gesellschaft für Neurologie) classifies non-traumatic SCIs according to Table 1.1.

Table 1.1 Causes of non-traumatic spinal cord injury

1. Spinal cord compression	2. Myelitis	3. Myelopathy	4. Demyelination
– Tumors	– Viral	– Arteriovenous malformation	– Multiple sclerosis
– Disc herniation	– Bacterial	– Ischemia	– Acute disseminated encephalomyelitis (ADEM)
– Spondylodiscitis	– Mykogene	– Radiation damage	
– Hemorrhage		– Toxic	– Neuromyelitis optica
– Spinal canal stenosis			– Acute transverse myelitis
			– Collagenosis

SCI symptoms can also be caused by multiple small gas embolisms that occur when external pressure on the body is suddenly relieved (e.g., in the water). The 'decompression sickness' or Caisson disease emerges when scuba divers ascend to the surface too quickly. During fast depressurization, physically dissolved gas in the blood forms bubbles that block perfusion.

Congenital

Severe forms of developmental congenital malformations (spina bifida or myelomeningocele) result in the signs and symptoms of an SCI. This thesis does not include patients with congenital SCIs.

Epidemiology

Incidence/prevalence

According to a recently published literature review, the incidence rates for traumatic SCI vary across geographical regions: the number of new cases per million inhabitants ranged from 2.3 (Canada) to 83 (Alaska) [26]. Other researchers reported similar variations in their results [27, 28]. Prevalence seems to be less accurately recorded; available data showed prevalence per million persons ranging from 236 (India) to 1,800 (USA) [26]. Compared to stroke [29], SCIs occur relatively rarely.

There are fewer epidemiologic data available for non-traumatic SCIs. However, two large population-based studies showed that the number of patients with non-traumatic SCIs exceeds that of traumatic cases [30, 31]. In a nationwide Australian study, the incidence of non-traumatic SCI was reported to be 26.3 cases per million per year [31].

Age at injury
The average age at which a traumatic SCI occurs has increased over the last decades. In the USA, the average age at injury grew from 29 years (in 1973-1979) to 41 (in 2005-2010). In a European network of SCI rehabilitation centers [32], the average age at injury was 45 years (in 2005-2010) (Wirz, unpublished). With an average age of approximately 61 years, patients with non-traumatic SCIs are clearly older at onset [28, 30, 31, 33, 34].

Male/female distribution
Though about 80% of traumatic SCI cases occur in men [25-28], the ratio is balanced in the group of patients with non-traumatic SCIs [30, 31, 33, 34].

Lesion characteristics
According to registers in the USA [2] and Europe [32], the most frequent condition after a traumatic SCI is incomplete tetraplegia (41% and 33%) followed by complete paraplegia (22% and 27%), incomplete paraplegia (21% and 23%) and complete tetraplegia (16% and 17%). Non-traumatic SCI tends to result more frequently in incomplete paraplegia [33, 34].

REHABILITATION

After an SCI of any origin, patients undergo a multidisciplinary rehabilitation where the primary aim is to maximize patients' independence in performing daily life activities and participating in life situations. Until about the 1990s, rehabilitation after a neurological event (e.g., SCI) focused primarily on preventing complications that resulted from impairment [35, 36]. Driven by the results and conclusions of physiological and behavioral animal studies [7, 8, 37], the rationale behind intervention strategies started to fundamentally change. A more comprehensive understanding of the neurological conditions became increasingly established; it not only focused on impairment but also on activities, participation and environmental factors. The framework of the International Classification of Functioning Disability and Health [38], which evolved from Nagi's seminal work [39], expresses that new understanding. In accordance with this change of paradigm, interventions and assessments were challenged and new approaches were developed. For example, activity-

dependent neural plasticity became a major concept within neurological rehabilitation [40]. Physiotherapists are confronted with the tasks of implementing knowledge derived from basic research and providing scientific backgrounds for their empirically based interventions.

Prognosis/recovery

The impairments seen after an SCI exhibit not only a large variation in terms of their clinical presentation at onset but also with regard to their recovery [41]. Patients with a complete SCI (i.e., AIS A) tend to remain at that level and show only some recovery in the segments adjacent to the lesion [42, 43]. However, activity-related changes can also be observed in this patient group [44]. Most likely, the basis for these improvements is compensation and adaptation. For example, the use of a wheelchair can be considered to be a compensatory strategy for overcoming the loss of motor function in the lower extremities, or an indwelling catheter can compensate for the impaired voiding function of the bladder.

In contrast, patients with incomplete SCI lesions frequently show marked recovery from impairment within the first year after injury [41, 45, 46]. The main changes in walking function can be observed within the first half year [47], a time period when rehabilitation usually takes place. Improvements in impairment level and activities seem to be based on compensation/adaptation but also on activity-dependent neural plasticity that is exploited by functional training and spontaneous recovery of function [48, 49].

Rehabilitation of mobility

Among other domains, mobility is a typical target for physical therapy interventions [50]. Depending on the neurological motor deficit, mobility is attained either by using a wheelchair or regaining locomotor ability. In the latter case, walking aids and orthotics may be required.

Predictors for regaining ambulation after an SCI are the initial motor score (specifically that of the lower extremities), partial sensory sparing, age, somatosensory evoked potentials [51-53] and mobility assessments made by physical therapists [54]. Patients with an incomplete AIS B or C SCI typically exhibit an extensive impairment at the beginning of rehabilitation. Volitional leg muscle activation is not possible or hardly possible and mobility is restricted to the wheelchair. However, as highlighted earlier about these cases (i.e., AIS B and C), the prognosis for regaining walking function is high. But that can be hampered if during the period of impaired

mobility and non-use of the locomotor system a secondary worsening by maladaptive plasticity takes place (which is elsewhere referred to as 'learned non-use') [55].

From this point of view, it is important to start locomotor training as early as possible, even though patients do not yet have voluntary motor control of their leg movements. The locomotor system can be activated (Chapter 2, [17]) in this early phase by using adequate supporting training devices (Chapter 7, [56]). In such a way, the spinal locomotor centers are activated when adequate proprioceptive afferent input is provided. When patients eventually start to regain some voluntary control of their leg movements, the support can gradually be reduced. Studies have shown that the improvement of function exceeds that of neurological deficit (Chapter 3). The goal of the supported locomotor training is to enable patients to ambulate over ground.

AIM OF THE THESIS

This thesis focuses on the rehabilitation of ambulatory function. Rehabilitation interventions and the ways their effectiveness is assessed have undergone substantial development in the last few years.

This thesis includes three main sections:

i) Are concepts derived from basic research applicable to human subjects with an SCI?
   a. the spinal locomotor center *(Chapter 2)*
   b. the interrelation of the ICF (*Chapter 3)*
   c. an animal lesion model *(Chapter 4)*

ii) Is the use of robots feasible and effective? *(Chapters 7, 8 and 9)*

iii) How valid and reliable are measurements of walking function and falls which were originally developed for other patient populations? *(Chapters 5 and 6)*

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CHAPTER 2

Long term effects of locomotor training in spinal humans

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ABSTRACT

The long term effects of locomotor training in patients with spinal cord injury (SCI) were studied. In patients with complete or incomplete SCI coordinated stepping movements were induced and trained by bodyweight support and standing on a moving treadmill. The leg extensor muscle EMG activity in both groups of patients increased significantly over the training period, associated with improved locomotor ability in those with incomplete SCI. During a period of more than 3 years after training, the level of leg extensor EMG remained about constant in incomplete SCI in those who regularly maintained locomotor activity. By contrast the EMG significantly fell in those with complete SCI. The results suggest a training induced plasticity of neuronal centres in the isolated spinal cord which may be of relevance for future interventional therapies.

Keywords. locomotion; spinal cord injury; leg muscle EMG activity; motor learning

INTRODUCTION

It has been known for several years that patients with spinal cord injury (SCI) profit from specific locomotor training experiments, [1-3] based on cat studies. In the spinal cat the generation of coordinated leg muscle EMG activity on a moving treadmill was first described in 1980 [4]. Similar step-like automatic movements are present at birth and in anencephalic children [5]. Evidence arose that in adult humans also, spinal interneuronal circuits exist which are involved in the generation of locomotor activity [2, 6]. The locomotor function of incomplete paraplegic patients was shown to profit by specific training on a treadmill with partial body weight support [3, 7]. Certain guidelines must be followed to make the training effective [2, 6, 7]. The beneficial effect of this training critically depends on a physiological proprioceptive afferent input - for example, from load receptors [8] - to the spinal locomotor centres. Even in patients with a complete SCI, a locomotor pattern could be induced [1]. The aim of this study was to investigate the course of locomotor EMG activity after the end of locomotor training in patients with complete and incomplete SCI.

PATIENTS AND METHODS

General procedures

Consent was obtained from patients and the local ethics committee to make recordings in 32 patients with SCI. The clinical diagnosis of spinal cord lesion was confirmed by electrophysiological [9] and radiological [10] examinations. Patients with peripheral nerve damage were excluded. Thirty two patients had either a complete motor SCI according to the American Spinal Cord Injury Association (ASIA) classification [11] (A or B (n=16; mean age 35 (SD 12) years)) or had an incomplete motor SCI (ASIA C (n=2) or D (n=14) (mean 35 (SD 16 years)) (Table 2.1). The level of lesion ranged from C4 to T12 (one patient with incomplete SCI at L3) with about one third at the cervical and two thirds at the thoracic level (see Table 2.1).

All patients were admitted to our centre between 1993 and 1997 for primary rehabilitation. They underwent daily locomotor training on a treadmill (roughly 300 m of walking (about 15 minutes), 1.5 km/h speed, 5 days a week) starting between day 32 to 347 after SCI (mean 96 (SD 64)). The training on average lasted 137 days (SD (SD 72). In all patients with complete SCI and at the beginning of the training in most patients with incomplete SCI (13 of 16), leg movements had to be assisted by physiotherapists and body weight had to be partially unloaded. Unloading was achieved by suspending the patients over the treadmill by a parachute harness connected to counterweights. The amount of unloading was adapted to the

Table 2.1 Patients with SCI included in the study

Patient No	Sex	Age (y)	Level of lesion	ASIA score at beginning of treadmill training	ASIA score at end of treadmill training	Duration of treadmill training (days)
Complete SCI						
1	M	46	C5	A	A	343
2	M	23	C6	A	A	219
3	M	28	C6	B	B	158
4	M	42	C7	A	A	101
5	M	21	C7	A	A	210
6	M	42	T1	A	A	139
7	M	41	T1	A	A	85
8	F	19	T1	A	A	112
9	M	53	T1	B	B	148
10	M	27	T1	A	A	71
11	M	35	T10	A	A	90
12	F	14	T3	A	A	120
13	M	50	T4	A	A	273
14	M	33	T6	A	A	84
15	M	26	T6	A	A	103
16	M	53	T8	B	B	113
					Mean:	148
Incomplete SCI						
17	M	24	C4	C	C	288
18	M	51	C4	C	D	126
19	M	47	C4	D	D	107
20	M	72	C6	D	D	174
21	M	13	C7	D	D	147
22	M	20	C8	D	D	165
23	M	33	L3	D	D	98
24	M	37	T10	C	D	36
25	M	30	T11	C	D	49
26	M	32	T11	D	D	91
27	F	29	T11	C	D	175
28	M	39	T11	D	D	35
29	M	31	T12	C	D	196
30	M	23	T12	C	D	103
31	M	59	T7	D	D	154
32	M	11	T7	C	C	60
					Mean:	125

Abbreviation: SCI, spinal cord injury

patients' capability of performing stepping movements (up to 80% of body weight). After training had finished, 11 patients with incomplete SCI needed neither unloading nor external assistance and were able to perform stepping movements on nor-

mal ground conditions; two patients could walk without unloading but needed some assistance. In all patients with complete SCI body weight support could be reduced during the course of the training, although none of these patients could perform stepping movements without assistance after finishing locomotor training. Recordings at three points were made weekly: EMG activity from the gastrocnemius medialis muscle using surface electrodes; the force exerted on the treadmill using force plates located underneath the treadmill; and from movements of the knee joints using mechanical goniometers fixed at the lateral aspect of the right and left knees. Follow up recordings were also made after finishing the locomotor training as outpatients. The number of outpatient measurements and the intervals between them varied due to the availability of the patients (a mean of five measurements over a mean period of 1.9 years (SD 1.4), range 0.13–5.8 years)). We also analysed the time course of the amplitude of muscle action potentials (MAPs) of the abductor hallucis muscle evoked by tibial nerve stimulation in four patients with complete SCI, for more than 4 years.

Data analysis

The EMG recordings were amplified (μV amplifier; bandpass filter, 30–300 Hz) and, together with the biomechanical signals, were converted (a/d) into a digital signal and transferred to a PC system. Signals were sampled at 500 Hz. The EMG signals were rectified and averaged over 20 step cycles. The force signal indicating the heel strike and beginning of the stance phase served as a trigger to average the EMG signal and to normalize the recordings to one stride cycle (for further details see Dietz et al [1, 6]. To investigate changes in amplitude of EMG activity in the gastrocnemius medialis muscle as a function of time, the signal energy (root mean square (RMS)) was determined for the stance (5%–25% before the end of the stance phase) and for the swing phase (5%–25% after the end of stance). The knee joint signal was used to detect the end of the stance phase. During the stance phase, the main activation and during swing no activation of the gastrocnemius medialis muscle was expected to occur [6]. The RMS during swing was subtracted from the RMS during stance to eliminate noise and tonic muscle activation. To allow intersubject comparison within the two groups of patients with complete and incomplete SCI, measurements were normalised to the mean RMS amplitude of the three final recordings before finishing locomotor training. These values have been correlated with the time elapsing after discharge. Because the number of the recordings differed between patients, Pearson's weighted correlation coefficient was taken for calculation. A Dantec Keypoint 1000 EMG machine was used to record M waves. The maximal amplitude of muscle action potentials was obtained by a supramaximal stimulation (single rectangular wave stimuli of 0.5 ms duration, <100 mA) of the tibial nerve at the level of the ankle. The M waves (MAPs) were recorded in four

patients over the abductor hallucis muscle using surface electrodes. The maximal MAP amplitude (baseline to peak) was determined. The registration was done before, during, and after the locomotor training in patients with complete SCI to assess whether muscle atrophy due to disuse had occurred. The MAP amplitude of the four patients has been correlated with the time elapsing after discharge (Pearson's correlation coefficient).

RESULTS

Figure 2.1 shows two examples of gastrocnemius muscle EMG during one step cycle of (A) a patient with complete paraplegia T4 and (B) a patient with incomplete tetraplegia C4 (central cord syndrome). The EMG signals were rectified, averaged (n=20 step cycles), and smoothed. The black lines represent EMG activity of the gastrocnemius medialis muscle at the end of locomotor training. The grey lines indicate the EMG activity at (A) 335 days and (B) 893 days after finishing locomotor training. In the patient with incomplete SCI the amplitude of the EMG signal was somewhat larger during early stance during the late recording, but otherwise similar at the two time points. In the patient with complete SCI the EMG signal was considerably reduced in amplitude during the late recording.

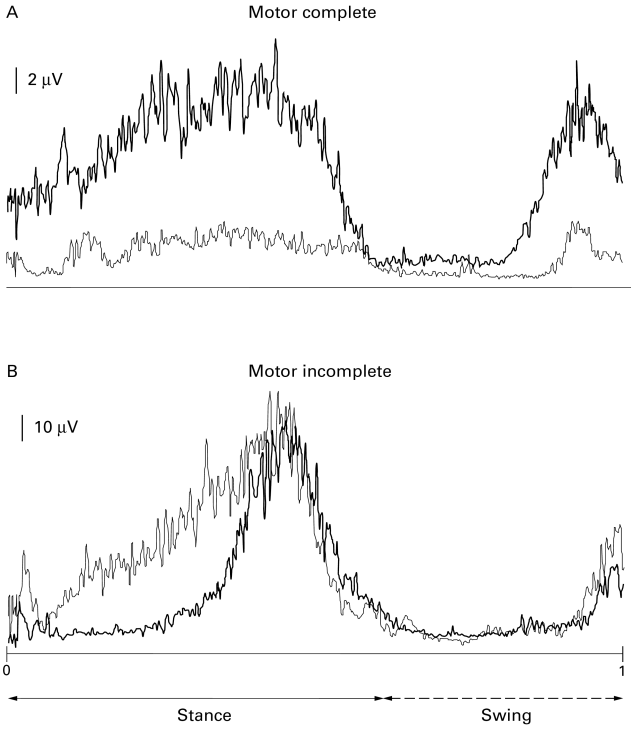

Figure 2.1 Rectified and averaged (n=20 strides) gastrocnemius EMG during one step cycle of a patient with (A) complete paraplegia T4 and (B) a patient with incomplete tetraplegia C4. The black lines represent the EMG activity at the end of the locomotor training. The grey lines indicate the activity at (A) 335 days and (B) 893 days after finishing locomotor training. Note the different calibrations of the EMG signal in (A) and (B).

Figure 2.2 shows the course of locomotor activity in patients (A) with complete and, (B) incomplete SCI over time after locomotor training had finished. In both groups of patients there was a significant ($p>0.001$) increase of EMG activity of the gastrocnemius muscle during the period of locomotor training (left side of time=0). This increase seemed to be greater in the group of patients with incomplete SCI. In patients with complete SCI the absolute level of RMS amplitude at this time was about one third of the corresponding activity level seen in incomplete paraplegic patients. After finishing locomotor training all patients with incomplete SCI used their locomotor capability every day on normal ground conditions (see methods). In these patients EMG activity of the gastrocnemius medialis muscle changed marginally over time after the end of training ($r=-0.01$; $p>0.05$, see fig 2.2 A. No patient showed a significant decline). By contrast, all patients with complete SCI never performed stepping movements after locomotor training stopped. These patients developed a significant decrease of gastrocnemius medialis muscle EMG activity over

time (r=−0.29; p<0.01, see fig 2.2 B). The regressions between patients with complete and those with incomplete SCI were significantly different (p<0.01). Neurographic recordings were performed over time in four patients with complete SCI to assess eventual signal changes in EMG activity due to muscle atrophy. The MAP amplitude (abductor hallucis muscle) evoked by tibial nerve stimulation did not change over time (r=0.05; p>0.05).

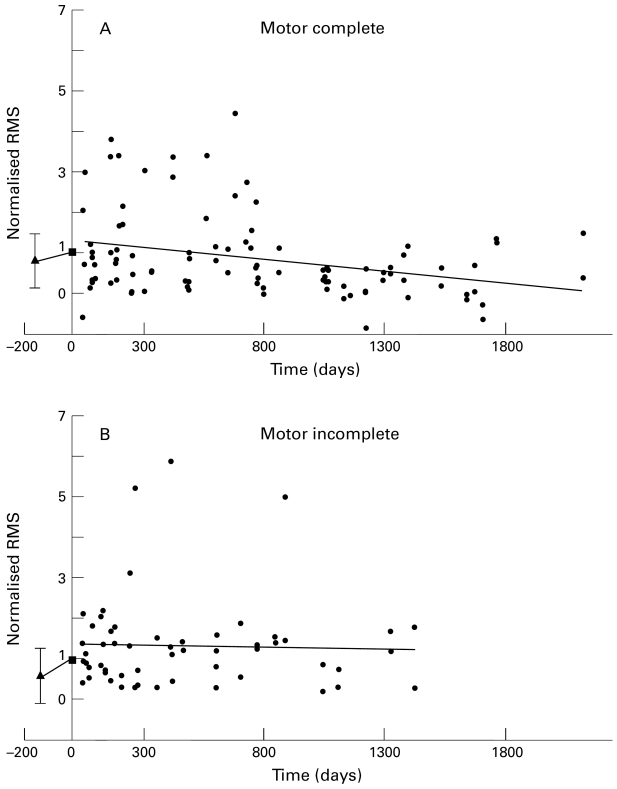

Figure 2.2 Course of gastrocnemius EMG activity after finishing locomotor training: (A) at t=0, 16 patients with complete motor paraplegia (ASIA A or B; n=99 recordings) and (B) 16 patients with incomplete paraplegia (ASIA C or D; n=55 recordings). The RMS values were normalised to the mean of the final three EMG recordings before finishing locomotor training (filled squares). Each point represents one recording (average 5/patient). The filled triangle reflects the normalised mean RMS amplitude of the first three recordings of all patients at the beginning of locomotor training. In patients with complete paraplegia the EMG amplitude declines over the time course (y=−0.0006x+1.3039; r=−0.29; p<0.01) whereas in incomplete paraplegic patients the level of EMG activity remains about constant (y=0.0000424x+1.3527; r=−0.008; p>0.05).

DISCUSSION

Several reports indicate that patients with incomplete SCI profit from locomotor training [2, 6]. The basis for this improvement in locomotor activity seems to be mainly due to an adaption of spinal neuronal networks to a physiological proprioceptive input after SCI. In patients with incomplete SCI a strengthening of cortical input [12] might also contribute to the functional improvement. The aim of this study was to evaluate the long term effects of such training on the leg extensor EMG activity in patients with incomplete and complete SCI. We concentrated on the EMG activity of the gastrocnemius medialis muscle, as this muscle was shown earlier [1, 6] to be most sensitive to locomotor training (by contrast with the tibialis anterior muscle) and as a consequence was overriding antigravitational function during locomotion. The results indicate that a regular locomotor training is effective in improving locomotor (gastrocnemius medialis EMG) activity in both patients with complete and those with incomplete SCI. Different long term effects of this training on locomotor activity between the two groups of patients was found. In patients with incomplete SCI who regained ambulatory capacity, either functional or therapeutic [9] leg extensor EMG activity did not change over time after finishing locomotor training. All these patients used their "learned" locomotor activity daily to walk at least short distances. Obviously this practice is sufficient to maintain the level of locomotor activity achieved during training. However, there is evidently no futher improvement in the more practical use of the locomotor pattern.

Patients with complete SCI could not use their acquired locomotor activity after finishing locomotor training as they remained unable to induce stepping movements. These patients lost the "learned" capacity of spinal neuronal networks to produce reasonable leg extensor EMG activity during assisted walking. The preserved MAP amplitude over time indicates that the decline in EMG activity is not due to muscle atrophy because of disuse, or peripheral nerve degeneration. It is recommended that locomotor training is started in patients with incomplete SCI as early as possible so as to use a long training period and to establish optimal conditions for the time when some supraspinal control is regained. By such an approach a high level of locomotor function can be achieved. For patients with complete SCI the results may be of importance for future interventional therapies promoting some regeneration. In such a situation a maintained level of trained locomotor activity may be of benefit to regain locomotion.

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CHAPTER 3

Muscle force and gait performance:
Relationships after spinal cord injury

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ABSTRACT

Objectives. To relate locomotor function improvement, within the first 6 months after spinal cord injury (SCI), with an increase in Lower Extremity Motor Score (LEMS) and to assess the extent to which the level of lesion influenced the outcome of ambulatory capacity. *Design*: Longitudinal and cross-sectional analyses. *Setting*. Seven SCI rehabilitation centers. *Participants.* Patients (N=178) were analyzed longitudinally (group A, motor complete; group B, motor incomplete, nonwalking or group C, motor incomplete and able to stand). The cross-sectional analysis included 86 patients (paraplegic, n=46; tetraplegic, n=40; group 1 with limited and group 2 with unrestricted walking function 6mo after SCI). *Interventions*. Not applicable. *Main outcome measures*. Walking Index for Spinal Cord Injury (WISCI), gait speed, and LEMS. *Results*. For group A, 24.8% of the patients improved in LEMS (median range, 0–10) and 7.7% in walking function (WISCI median range, 0–8; mean gait speed range, 0 to .14±.10m/s). For group B, LEMS improved in 93.5% of the patients (median range, 14–28) and walking function in 84.8% of the patients (WISCI median range, 0–10; mean gait speed range, 0 to .41±.45m/s) (P<.001). For group C, LEMS and walking function improved in 100% of the patients (LEMS median range, 29–41; WISCI median range, 8–16; mean gait speed range, .36±.29m/s to .88±.44m/s) (P=.001). In groups B and C, the improvement of walking function was greater than in LEMS. The cross-sectional analysis showed that group 1 patients with tetraplegia had more muscle strength (median LEMS, 31.5), and equal walking function (WISCI, 8; walking speed, 0.4±0.3m/s) compared with patients with paraplegia (LEMS, 23; P<.01; WISCI, 12; P=0.6; speed, 0.4±0.3m/s; P=.68). In group 2, patients with tetraplegia had slightly more strength (LEMS, 48) and equal walking function (WISCI, 20; walking speed, 1.4±0.4m/s) compared with patients with paraplegia (LEMS, 45; P<.05; WISCI, 20; P=1.0; speed, 1.4±0.3m/s; P=.89). *Conclusions*. An improvement in locomotor function does not always reflect an increase in LEMS, and LEMS improvement is not necessarily associated with improved locomotor function. LEMS and ambulatory capacity are differently associated in patients with tetra- and paraplegia. Functional tests seem to complement clinical assessment.

Keywords. Locomotion; Paraparesis; Rehabilitation; Spinal cord injuries; Treatment outcome.

INTRODUCTION

In the United States 11,000 people experience a spinal cord injury (SCI) every year [1]. Nearly 53% of these injuries are incomplete, that is, some sensory and/or motor function is preserved below the level of the spinal cord lesion. About 70% of initial incomplete SCI subjects regain some ambulatory function [2-4].

To quantify rehabilitation outcomes after SCI and other disorders, internationally standardized measures should be applied. Such a classification system grades the extent of pathology and serves as a valid measure that accurately reflects the patient's actual impairment. For subjects with SCI, the American Spinal Injury Association (ASIA) established a standardized neurologic assessment (ie, the ASIA classification) [5]. The ASIA classification focuses on the motor and sensory deficits after a spinal lesion. More recently developed classifications, such as the International Classification of Functioning, Disability and Health (ICF) [6], cover a much broader aspect of functioning and disability. The ICF encompasses different domains, including the perspective of the body, the individual, and the society. In this conceptual framework, functioning and disability are subdivided into the components of (1) body functions and structures and (2) activities and participation. These components are interacting, but not in a linear and predictable one-to-one relationship.

The ASIA protocol has been extensively used as a standardized assessment tool to document the neurologic deficit after a SCI [7-12]. Additional assessments have to be applied for the assessment of the activity limitation in order to enhance comprehensive outcome measurement. Previous studies have shown that after an SCI, preserved voluntary muscle contraction measured using the ASIA protocol is highly correlated with walking ability [2, 4, 13-15]. Nevertheless, some aspects of the relationship between muscle "force and function" are not yet solved.

About 51% of all patients with an incomplete SCI experience a cervical lesion [1]. In these patients, not only the lower extremities and trunk muscles are affected but also muscles of the upper extremities, that is, the supportive function of the arms is weak. Hence, for the achievement of a comparable walking ability we hypothesized, that subjects with tetraplegia compared with subjects with paraplegia require higher motor scores of lower extremities to compensate for this deficit.

The aim of this study was to evaluate the relationship between locomotor function improvement and an increase in lower-limb motor scores. This was analyzed using a longitudinal approach. In addition, we studied to what extent the level of lesion influenced outcome of locomotor function using a cross-sectional approach.

METHODS

General procedures and participants

The study was part of the European Multicenter Study about Human Spinal Cord Injury (EMSCI) and was carried out in 7 European SCI rehabilitation centers over a period of 20 months. The protocol of the study was approved by the local ethics committee and all participants were informed and gave written consent.

In the 7 SCI rehabilitation centers, all subject with traumatic or ischemic SCI who had been referred for primary rehabilitation were examined with the same clinical assessments according to a fixed timeframe: within the first week after the injury and consecutively after 1, 2, 6, and 12 months [16]. The results of these assessments were stored anonymously in a central electronic database. For this retrospective study, a query of this database was performed in June 2005. The query included a key identifier, age, sex, level of lesion, date of the lesion, test dates, results of the Lower Extremity Motor Score (LEMS), Walking Index For Spinal Cord Injury (WISCI), and gait speed using the 10-meter walking test (10MWT) 1 and 6 months after injury. We excluded participants who were aged under 15 or over 70 or with an incomplete database record. In addition, subjects with SCI who exceeded 75% of a scale (for LEMS: 0.75x50=37; for WISCI, 0.75x20=15) 1 month after SCI were excluded. Chances for further improvement in such patients are small. Moreover, ceiling effects cannot be excluded. Such ceiling effects are likely to occur with both the WISCI and the LEMS but less with the self-selected walking speed using the 10MWT.

For the comparison between the improvement of ambulatory function and motor impairment, a longitudinal approach with 2 time points was chosen. To pool patients with comparable potential to recover voluntary muscle force and ambulatory function patients were categorized to 1 of 3 groups based on the assessment made 1 month after SCI: (1) group A (motor complete and nonwalking): patients with neither voluntary muscle contraction in the lower extremity nor walking function (LEMS, 0; WISCI, 0); (2) group B (motor incomplete and nonwalking): patients with some preserved voluntary muscle strength but no walking function (1≤LEMS≤37; WISCI, 0); and (3) group C (motor incomplete and standing or walking): patients with preserved voluntary muscle contraction and walking function (1≤LEMS≤37; 1≤WISCI≤15).

In addition, a cross-sectional analysis of patients who regained ambulatory function 6 months after SCI was performed. The goal of this analysis was to compare the differences in LEMS, WISCI, and gait speed between patients with paraplegia and tetraplegia in 2 separate groups: patients who achieved only limited walking function with the help of walking aids (WISCI <20) were categorized to group 1. All

patients who regained unrestricted ambulatory function (WISCI, 20) were summarized in group 2.

Outcome measures

Examinations were performed 1, 3, 6, and 12 months after the injury by experienced physicians (ASIA assessment) and physical therapists (assessment of walking). For this analysis, results of the first- and sixth-month examinations were used. To standardize the testing procedure, regular workshop meetings and additional training were organized for the examiners.

The voluntary muscle strength of 5 key muscles (hip flexors, knee extensors, ankle dorsiflexors, toe extensors, ankle plantarflexors) of both lower extremities (LEMS) was tested in accordance with the standard neurologic assessment developed by ASIA [5]. Each muscle was given a value between 0 and 5 according to the strength of voluntary muscle contraction. Maximum and minimum LEMS were 50 and 0, respectively.

To assess walking performance, the revised version of the Walking Index for Spinal Cord Injury (WISCI II) [17,18] and the 10MWT [19] were used. The WISCI II describes the walking status of a patient based on the requirements of assistance and/or bracing and/or walking aids. The ordinal scale ranges from 0 (neither standing nor walking function) to 20 (independent walking). The 10MWT reflects the time necessary for walking 10m. Subjects were instructed to walk in a straight line at a comfortable self-selected pace over the distance of 14m. Walking time was taken after the subject walked 2m and was stopped 2m before the finish line to account for potential acceleration and deceleration effects. They could use their preferred assistive device, including minimal physical assistance. Gait speed (in m/s) was calculated from the results of the 10MWT.

Data analysis

Given the fact that LEMS and WISCI are ordinal-scaled variables, nonparametric tests were applied and medians are given. Gait speed is presented as mean ± standard deviation. SPSS[a] for Windows was used for the statistical analysis.

Patient groups A, B, and C. Wilcoxon signed-rank test was used to analyze longitudinally the course of LEMS and walking function (ie, WISCI, gait speed) between the first and the sixth month after SCI. To compare the improvements between LEMS, WISCI, and gait speed, results obtained 1 month after the injury were subtracted from those obtained 6 months after the injury. These differences were divided by the respective normative value. The normative value for LEMS is 50; for WISCI, 20; and for gait speed, 1.46m/s [20]. The Wilcoxon signed-rank test was used to compare these normalized differences.

Patient groups 1 and 2. For this cross-sectional analysis, Mann-Whitney U tests were applied to compare LEMS, WISCI, and gait speed between patients with paraplegia and tetraplegia within each group.

RESULTS

The database contained 504 records when the query was performed. Of these patients, 284 had incomplete data records, that is, not all 3 tests were completed at both time points, or information about age or date of measurement were lacking. Thirteen patients were excluded because of their age (<15y, >70y). For the longitudinal analysis, 31 patients were excluded because the LEMS and/or WISCI exceeded 75% of the maximum value 1 month after SCI. The analysis was performed on 178 patients. For the cross-sectional analysis, a subgroup of 86 patients who regained ambulatory function 6 months postinjury was included. For further characteristics see Table 3.1.

Table 3.1 Characteristics of the Patient Groups

Group		Tetraplegia	Paraplegia	Age (y)	Sex	
					Female	Male
A[a]		49	68	35.3±14.1	25	91
B[a]		24	22	44.1±16.4	16	30
C[a]		3	12	42.1±14.4	7	8
1[b]	Tetra	16		46.2±12.8	2	14
	Para		33	37.7±15.4	14	19
2[b]	Tetra	24		42.2±14.1	3	21
	Para		13	37.1±10.6	2	11

NOTE. The assignment to the groups A, B, and C was made according to the disability 1 month after SCI.

[a] Group A, motor complete and non-walking; group B, motor incomplete and non-walking; and group C, motor incomplete and standing or walking.

[b] Groups 1 and 2 consist of patients who regained ambulatory function 6 months after SCI: (1) patients with limited walking function (WISCI <20); and (2) patients with unrestricted walking function (WISCI, 20).

Course of motor scores and walking function

In group A (i.e. motor complete and non-walking 1 month after the injury, n=117), 29 (24.8%) patients improved their LEMS from 0 to a median of 10. The most frequent improvement was from 0 to 1. Eighty-eight (75.2%) patients remained at a 0 value, which means complete paralysis. Nine (7.7%) patients improved in the WISCI from 0 to a median of 8, and in the 10MWT to an average gait speed of .14±10m/s. In 108 (92.3%) patients, walking function (ie, WISCI, gait speed) did not change. Although the changes in LEMS and WISCI had no clinical impact, the Wilcoxon

signed-rank test revealed a significant improvement of the total group (for LEMS, P<.001; for WISCI, P<.01).

In group B (ie, motor incomplete and nonwalking, n=46), LEMS improved in 43 (93.5%) patients, from a median of 14 to 28, that is, a relative improvement of 24%±18%. However, in 3 (6.5%) patients, LEMS decreased.

WISCI improved in 39 (84.8%) patients, from 0 to a median of 10, that is, relative improvement of 52%±33%. In 7 (15.2%) patients, WISCI did not change.

Gait speed improved in 35 (76.1%) patients, from 0 to an average value of .41±.45m/s, that is, relative improvement of 28%±31%. No change in gait speed was observed in 11 (23.9%) patients.

For the total group, the overall improvement in LEMS, WISCI, and gait speed was significant (P<.001). WISCI improved to a larger extent compared with LEMS (P<.001). No difference was evident between the relative improvements of LEMS and gait speed (P=.54).

In group C (ie, motor incomplete and standing or walking, n=15), all patients improved in LEMS, WISCI, and gait speed. The median LEMS 1 month after the injury was 29 and improved to 41 at the sixth month after the SCI, which corresponds to a relative improvement of 23%±12%. The corresponding values for WISCI were 8 one month postinjury and 16 five months later. This reflects a relative improvement of 46%±20%. Gait speed improved from .36±.29m/s to .88±.44m/s, that is, a relative improvement of 36%±23%. The overall improvements of LEMS, WISCI, and gait speed was significant (P=.001). WISCI (P<.01) and gait speed (P<.05) showed a greater relative improvement than LEMS. See also Table 3.2 and Figure 3.1.

Table 3.2 LEMS, WISCI, and gait speed at the first and sixth months after SCI of patients in groups A, B, and C

Group	LEMS			WISCI			Gait Speed		
	1 M	6 M	RI (%)	1 M	6 M	RI (%)	1 M	6 M	RI (%)
A	0	0	6±12	0	0	3±11	0	.01±.05	0.7±3
B	14	28	24±18	0	10	52±33	0	.41±.45	28±31
C	29	41	23±12	8	16	46±20	.36±.29	.88±.44	36±23

NOTE. Values are median and mean ± SD.

Abbreviation: LEMS, lower extremity motor score; WISCI, Walking Index for Spinal Cord Injury; M, month; RI, relative improvement.

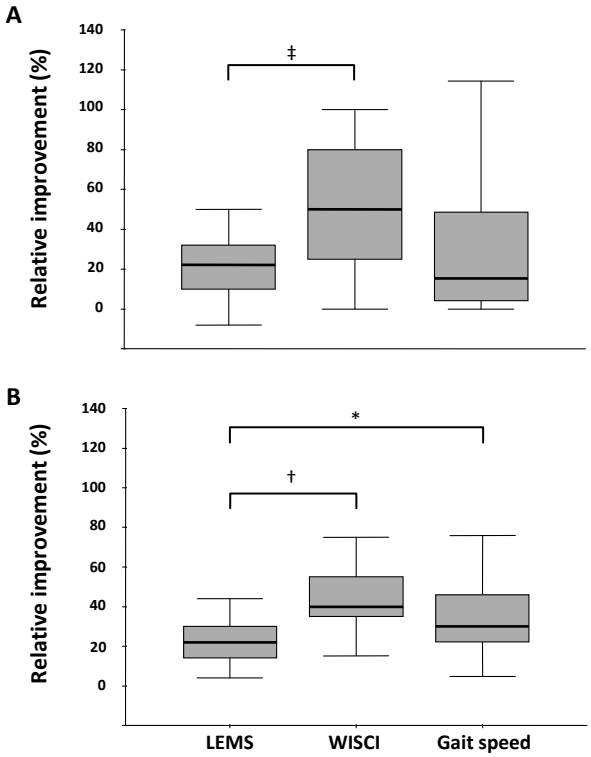

Figure 3.1 Relative improvements of LEMS, WISCI, and gait speed (difference between measurement at 6 months and at 1 month divided by the respective normative value). (A) Motor incomplete patients who were not able to stand or walk 1 month after SCI; and (B) patients who were motor incomplete and able to stand or walk 1 month after SCI. *P<.05; †P<.01; ‡P<.001.

Outcome of subjects with tetraplegia versus paraplegia

Subjects with tetraplegia of group 1 who achieved only limited walking function 6 months after the injury (WISCI <20, n=16) showed a median LEMS of 31.5, a median WISCI of 8, and a mean walking speed of 0.4±0.3m/s. By comparison, the corresponding values of patients with paraplegia (n=33) were 23 for the LEMS (P<.01), 12 for the WISCI (P=.6), and 0.4±0.3m/s for the walking speed (P=.68).

Subjects with tetraplegia in group 2 (n=24), who could walk without restrictions (WISCI, 20), showed a median LEMS of 48, a median WISCI of 20, and a mean walking speed of 1.4±0.4m/s. Patients with paraplegia (n=13) showed a median LEMS of 45 (P<.05), a median WISCI of 20 (P=1.0), and a mean walking speed of 1.4±0.3m/s (P=.89). See also Table 3.3 and Figure 3.2.

Table 3.3 Comparison of LEMS, WISCI, and gait speed between patients with tetraplegia and paraplegia in 2 groups

Test	Group 1		Group 2	
	Tetraplegia (n=16)	Paraplegia (n=33)	Tetraplegia (n=24)	Paraplegia (n=13)
LEMS	31.5	23	48	45
WISCI	8	12	20	20
Gait speed	0.4±0.3	0.4±0.3	1.4±0.4	1.4±0.3

NOTE. Values are median and mean ± SD.
Group 1 is patients with limited walking function (WISCI <20); group 2 is patients with unrestricted walking function (WISCI, 20).

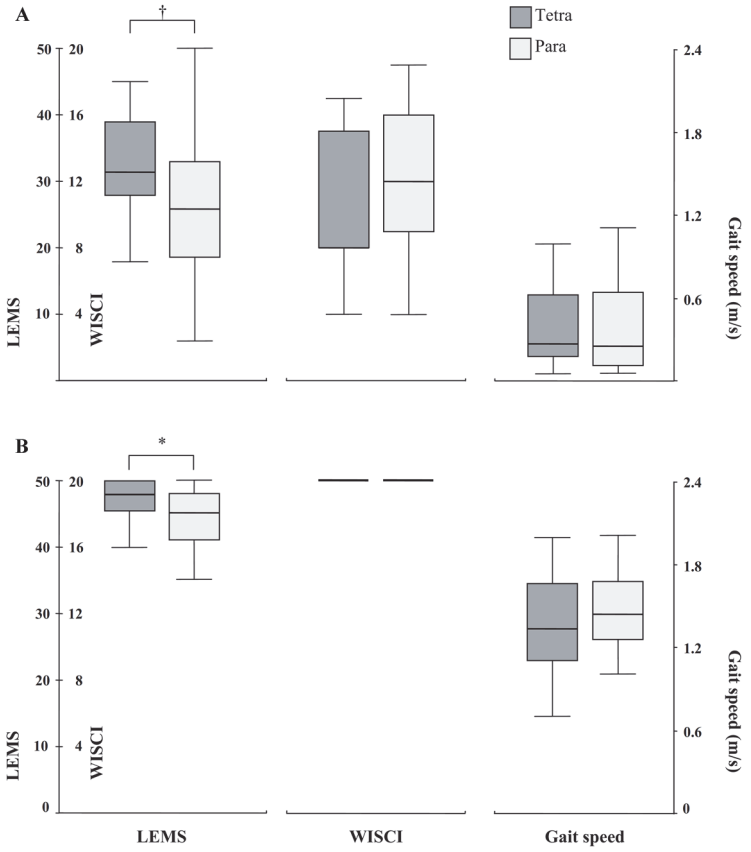

Figure 3.2 Comparison of LEMS, WISCI, and gait speed between patients with tetraplegia (Tetra) and paraplegia (Para) who achieved (A) limited, and (B) unrestricted walking function 6 months after the injury. *P<.05; †P<.01.

DISCUSSION

After an SCI, the remaining voluntary muscle force of key muscles can be quantified by internationally accepted protocols, such as the ASIA classification [5]. The ASIA motor scores represent a simple clinical measure reflecting the walking ability of patients with SCI [13,14]. Other studies showed that particular muscles around the hip [15] or knee extensor strength [4] are associated with ambulatory function. These studies focused on correlations or predictions at a certain point in time. We evaluated the relationship between ASIA motor scores and the locomotor function during the first 6 months after a SCI. Our results indicated that (1) ASIA motor score and locomotor function are closely related, even in subgroups of patients with SCI, which is in line with other studies (eg, Burns et al [2]), (2) the degree of recovery of locomotor function does not parallel the change in motor scores obtained during the first 6 months after SCI, and (3) among patients who achieved limited ambulatory function 6 months after SCI, patients with tetraplegia need a substantially higher LEMS compared with patients with paraplegia. Nevertheless, if patients with tetraplegia achieve a basic walking function, they are more likely to become unrestricted walkers.

Course of LEMS and locomotor function

As has been shown in this study, an increase in motor score is not always associated with an improvement in function. Conversely, an improvement in locomotor function between 1 and 6 months after SCI in patients both with incomplete tetraplegia and paraplegic is associated with a variable increase in LEMS. Along the same line Wirz et al [21] showed that locomotor training by a robotic device (Lokomat) in patients with chronic SCI resulted in a significant improvement of locomotor ability, which was not associated with an increase in LEMS. This might be due to an extra-activation of lower-extremity muscles by the automatic proprioceptive feedback during locomotion [22]. In addition, locomotor training affects many muscles and activates them in a functional way, resulting in a better coordination of synergistic muscles [22, 23]. This might lead to a better functional result than any other physical therapy because training effects were shown to be specific to the focus of the therapy [24].

Another study [25] which focused on the efficacy of a treatment, that is, the application of high doses of methylprednisolone, has shown a small increment in ASIA score compared with controls. However, in this study it remained open whether the observed improvements on the level of the body functions were associated with an improved activity i.e. ambulatory function. Recently, this treatment has been questioned (eg, Hurlbert [26]). According to our observations the effect of this

treatment on outcome, that is, a small increase of ASIA score, might not reflect improvement in function in all patients.

Difference between outcome in subjects paraplegia and tetraplegia

Patients with paraplegia and tetraplegia who became ambulatory 6 months after SCI demonstrated a similar locomotor function according to WISCI and walking speed. However, in patients with tetraplegia all lower-extremity "key" muscles had to reach a functional level of muscle contraction to permit locomotor function. In contrast, patients with paraplegia achieved this performance already at lower LEMS. This became evident in patients with limited walking function (ie, WISCI<20). This difference is suggested to be due to the additional weakness of trunk and upper-limb muscles in patients with tetraplegia, which requires substantially more lower-extremity muscle force to compensate for the postural instability. If this stability is provided, a further increase in LEMS was associated with a steep improvement in locomotor ability. Consequently, ambulatory patients with tetraplegia achieved a higher level of walking function than patients with paraplegia. In contrast, if the LEMS remains below a certain level, only patients with paraplegia become ambulatory while patients with tetraplegia remain wheelchair-bound.

Methodological considerations

This study has some limitations. First, incomplete data records are inherent to a multicenter database, reflected by a high exclusion rate. Second, on the one hand, the multicenter nature of this study enables access to a substantial number and broad spectrum of subjects. However, reliability of the procedures is hard to ensure due to multiple examiners. This applies in particular to the clinical, non-apparative assessments. To keep random and systematic error as small as possible, regular workshop meetings were organized and datasets were tested for plausibility by an independent person. The assessment of reliability was not a focus of this study and was therefore not further explored. Third, for the assessment of voluntary muscle force, a limitation and source of bias might be the use of clinical motor scores rather than objective measures (eg, dynamometry). Fourth, despite the straightforward aim of this study (ie, comparing muscle force and functional walking scores), no unambiguous statistical method is available to directly compare the different variables.

CONCLUSIONS

The effectiveness of new interventional physical or drug therapy should be assessed not only by a standardized neurologic examination (e.g. ASIA), but also by internationally accepted activity assessments. Motor and sensory scores reflect spontaneous recovery of spinal cord function as they depend on the integrity of corticospinal connections (i.e. voluntary muscle contraction). By a combined assessment of force and function, the effectiveness of any new interventional therapy might become comprehensively assessed.

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CHAPTER 4

Outcome after incomplete spinal cord injury:
Central cord syndrome versus Brown-Séquard syndrome

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ABSTRACT

Study design. Retrospective analysis of prospectively collected data. *Objective*. A hemisection of the spinal cord is a frequently used animal model for spinal cord injury (SCI), the corresponding human condition, i.e. the Brown- Sequard syndrome (BS), is relatively rare compared to the central cord syndrome (CC). The time-course of neurological deficit, functional recovery, impulse conductivity and rehabilitation length of stay (LOS) in BS and CC subjects were compared. *Setting*. Nine European Spinal Cord Injury Rehabilitation Centers. *Methods.* Motor score, walking function, daily life activities, somatosensory evoked potentials and LOS were evaluated one and six months after SCI and were compared between age-matched groups of tetraparetic BS and CC subjects. *Results*. For all analyzed measures no difference in the time-course of improvement was found in 15 matched pairs. *Conclusion*. In contrast to the assumption of a better outcome of subjects with BS, no difference was found between the two incomplete SCI groups. This is of interest with respect to the different potential mechanisms leading to a recovery of functions in these two SCI subgroups.

Keywords. Quadriplegia, Central cord syndrome, Brown-Sequard syndrome, Recovery of function, Walking, Electrophysiology.

INTRODUCTION

The consequence of trauma to the spinal cord is a partial or complete loss of motor, sensory and autonomic functions below the level of lesion. According to European and American databases the proportion of traumatic patients experiencing an incomplete spinal cord injury (SCI) amounts to 52.8% and 44.3% respectively [1]. Within the spectrum of incomplete damage to the neural structures within the spinal canal five distinct syndromes can be separated: the Central Cord- (CC), the Brown-Sequard- (BS), the Anterior Cord-, the Conus Medullaris- and the Cauda Equina syndromes [2, 3].

A comprehensive overview of the clinical characteristics of these syndromes is provided elsewhere [4]. Most common is the CC, occurring in approximately 9% of all traumatic SCIs [4]. It is characterized by a pronounced loss of motor function in the upper extremities due to a lesion of the central region of the cervical spinal cord [5]. Typically, the CC results from a hyperextension of the cervical spine during a fall, mainly in older patients with a pre-existing cervical spondylosis [6]. The prognosis for a functional recovery of the CC has been suggested to be rather favorable, depending on the age of the subject [5-12].

The BS is caused by an injury restricted to one side of the spinal cord resulting in an ipsilateral paresis and loss of deep sensation and a contralateral loss of pain and temperature sensation [13]. The BS accounts for only about 3% of all traumatic SCI [4]. A pure form of BS occurs rarely. Therefore, clinically the criteria for classifying a BS were broadened. The “Brown-Sequard-plus” syndrome encompasses SCI subjects suffering from an asymmetric paresis combined with relatively pronounced analgesia on the less paretic side [14, 15]. Patients with a BS are suggested to have a favorable prognosis for functional recovery [4, 15, 16]. According to textbooks [17], the BS is thought to have a better outcome than the CC. Such a difference in outcome is of interest with respect to the possibility of different mechanisms underlying spontaneous functional recovery after an incomplete SCI in humans. Furthermore, unilateral lesions of the spinal cord, i.e. injuries that correspond to the BS, are frequently used in animal research as models to investigate new interventions for spinal cord repair [18].

The aim of the present study was to determine whether different types of incomplete SCI differ in outcome. Specifically it was of interest to evaluate and compare the course of neurological, functional and electrophysiological measures in BS and CC subjects.

MATERIALS AND METHODS

This retrospective review encompassed data from an European network of nine SCI rehabilitation centers (EMSCI) [19]. Local Ethics Committee of all centers approved the data collection and all subjects gave written, informed consent.

Subjects and general procedures

All patients experienced a traumatic or ischemic SCI and were referred to one of the participating centers. They were examined according to the EMSCI protocol [19]. Patients with a traumatic brain lesion, peripheral nerve damage or polyneuropathy were excluded.

For this study, the EMSCI database was screened for tetraparetic patients with either a pronounced loss of motor function of the upper extremities (CC) or restricted to one side (BS). The criterion for differential paresis in this study was an arbitrarily defined difference in ASIA motor score of 19 or more points between the upper and lower extremities (CC) or the right and left side of the body (BS), respectively (see 'Clinical, functional and electrophysiological examinations'). Previous studies applied different cut-off values which in general were lower [3, 8, 11]. The relatively greater difference in ASIA motor score allowed us to include patients with clear representations of the respective syndromes. In order to ensure comparable groups regarding neurological level of lesion and age, we formed two matched groups from all patients who fulfilled the above-mentioned criteria.

Data assessments

Examinations were performed at one and six months after SCI by specialized and trained physicians (neurological examination and neurophysiological recordings) and therapists (walking and daily life functional tests). The results of these examinations were sent anonymously to a central database.

Clinical, functional and electrophysiological measures

Motor score (MS) was assessed according to the international standard classification of the American Spinal Injury Association (ASIA) [2]. Total MS and MS of more and less impaired extremities of the body were used for comparison of the two groups. While the total MS and its recovery is expected to be similar in both groups of patients one would assume a substantial difference in the distribution of the voluntary muscle strength as measured with the MS. Therefore MS sum was calculated for upper (more impaired) and lower limbs (less impaired) for CC subjects and for the weak (more impaired) and the strong (less impaired) sides for patients presenting with BS, respectively.

Walking function was assessed using the Walking Index for Spinal Cord Injury II (WISCI II) [20] and the ten Meter Walk Test (TMW) [21].

The degree of disability during daily tasks performance (i.e. self-care, respiration and sphincter management as well as mobility) was examined using the Spinal Cord Independence Measure (SCIM II) [22].

Neurophysiological recordings were obtained from ascending (somatosensory evoked potentials-SSEP) pathways. For the present study, signal amplitudes were used for analysis [19]. As shown recently 1SSEP amplitudes reflect to some extent recovery of function in incomplete SCI, while spinal conductivity does little change during the course of a SCI. Analogous to the analysis of the motor scores, the amplitudes of the more and less affected extremities were separately explored.

Data analysis

The level for statistical significance for all analyses was set at p=0.05.
Chi-Square and T-tests were used to control for equality of groups regarding sex, age and neurological level.

Differences between one and six months after SCI were calculated to evaluate changes in the outcome measures. These changes were compared within and between the two groups.

Given the limited number of participants, non-parametric methods were applied, i.e. for the within-group comparisons Wilcoxon's Signed Rank test, and for the between-group comparisons the Mann-Whitney U test.

Not all data were available for all patients at both time points. For every comparison, we therefore checked if matching was violated by the drop-outs the above mentioned methods (i.e. Chi-Square for sex and neurological level and T-tests for age).

Microsoft Excel 2002 (Microsoft, Redmont, WA) and SPSS for Windows 14.0 (SPSS Inc, Chicago, IL) were used for the analysis.

RESULTS

Sample characteristics

Two groups were formed, i.e. (i). 15 subjects with BS and (ii). 15 subjects with CC. In the BS group the mean motor score difference between the strong and weak side was 26.93±5.69 points. In addition, the sensory criterion relating to pain (contralateral reduction of ASIA pin prick sensation) was present in 9/15 individuals and touch sensation (ipsilateral ASIA light touch) was reduced in 2/15 patients. In CC subjects

the difference in motor score between lower and upper extremities was 23.14±3.84 points.

The groups were similar regarding age, neurological level of the lesion and sex (Table 4.1). This was true also for all comparisons that did not include the whole sample. The etiology of the SCI was traumatic, except for two cases in the BS group where ischemia was the reason for the paralysis.

Table 4.1 Characteristics of subjects included in the study

		Central Cord	Brown-Sequard
n		15	15
Sex m/f		8/7	10/5
Age mean (SD/range)		49.2 (18.55/19-82)	48.4 (18.29/20-78)
Neurological Level	C2	1	2
	C3	1	2
	C4	8	6
	C5	3	5
	C6	2	0

ASIA motor score

The total MS improved significantly from the first to the sixth month after SCI for both BS and CC groups. Between groups, there was neither a difference in total MS at the first or sixth month.

In the BS group, the MS of arms and legs improved on both the more and less impaired sides, but to a greater degree on the more affected side. The same observation was made in the CC group. The MS of the arms (more impaired) and legs (less impaired) improved significantly but the recovery was more pronounced in the arms. No difference between BS and CC was found for the sum scores from the more and the less affected limbs (Table 4.2(a) and Fig 4.1). In order to recognize the influence of a possible ceiling effect on the course of recovery, MS values of the early examination (i.e. one month after SCI) were evaluated. Only 2/15 patients scored 25 points on the upper extremity motor score (UEMS) and 6/15 on the lower extremity motor score (LEMS) on the less impaired side of the BS group. In the CC group only 2/15 patients achieved maximum scores in LEMS in the early examination.

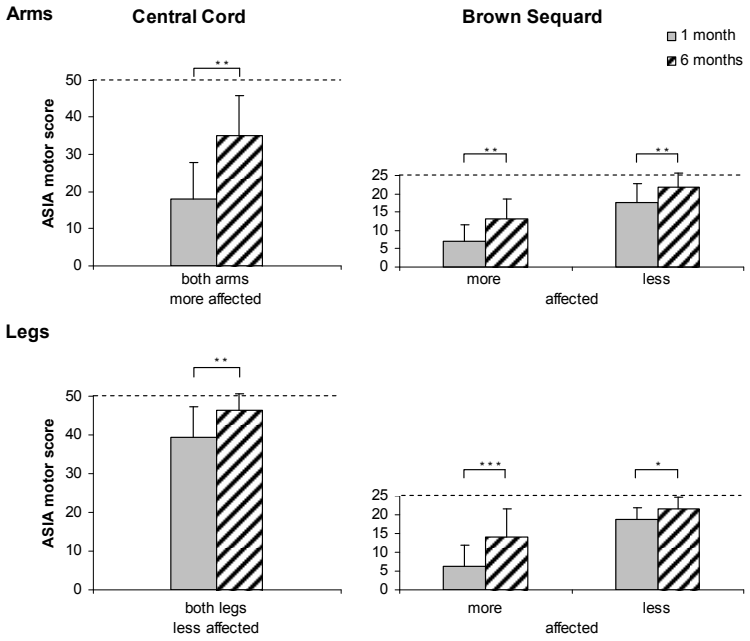

Figure 4.1 Mean values of the ASIA motor scores examined one and six months after SCI for patients with a Central Cord and Brown-Sequard syndrome (**P*≤0.05, ***P*≤0.01; ****P*≤0.001). Dashed lines represent the maximum values of the motor scores.

Walking function

Both groups of subjects showed significant improvement in walking function (Table 4.2(b) and Fig 4.2). There was no statistical difference between the groups regarding the initial and final values in the TMW and WISCI II tests.

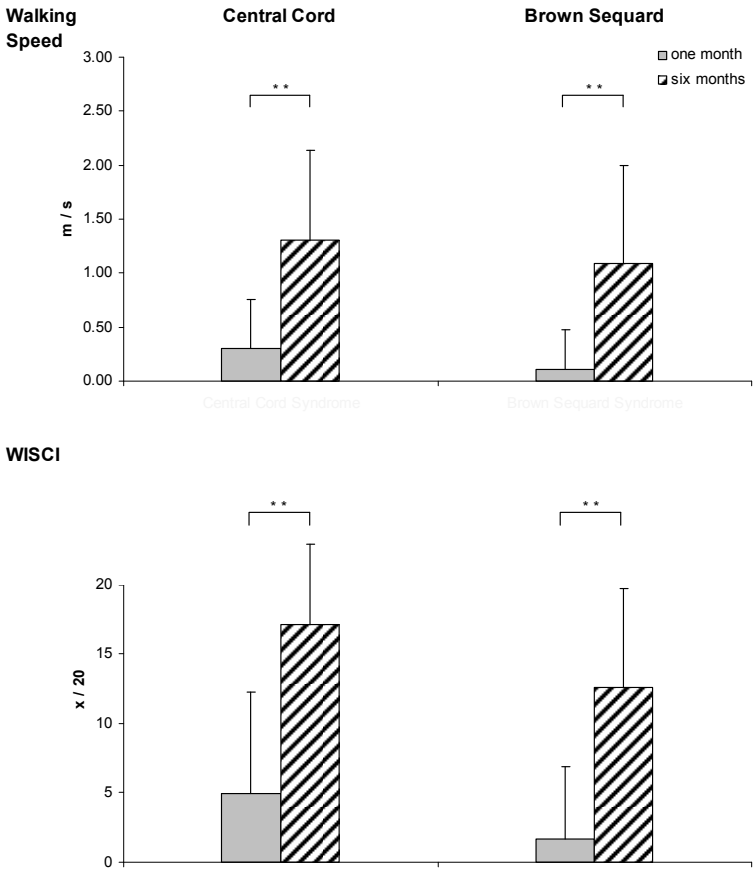

Figure 4.2 Changes in walking tests achieved between one and six months after SCI for patients with Central Cord and Brown-Sequard syndrome (Walking speed assessed using the 10-Meter Walk test, WISCI: Walking Index for Spinal Cord Injury; ** $p<0.01$).

Table 4.2 Mean standard deviation (a) ASIA motor score; (b) walking function; (c) SCIM; and (d) amplitudes of SSEPs examined at 1 (1M) and 6 (6M) months after SCI

	Central Cord	Brown-Séquard	
(a) Motor scores			
Total score			
1M	59.43 ± 17.61 (14)	53.09 ± 14.73 (15)	p= 0.295
6M	81.69 ± 13.14 (13)	71.69 ± 14.48 (13)	p= 0.072
More impaired extremities [a]			
1M	18.14 ± 9.72 (14)	13.07± 7.92 (15)	p= 0.155
6M	35.23 ± 10.46 (13)	27.15 ± 11.58 (13)	p= 0.095
Less impaired extremities [a]			
1M	40.80 ± 8.16 (15)	40.00 ± 7.87 (15)	p= 0.677
6M	46.46 ± 4.12 (13)	44.54 ± 5.43 (13)	p= 0.309
Change between 1st and 6th month			
More affected extremities [a]	18.67 ± 8.88 (12)	15.15 ± 10.22 (13)	p= 0.320
Less affected extremities [a]	6.85 ± 5.03 (13)	5 ± 5.35 (13)	p= 0.336
	p= 0.002	p= 0.006	
(b) Walking tests			
Walking speed (ms^{-1})			
1M	0.3 ± 0.46 (15)	0.11 ± 0.37 (15)	p= 0.104
6M	1.31 ± 0.83 (12)	1.09 ± 0.91 (9)	p= 0.454
Change	1.12 ± 0.66 (12)	0.91 ± 0.9 (9)	p= 0.355
WISCI II [b]			
1M	0 (15)	0 (15)	p= 0.192
6M	20 (13)	13 (13)	p= 0.078
Change	16 (13)	9 (13)	p= 0.161

Continued on next page

Table 4.2 cont.

	Central Cord	Brown-Séquard	
(c) Spinal Cord Independence Measure			
Total score			
1M	29.15 ± 24.31 (13)	30.07 ± 22.82 (15)	p= 0.747
6M	74.69 ± 31.51 (13)	68.15 ± 26.65 (13)	p= 0.303
Change	45.54 ± 47.25 (13)	38 ± 24.89 (13)	p= 0.137
Self-care			
1M	3.23 ± 5.22 (13)	4.8 ± 5.39 (15)	p= 0.228
6M	13.5 ± 6.83 (12)	13.85 ± 5.6 (13)	p= 0.890
Change	11.58 ± 5.65 (12)	8.77 ± 5.66 (13)	p= 0.209
Respiration and sphincter management			
1M	18.77 ± 10.68 (13)	18.87 ± 9.77 (15)	p= 0.625
6M	32.77 ± 11.92 (13)	31.38 ± 10.41 (13)	p= 0.630
	p= **0.023**	p= **0.005**	
Change	14 ± 18.66 (13)	13.15 ± 10.73 (13)	p= 0.328
Mobility			
1M	7.15 ± 11.21 (13)	6.4 ± 9.93 (15)	p= 0.608
6M	29.46 ± 15.13 (13)	22.92 ± 13.14 (13)	p= 0.239
Change	22.31 ± 21.79 (13)	16.1 ± 13.14 (13)	p= 0.123
(d) Somatosensory evoked potentials			
Change between first and sixth month			
More affected extremities [a]	1 ± 2.54 (8)	0.94 ± 0.84 (9)	p= 0.386
Less affected extremities [a]	0.65 ± 1.14 (8)	- 0.39 ± 2.18 (9)	p= 0.177
	p= 0.779	p= 0.051	

Abbreviations: ASIA, American Spinal Injury Association; SCIM, Spinal Cord Independence Measure; SSEP, somatosensory evoked potential; WISCI, Walking Index for Spinal Cord Injury.
The number of included subjects is indicated in parentheses.
[a] The more affected limbs are both arms in CC and the arm and leg of the paretic side in BS. The same applies for the less affected sides.
[b] median values are reported; significant differences are given in bold.

Spinal Cord Independence Measure

There was a significant improvement in the total scores of the SCIM and its sub scores in both groups. No difference between BS and CC was found in the values obtained at one and six months after SCI, or in the mean changes (Table 4.2(c) and Fig 4.3).

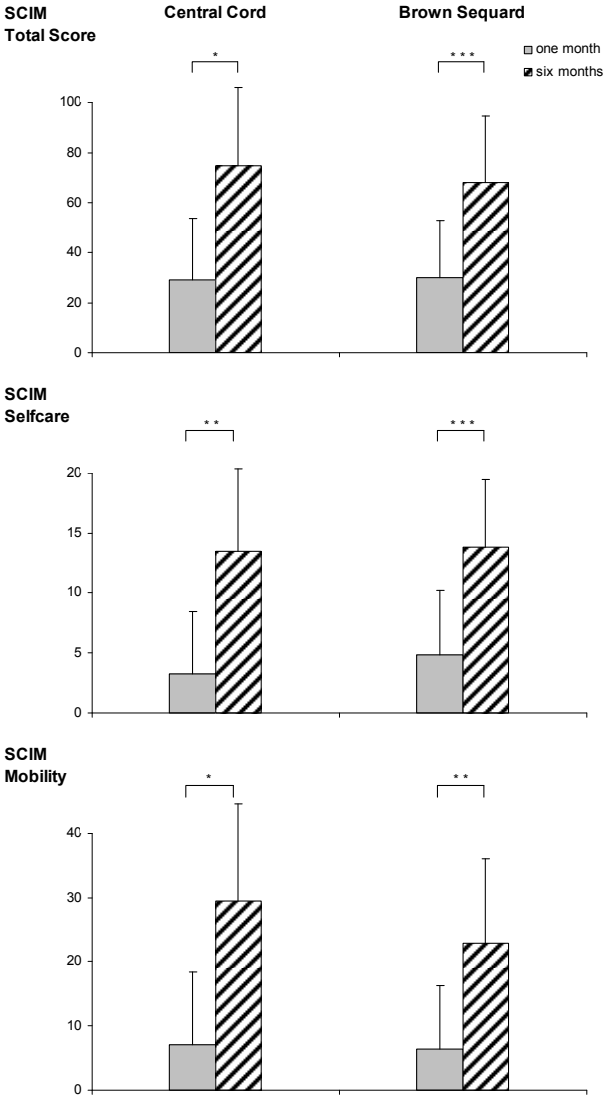

Figure 4.3 Changes in the Spinal Cord Independence Measure for the total score, and two sub-scores, between one and six months after SCI for patients with Central Cord and Brown-Sequard syndrome (*p≤0.05, **p≤0.01, ***p≤0.001).

Somatosensory evoked potentials

No significant change was observed in SSEP amplitudes of N. ulnaris and N. tibialis. In the BS group there was a positive trend in improvement (p=0.051) of the summed amplitudes of N. ulnaris and N. tibialis on the more affected side. However, there was no group difference in initial and final values (Table 4.2(d) and Fig 4.4A). The clinical examination provides a rather rough measure of the sensory deficit. Therefore no correlation with SSEP can be expected.

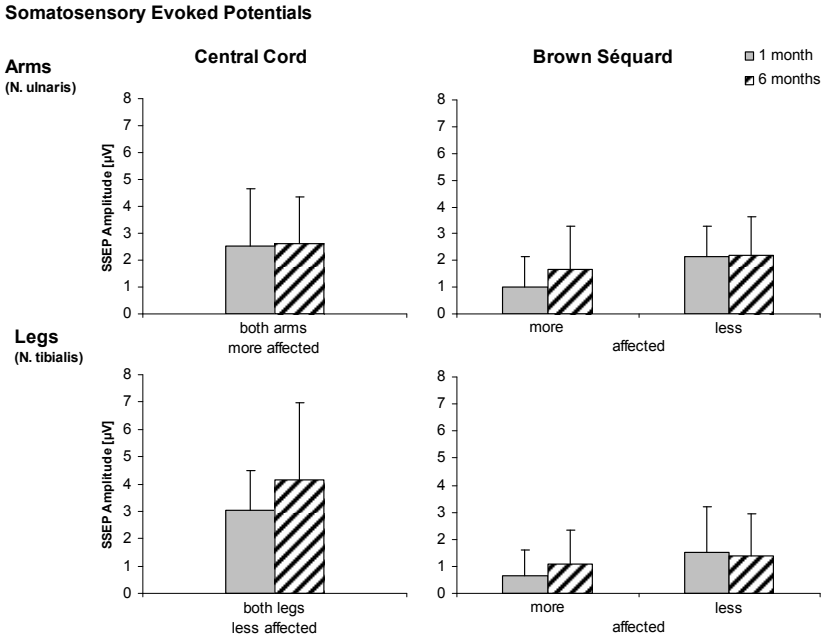

Figure 4.4 SSEP amplitudes at one and six months after SCI for the group of subjects with Central Cord and Brown-Sequard syndrome.

Rehabilitation length of stay

Subjects with CC stayed shorter in rehabilitation than BS subjects (113.5±81.8 days vs. 131.9±52.2 days). However this difference was not statistically significant.

DISCUSSION

The aim of this study was to explore the extent to which the neurological, functional and electrophysiological recovery differs between BS and CC subjects which might be due to a different anatomical damage of spinal tracts associated with these two

types of an incomplete SCI. Studies with reasonable number of participants comparing specifically the outcome of BS and CC are rare. In humans, the incidence of the BS is lower compared to the CC, but lateral hemisections of the spinal cord are frequently used in animal research to model SCI. However, no clear-cut criteria are defined for BS and CC. Therefore, we followed the algorithm proposed elsewhere [4]. Compared to the MS, the evaluation of sensory scores is generally less reliable [23]. Nevertheless the differential sensation criterion of the BS group was fulfilled in most subjects.

A bimodal age-distribution of patients with CC suggested that this group might consist of two different populations regarding etiology and outcome [7, 9, 11, 12, 14]. At the time of the analysis, the EMSCI network included approximately 1000 SCI patients. From this population, only 30 patients who were matched regarding age and neurological level of lesion fulfilled our inclusion criteria. The age of our sample was slightly older than the age at injury of the general SCI population [24].

In two BS patients the reason for the SCI was an ischemia. We did not consider this fact further since the results of a previous study suggest that the outcome is similar in ischemic and traumatic SCI [25].

It was assumed that BS has a better outcome than the CC [17]. Such a difference might also be expected on the basis of animal experiments [26, 27]. Mechanisms underlying functional recovery after unilateral SCI (BS) in animals, e.g. compensatory sprouting of spared fibre tracts above and below the lesion site might also play a role in the human situation [26]. Interestingly, BS and CC subjects recovered to about the same extent suggesting equally efficient mechanisms of functional recovery in these two anatomically dissimilar types of SCI. However, one has to be aware that the human Brown-Sequard Syndrome can only insufficiently reflect the hemisection animal model. However, the small patient group studied here can hardly allow drawing serious conclusions about the mechanisms underlying the recovery of function after a SCI.

Course of motor deficit

In line with the literature, recovery of motor deficits was seen in both syndromes [5, 10, 11, 13, 17-19]. Notably, the change in MS was significant on both the more and the less impaired limbs. Nevertheless, the rate of recovery was greater on the more than less affected limbs, which might be due to 2 facts: 1. A greater gradient on the more affected side might lead to stronger effects on neuronal plasticity to become maximally exploited; 2. On the less affected side a ceiling effect might lead to a less powerful recovery, i.e. the less impaired limbs may have already early achieved scores near the maximum. However, even when the subjects were excluded who achieved maximum scores already in the early examination the result did not change.

Recovery of walking function

In line with the literature [12], the favorable recovery of walking function in CC subjects corresponds to the fact that arms are more impaired than legs in this syndrome by definition. Most incomplete SCI subjects regain ambulatory function [8, 10, 13]. However, in our sample, approximately two thirds of CC and only one third of BS patients became unrestricted walkers within the first 6 months after a SCI. Overall the difference in outcome of walking function was not significant. The observation that walking function in BS subjects changes to a similar extent was also noted elsewhere [8, 5]. While in the study of McKinley the subscore "mobility" of the Functional Independence Measure (FIM) was similar at admission, patients with BS achieved even higher discharge values as compared to CC [4]. In our study, patients with BS had lower admission and discharge values in the WISCI II test but showed similar changes as patients with CC.

Course of somatosensory recordings

Since the number of measurements was limited, the results of the neurophysiological recordings have to be considered carefully. The observation that somatosensory evoked potentials (SSEP) showed little change, i.e. behaved differently from the recovery in function after a SCI is in line with an earlier study on incomplete and complete SCI subjects 1. The SSEP recordings reflect the sensory deficits after a SCI, while the clinical examination provides only a rough measure (3 items). Therefore no close relationship between these measures can be expected.

Study limitations

In the animal model, the pure form of the BS syndrome can be investigated due to a controlled experimental lesion of the spinal cord (the lateral hemisection). The accuracy of these lesions can be verified by histological examinations. In contrast, the occurrence of a pure BS in humans is rare. For practical reasons, the categorization to either the CC or BS group was based on MS. This might have led to some misclassifications since the BS is further characterized by a contralateral loss of pain and temperature sensation below the level of lesion [15], which was not present in all BS subjects included. In addition, the classification of patients as CC based on upper to lower limb MS differences without imaged verification of pathology, is at risk of including patients with bilateral cortico-spinal (i.e. dorsifunicular) involvement rather than central neuropathology alone. This limits the interpretation about which tracts recover function.

Additionally, the samples of CC and BS subjects were of limited size which raised the chance that we accepted the Null-Hypotheses although there were real differences in the change of the measures evaluated.

CONCLUSIONS

This study shows that there is no difference in the functional recovery between BS and CC subjects over the first six months after a SCI, although spinal tracts were differentially affected.

The spinal cord seems to have the capacity to compensate for a damage that does not depend on the integrity of a specific tract [28]. Finally, such a study on a sub-population of SCI subjects requires the formation of clinical networks which apply standardized examinations at distinct time-points are a prerequisite to enable the study of such a subpopulation of spinal cord injured subjects.

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CHAPTER 5

Standardized assessment of walking capacity after spinal cord injury:

The European network approach

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ABSTRACT

Objectives. After a spinal cord injury (SCI), walking function is an important outcome measure for rehabilitation and new treatment interventions. The current status of four walking capacity tests that are applied to SCI subjects is presented: the revised Walking Index for Spinal Cord Injury (WISCI II), the 6 minute walk test (6MinWT), 10 meter walk test (10MWT) and the timed up and go (TUG) test. Then, we investigated (1) which categories of the WISCI II apply to SCI subjects who participated in the European Multicenter Study of Human Spinal Cord Injury (EM-SCI), and (2) the relationship between the 10MWT and the TUG. *Methods.* In the EM-SCI, the walking tests were applied 2 weeks and 1, 3, 6 and 12 months after SCI. We identified the WISCI II categories that applied to the EM-SCI subjects at each time point and quantified the relationship between the 10MWT and the TUG using Spearman's correlation coefficients (ρ) and linear regression. *Results*. Five WISCI II categories applied to 71% of the EM-SCI subjects with walking ability, while 11 items applied to 11% of the subjects. The 10MWT correlated excellently with the TUG at each time point (ρ>0.80). However, this relationship changed over time. At one year after SCI, the time needed to accomplish the TUG was 1.25 times greater than the 10MWT time. *Discussion*. Some categories of the WISCI II appear to be redundant, while some discriminate to an insufficient degree. In addition, there appear to be ceiling effects, which limit its usefulness. The relationship between the 10MWT and TUG is high, but changes over time. We suggest that, at present, the 10MWT appears to be the best tool to assess walking capacity in SCI subjects. Additional valuable information is provided by assessing the needs for walking aids or personal assistance. To ensure comparability of study results, proposals for standardized instructions are presented.

Keywords. Standardization; Instructions; Guidelines; Timed walking test; WISCI II; SCI; Gait; Neurorehabilitation.

INTRODUCTION

The need for sensitive assessment tools in the field of neurological rehabilitation is obvious [1]. Current assessment tools have been designed largely to document functional outcome changes great enough to monitor clinically relevant improvements. These large changes are what have been considered as being most relevant for the patients and health insurance companies, and their assessment influences both (post) clinical and rehabilitation decision making (e.g. can a patient already be discharged from rehabilitation? Is this patient independent enough to return to his or her home environment?). However, today, we are full of expectations that in the near future new interventions will restore or repair damaged neural structures. Therefore, assessment tools should be able to detect smaller changes in function. On the one hand, more sensitive tools should be capable of detecting small improvements, thus demonstrating possible positive treatment effects. Although small, clinically-irrelevant treatment effects might be considered meaningless for the patient, they could demonstrate the 'proof of principle' of a new intervention. On the other hand, harmful interventions could be stopped as early as possible by the use of more sensitive measures, before the patient's condition becomes seriously affected. Thus, all of these considerations should be taken into account when evaluating assessment tools on their usefulness for clinical studies at present (see also [2]).

European Multicenter Study of Human Spinal Cord Injury

The European Multicenter Study of Human Spinal Cord Injury (EM-SCI; see also www.emsci.org) was founded in 2003 [3]. Five (at present 19) spinal cord injury rehabilitation centers across Europe standardized the assessment of their acutely injured patients. The aims of this initiative were (1) to document the time course and extent of natural recovery after a spinal cord injury (SCI) achieved with current rehabilitative approaches, (2) to introduce and to validate assessment procedures, (3) to improve diagnosis and prediction of outcomes after SCI and (4) to prepare the clinical basis for new interventional studies. The multicenter approach of this project ensured the capture of a sufficient number of cases with a broad spectrum of neurological and functional deficits. Assessments were chosen to cover several domains of a spinal cord injury i.e. impairment and disability. Time points of assessments were set according to the natural recovery and practical aspects. SCI subjects were assessed within 2 weeks after SCI and after 1 month (time window: 16 – 40 days), 3 months (70 – 98 days), 6 months (150 – 186 days) and 12 months (300 – 400 days).

The neurological examinations encompassed the standardized assessment established by the American Spinal Injury Association (ASIA) [4]. In addition, neuro-

physiological recordings were performed on the long sensory and motor tracts (somato-sensory evoked potentials and motor evoked potentials, respectively) and on the segmental level (electromyography and nerve conduction velocity). To assess the level of independence in SCI subjects, the revised Spinal Cord Independence Measure (SCIM II) [5] was applied, while walking capacity was assessed using the revised version of the Walking Index for Spinal Cord Injury (WISCI II; Fig. 5.1) [6], the 6 minute walk test (6MinWT) [7], the 10 meter walk test (10MWT) [7] and the timed up and go test (TUG) [7].

There were several reasons for performing these particular walking capacity tests. The WISCI was already tested for validity and reliability for SCI subjects [8] and was replaced in 2001 by the WISCI II (Fig. 5.1) [6]. Indeed, valuable information can be obtained by scoring the walking aids and / or physical assistance needed by the patient. The three timed tests were chosen as each of them was expected to reflect different aspects of walking capacity. The 6MinWT was chosen because of its relationship with cardio-vascular endurance [9], while the 10MWT was chosen as a measure to determine short duration speed that could be relevant for in-home activities. The TUG should relate with balance [10]. All tests were performed at preferred speed, as this might reflect the level of performance of the SCI subject in the community.

Figure 5.1 Revised version of the Walking Index for Spinal Cord Injury (WISCI II). Reprinted by permission from Macmillan Publishers Ltd 6.

Level	Description
0	Client is unable to stand and/or participate in assisted walking.
1	Ambulates in parallel bars, with braces and physical assistance of two persons, less than 10 meters.
2	Ambulates in parallel bars, with braces and physical assistance of two persons, 10 meters.
3	Ambulates in parallel bars, with braces and physical assistance of one person, 10 meters.
4	Ambulates in parallel bars, no braces and physical assistance of one person, 10 meters.
5	Ambulates in parallel bars, with braces and no physical assistance, 10 meters.
6	Ambulates with walker, with braces and physical assistance of one person, 10 meters.
7	Ambulates with two crutches, with braces and physical assistance of one person, 10 meters.
8	Ambulates with walker, no braces and physical assistance of one person, 10 meters.
9	Ambulates with walker, with braces and no physical assistance, 10 meters.
10	Ambulates with one cane/crutch, with braces and physical assistance of one person, 10 meters.
11	Ambulates with two crutches, no braces and physical assistance of one person, 10 meters.
12	Ambulates with two crutches, with braces and no physical assistance, 10 meters.
13	Ambulates with walker, no braces and no physical assistance, 10 meters.
14	Ambulates with one cane/crutch, no braces and physical assistance of one person, 10 meters.
15	Ambulates with one cane/crutch, with braces and no physical assistance, 10 meters.
16	Ambulates with two crutches, no braces and no physical assistance, 10 meters.
17	Ambulates with no devices, no braces and physical assistance of one person, 10 meters.
18	Ambulates with no devices, with braces and no physical assistance, 10 meters.
19	Ambulates with one cane/crutch, no braces and no physical assistance, 10 meters.
20	Ambulates with no devices, no braces and no physical assistance, 10 meters.

Validity, reliability and responsiveness of the WISCI II

The Walking Index for Spinal Cord Injury (WISCI) was carefully and specifically designed by Ditunno and colleagues for SCI subjects [8] (for a review see ASIA/ISCOS [11]). Clinical experts described 19 items based on literature review and consultation with colleagues. These items were hierarchically rank ordered by several international experts from most-impaired to least. This was followed by several stages investigating concurrent and face validity, which resulted finally in a group consensus. This version was then subject to an international reliability study, in which videotapes of a representative group of patients was shown to several experts. Indeed, an excellent reliability was found. In the revised scale (WISCI II; Fig. 5.1) two categories were added and this scale has been used in several international studies [6]. The WISCI II correlated well with several other scales indicating concurrent validity: the Barthel Index (BI) and the Rivermead Mobility Index (RMI; for both: Spearman's correlation coefficient ρ=0.67), the Spinal Cord Independence Measure (SCIM; ρ=0.97) and the Functional Independence Measure (FIM; ρ=0.70) [12]. It should be noted, however, that the SCIM, FIM and WISCI II were retrospectively scored, based on the description of walking in the SCI subjects charts. Furthermore, the WISCI II correlated with the Lower Extremity Motor Score (LEMS; ρ=0.58). It also showed good correlations with the 6MinWT (Spearman's correlation coefficient ρ=0.60), the 10MWT (ρ=–0.68), and the TUG (ρ= –0.76) [7].

Sensitivity to detect changes over time (responsiveness) was also investigated [12]. It was concluded that the WISCI II was more sensitive to walking recovery, as the WISCI II score distribution was wider at discharge (12/21 items) compared to other scores (BI, 3/16 items; RMI, 2/3 items; SCIM, 5/9 items and FIM, 4/7 items). However, in another study, the responsiveness of the WISCI II was lower compared to the 6 MinWT and 10MWT in a select group of SCI subjects with good walking ability (WISCI II score >1 within the first month after SCI) [13]. While the timed tests could determine improvement in walking capacity between 1 and 3 months and 3 and 6 months after SCI, the WISCI II showed improvement only within the first 3 months. Similar results were observed in SCI subjects with poorer walking ability, who achieved a WISCI II score above one within 3 months after SCI [14]. In that study, the WISCI II showed significant improvement also between 3 and 6 months after SCI, although the median improvement was zero.

Critical reflection of the WISCI II

The authors of the WISCI wrote that 'the ranking of severity is based on the severity of the impairment and not on functional independence in the environment [6]. However, as the WISCI is applied to test an activity (walking), it can be questioned whether ranking based on impairment can be justified. For example, motor impairment recovers differently compared to walking ability [15]. The actual WISCI II rank-

ing results in a somewhat confusing order of the items and a strong non-linearity. From a physical therapist's point of view, independent walking should be scored better compared to walking that depends on the assistance of another person [7]. Such aspects are not considered in the WISCI II, as for example, category 16 (ambulates with two crutches, no braces and no physical assistance, 10 meters; see Fig. 5.1) is scored poorer than to 17 (ambulates with no devices, no braces and physical assistance of one person, 10 meters). Furthermore, non-linearity can be observed if a SCI subject always needs braces. This patient could improve theoretically from 1 to 2, 3, 5, 6, 7, 9, 10, 12, 15, to a maximum score of 18. Such jumps in score are difficult to interpret.

Reliability of the WISCI has been reported to be excellent [8]. However, the authors have investigated reliability by scoring photos or videos. This has the disadvantage that the initial process of determining what walking aids or physical assistance are needed by this patient is not included in the reliability testing. It can be considered relatively easy to observe and score what devices and/or assistance a chronic SCI patient uses to walk. However, at the acute stage, the decision as to what aids or assistance the SCI patient needs is determined by the therapist together with the patient. This decision making process has not been tested for reliability and might cause most variability in determining the appropriate WISCI II category.

The responsiveness of the WISCI II, i.e. its ability to detect changes over time, appears to be poor compared to the timed walking tests. On the one hand, this could be explained by the ceiling effect of the WISCI II: SCI subjects that need no aids or assistance (WISCI II score 20) cannot further improve, although for example walking speed might increase [12, 13]. On the other hand, the categories of the WISCI II can cover a broad range of dependency. Physical assistance is described as 'any physical contact with the subject, including contact guard', which could cover a broad spectrum of physical support. Similarly, a wide variety in braces is available with different levels of support. Therefore, some patients might still need braces, but smaller ones, or need physical assistance, but considerably less and walk at a higher speed. All this is not reflected in changes in WISCI II category.

An assessment tool such as the WISCI II is subjected to cultural differences. Some differences between Europe and the USA are reflected in the preferences for walking aids. For example, while axilla crutches are predominantly used in the USA, in Europe, forearm or Canadian crutches are more common. Forearm crutches are considered as 'partial bearing' devices, because they do not support the full weight and are primarily used to give body stability (as opposed to leverage, like axilla crutches provide). Furthermore, initially, the WISCI II considered a walker to be rigid, without the use of wheels [6]. However, walkers with wheels are regularly used in European centers. Now, the WISCI II also considers walkers with wheels, although this should be identified in the descriptors. Similarly, other devices used

for bracing such as ace wraps or splints should be coded as brace and described under 'other'. In German speaking countries, orthopedic shoes (Künzli - SwissSchuh AG, Windisch, Switzerland) are widely used to reduce drop foot and increase lateral stability. We suggest that these shoes should also be considered as 'braces'. However, should alpine boots that increase the passive stability around the ankle-foot joint be considered braces as well?

Furthermore, the WISCI II is subjected to new inventions in the field of walking devices. Therefore, the guidelines should be adapted from time to time (as stated by the authors). For example, we were recently confronted with a relatively new device that provides a seat and trunk support for the patient (Meywalk® 2000, Meyland-Smith, Taars, Denmark, Fig. 5.2). Should this be considered a wheelchair that allows forward movements by the legs (in this case, WISCI II category 0 might apply)? Or is this a walker with wheels and additional bodyweight support that compensates for the loss of upper extremity supportive function in tetraplegic patients (WISCI II category 13), as these patients need more leg muscle strength for walking compared to paraplegic patients [15]?

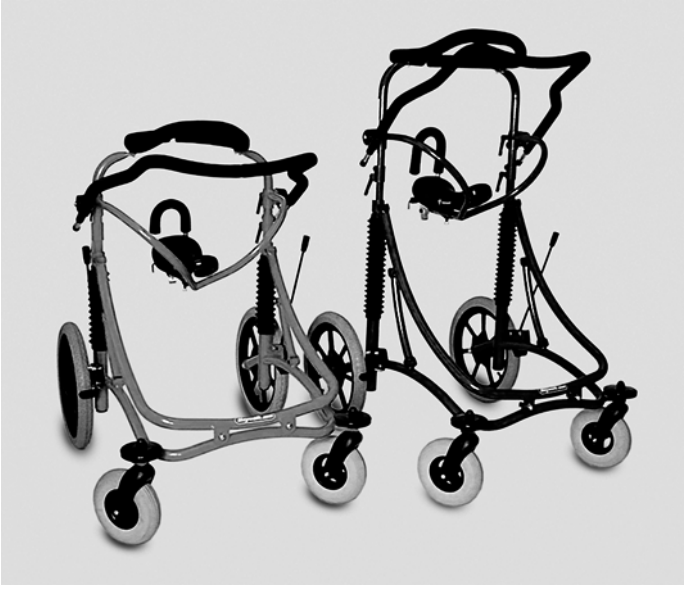


Figure 5.2 Meywalk® 2000 walking aid: WISCI II category 0 or 13?
Reprinted by kind permission from Meyland-Smith, Taars, Denmark.

General validity, reliability and responsiveness of the 6MinWT

We assume that no test has been more thoroughly investigated than the 6MinWT. The 6MinWT was originally applied to patients with respiratory diseases and chronic heart failure [9, 16]. In the cardio-respiratory domain, the 6MinWT is the test of choice (for reviews see [17, 18]). Indeed, in patients with primary pulmonary hypertension the distance walked during 6minutes correlated strongly with peak oxygen levels [19]. Also in patients with chronic obstructive airways and asthma, the 6MinWT correlated significantly with lung volume measurements [20]. This might be the reason why the 6MinWT has been applied to many different subject groups, with the aim of assessing cardiovascular endurance.

The 6MinWT has been tested for reliability in different patients groups. The 6MinWT is considered reliable when tested in healthy children [21] and elderly subjects [22], as well as in subjects with stroke [23, 24], acquired brain injury [25, 26], cerebral palsy [27], fibromyalgia [28, 29], multiple sclerosis [30] and cardiopulmonary disease [31, 32].

In patients with heart failure, the responsiveness of the 6MinWT is controversially discussed. In the RESOLVD study, the quality of life measures showed better responsiveness than the 6MinWT [32], while the responsiveness was considered good in elderly patients with heart failure [33]. In patients with chronic obstructive pulmonary disease, the endurance shuttle walking test was found to be more responsive compared to the 6MinWT [34]. Elderly subjects who underwent a functional training program showed less change in 6MinWT compared to a physical performance test [35]. However, the 6MinWT showed good responsiveness in patients with fibromyalgia [29]. Best initial estimates of small meaningful changes in elderly subjects were near 20m and of substantial change near 50m for 6MinWT [36]. For clinical use, small changes in the distance walked during 6minutes are detectable [36].

Validity, reliability and responsiveness of the 6MinWT in SCI patients

The 6MinWT has been applied to SCI patients in several studies [7, 13, 37-42] (for review, see also [11]). Concerning construct validity, the strength of the hip flexors at the less affected side correlated well with the distance walked during 6minutes [39]. Bilaterally, hip flexor and abductor muscle strength correlated best with the 6MinWT and gait speed [39]. A concurrent validity study showed that the 6MinWT correlated well with the WISCI II (ρ=0.60), the 10MWT (ρ=-0.95) and the TUG (ρ=-0.88) [7].

While interrater reliability can be considered good, intrarater reliability showed an improved 6MinWT performance between the first and second trial [7].

The responsiveness of the 6MinWT can be considered good in SCI subjects. Chronic SCI subjects who underwent a locomotor training program using a driven

gait orthosis improved their distance walked during 6minutes and gait speed, while the WISCI II showed no change [41]. In addition, in a small group of SCI subjects, both the 6MinWT and the 10MWT improved between 1 and 3 months and 3 and 6 months after SCI, while the WISCI II showed improvement only between 1 and 3 months [13].

Critical reflection of the 6MinWT

The standardization of the 6MinWT is more difficult compared to the 10MWT, as it depends strongly on the facilities. In some studies, the subjects performed the 6MinWT by walking up and down a pathway of a specific length. This has the advantage that it could also be applied in settings with limited space. However, walking speed might be negatively influenced by the turns. Indeed, in stroke patients who had to walk up and down, the 10MWT speed overestimated the 6MinWT speed [43], while when they walked in a square, the speeds were comparable [44]. Therefore, this test should be performed with the least amount of turns possible. Furthermore, as encouragement had a substantial impact on the distance walked during 6minutes in both cardiac and the respiratory patients [9], the test instructions should be rigorously standardized.

Although the reliability of the 6MinWT has been reported to be high, several studies indicated that the 6MinWT performance improved significantly after the first trial in healthy subjects [45] as well as in patients with cerebral palsy [27], fibromyalgia [29], SCI [7] and cardiopulmonary problems [9, 31]. It is therefore recommended that the subjects perform at least one test trial, before performing the actual measurement.

The 6MinWT appears to be redundant in some groups of patients with neurological disorders. Patients with stroke [44] and SCI [14, 39] showed no difference between short duration walking speed and speed during 6MinWT. This was even the case when tested at maximum walking speed [14]. It might indicate that in patients with neurological deficits, the distance walked during 6 minutes is not limited by cardiovascular impairments, but by other deficits, for example sensorimotor deficits. Indeed, in patients with stroke, there was no relationship between the 6MinWT and cardiovascular endurance [46]. Even in patients with severe lung diseases, the 6MinWT was rather related to muscle function than to cardiac or ventilatory impairment [47].

A selection bias could occur, as not all patients who are able to walk (WISCI II >1) perform the 6MinWT. Physical therapists tend not to test subjects who have poor walking ability, although these patients are allowed to take a rest during the 6MinWT. Especially at onset of the rehabilitation, this leads to a small number of patients who have performed the 6MinWT. Thus, especially in patients with poor

walking ability, a discrepancy might exist between short and long duration walking speed, which has not been assessed so far.

General validity, reliability and responsiveness of the 10MWT

The 10MWT represents a quick and easy measure and can be applied to any population able to ambulate the required distance (see also [11]). Reference values for gait speed exist for different ages and gender, although these were not derived from 10 meter testing [48]. The 10MWT was subject to concurrent or construct validation. It has been applied to both healthy subjects (e.g. elderly subjects [49]) and different patient groups with neurological disorders such as Parkinson's disease [50, 51], stroke [52-54] and multiple sclerosis [55]. In patients with cerebral glioma, the 10MWT correlated well with the Barthel Index [56]. In children with neuromuscular disease, the 10MWT correlated well with a 10minute walk, although the self-selected speed was higher for the 10MWT [57]. It has also been applied in patients with orthopedic disorders, e.g. with lower limb amputation [58]. Patients with a transtibial amputation walked faster compared to those with a transfemoral amputation [59].

The 10MWT showed good reliability in patients with mixed neurological diagnoses (ICC=0.93) [60], stroke [52], multiple sclerosis [30] and Parkinson's disease [50]. The 10MWT also showed good responsiveness in acute stroke patients [53, 61, 62], although the 5 meter walk test appeared to be more responsive compared to the 10MWT [63].

Validity, reliability and responsiveness of the 10MWT in SCI patients

Concerning construct validity, the strength of the hip flexors at the less affected side correlated well with gait speed [39]. Bilaterally, hip flexor and abductor muscle strength showed the highest correlations with gait speed [39]. Concerning concurrent validity, the 10MWT correlated well with the 6MinWT (ρ=-0.95), TUG (r=0.89) and WISCI II (ρ=-0.68) [7]. Compared to the TUG and 6MinWT, it showed better inter- and intrarater reliability in SCI, as the subjects' gait speed did not change between the first and second trial [7]. The 10MWT was more responsive than the WISCI II in SCI subjects. It assessed changes during SCI rehabilitation between month 3 and 6 after SCI [13] and in chronic SCI, it detected improvement in gait performance due to automated treadmill training [41], both unrevealed by the WISCI II.

Critical reflection of the 10MWT

Walking speed is considered a surrogate for the overall quality of gait (and motor function) [44]. However, gait speed is difficult to interpret. What is a meaningful gait speed for daily life and which increment in speed can be considered relevant? Gait speed has not been correlated with disability scales in SCI. It is therefore difficult to determine its relevance for daily life. The speed needed to safely cross a street was found to be 0.6m/s [64]. This was used to separate SCI subjects into functional and non-functional walkers. In elderly subjects, among several variables, a walking speed above 1.0m/s was associated with an independent lifestyle [65]. Perera et al. [36] found in elderly subjects that the best estimates of small, meaningful changes in gait speed were near 0.05m/s, while substantial changes were near 0.10m/s.
Similarly to the 6MinWT, the 10MWT has a floor effect for those subjects who are unable to walk 10meters. In addition, a ceiling effect might occur for those subjects who can walk a longer distance at the same speed. The latter effect is expected to be less for the 6MinWT.

In stroke, it has been shown that the 10MWT speed overestimated the long distance walking speed [43]. This was also the case for children with neuromuscular disease [57]. However, in a recent study, these findings could not be confirmed for SCI subjects [14]. The 10MWT speed did not differ from the 6MinWT speed 1, 3 and 6 months after SCI. This is in line with a recent study in stroke [44].

General validity, reliability and responsiveness of the TUG

The Get up and Go test [66] was modified by introducing a timed component (Timed Up and Go, TUG) [10]. The test was validated in frail, elderly subjects and was shown to correlate moderately with gait speed, the Berg Balance Scale and the Barthel Index [10]. Concurrent validity was good in patients with chronic stroke [67]. In patients with multiple sclerosis, the TUG correlated well with other static and dynamic balance tests, although all tests showed poor discriminative ability between fallers and non-fallers [68]. The discriminative ability of the TUG to predict falls was good in subjects with stroke [69], but contradicting findings exist in community-dwelling elderly people (Lin et al. [70] versus Shumway-Cook et al. [71]). The TUG could discriminate between geriatric subject groups who used different walking aids [72]. In children, the TUG could differentiate well between children with cerebral palsy or spina bifida and healthy ones, as well as between children of different ages [73]. Good concurrent validity was found in patients with lower limb amputation [74].

Reliability was excellent in young [73] and elderly [49, 70] healthy subjects, as well as in subjects with Parkinson's disease [75], chronic stroke [67] and lower limb amputations [74]. Reliability was poorer in patients with total hip and knee arthroplasties [76] and in elderly subjects, cognitive impaired or unimpaired [77].

The responsiveness of the TUG was good in young children in that it detected change over a period of five months [73]. It was also responsive in older subjects participating in geriatric rehabilitation [72]. It also detected deterioration and improvement in the early post-operative period after total hip and knee arthroplasty [76]. In patients with acute stroke, the responsiveness of the TUG was less compared to, for example, the 5meter walk test [63].

Validity, reliability and responsiveness of the TUG in SCI patients

Concurrent validity is good as a strong correlation was found between the TUG and the WISCI II (ρ=-0.76), the 6MinWT (ρ=-0.88) and the 10MWT (r=0.89) [7]. Reliability was high (r>0.97), but the Bland-Altman analysis showed that SCI subjects performed the second trial better than the first one, when tested by the same rater [7]. To our knowledge, no information exists about the responsiveness of the TUG in SCI subjects.

Critical reflection of the TUG

In patients with Parkinson's disease [50, 75] or SCI [7], test performance increased between the first and second trial, which influences reliability. It is therefore recommended that similarly to the 6MinWT, the subjects should perform a test trial at least once before performing the measurement.

The TUG correlated excellently with the 10MWT, which might indicate redundancy [7].

A slight disadvantage of the TUG is that it cannot be converted into speed, as can be done with the 10MWT and 6MinWT. The speed of subjects unable to perform the 10MWT or 6MinWT can be set at 0m/s. This is not possible for the TUG and makes statistical analyses more difficult.

An advantage of the TUG is that a more complex task is tested rather than 'just' walking, which might better reflect daily life activities. However, as it combines several important tasks in one test, it scores the whole composite of standing up, walking, turning and sitting down, which might decrease the sensitivity of the information gained. It might be more accurate to test the different phases separately: the sit-to-stand-to-sit test could be performed to test standing up and sitting down (see for example Csuka and McCarty [78]; Newcomer et al. [79] and Bohannon [80]). As this test should be performed with crossed hands, it might be more related to upper leg strength than the TUG, in which the subject can use the arms when standing up and sitting down. Walking could be tested by the 10MWT. Turning might be tested by timing and counting the number of steps needed to turn 360°, which has successfully been applied to elderly people [81] and patients with Parkinson's disease [82].

Aims of this study

This overview shows that the assessment of walking capacity has been extensively investigated in a variety of patient populations, but much less assessed in SCI patients. The aims of this study were to investigate: (1) which WISCI II categories apply to the EM-SCI subjects and (2) the relationship between the TUG and the 10MWT, as results from a previous study [7] might suggest that these tests provide similar information.

METHODS

Retrospective analyses were performed of the EM-SCI database. At the time of analysis, the EM-SCI database contained data from 917 subjects. The numbers of missing observations were largest at two weeks after SCI (difficult to assess at this early time point in most European centers) and 12 months (unfinished follow-up). To investigate which WISCI II categories applied to the SCI subjects, the frequency of each category was presented as a percentage for each time point. The percentages of each WISCI II category were averaged for all time points.

The walking tests were applied by trained physical therapists. The SCI subjects performed the 10MWT with a “flying start”, i.e. they walked about 14 meters, while the intermediate 10 meters were measured to compensate for acceleration and deceleration effects. The TUG was performed according to a previous study [10]. However, the SCI subjects initiated the test themselves, instead of responding to a “go” signal. The relationship between the 10MWT and the TUG was investigated using linear regression and correlation analyses. Again, separate analyses were performed for each time point.

RESULTS

Several WISCI II categories (Fig.5.1) applied rarely to the EM-SCI subjects (Table 5.1). Each of the categories 2, 7, 10, 14 and 18 applied on average to less than 1% of the SCI subjects with some walking ability (WISCI II >0; final column Table 5.1). In addition, the categories 3, 6, 11, 15, 17 and 19 applied to less than 2% of the SCI subjects with a WISCI II above 0. These 11 categories applied to 11% of walking EM-SCI subjects. In contrast, a large proportion (71%) of the SCI subjects with some walking ability could be categorized into the items 1, 8, 13, 16 and 20.

Table 5.1 Frequencies of WISCI II categories

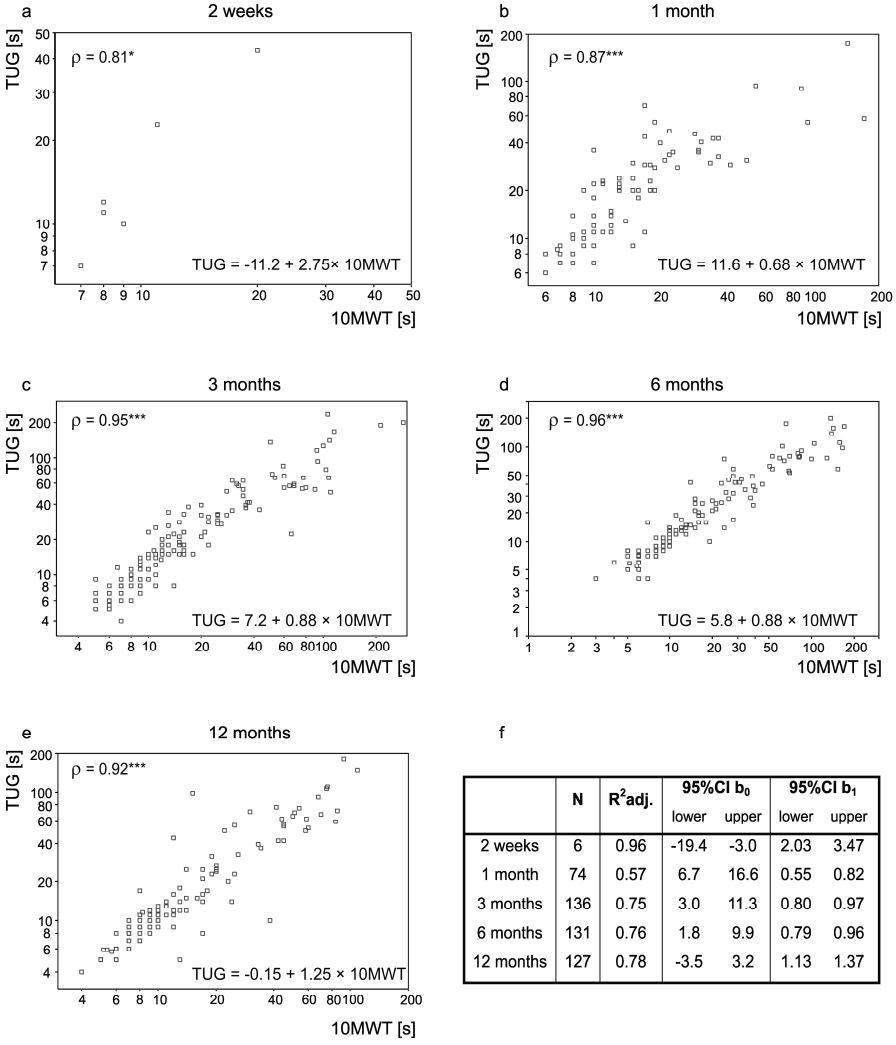
	2 weeks		1 month		3 months		6 months		12 months		Average[a]
WISCI II	n	%	n	%	n	%	n	%	n	%	%
0	504		646		485		333		213		
1	5	18.5	15	10.0	13	5.2	6	2.8	1	0.6	7.4
2		0.0		0.0		0.0		0.0		0.0	0.0
3	1	3.7	2	1.3	4	1.6	2	0.9	1	0.6	1.6
4	2	7.4	12	8.0	12	4.8	5	2.3	2	1.1	4.7
5	2	7.4	8	5.3	10	4.0	10	4.6	1	0.6	4.4
6		0.0	6	4.0	7	2.8	2	0.9	1	0.6	1.7
7		0.0	1	0.7	3	1.2	1	0.5	2	1.1	0.7
8	3	11.1	11	7.3	18	7.3	18	8.3	6	3.3	7.5
9	1	3.7	5	3.3	7	2.8	11	5.1	2	1.1	3.2
10		0.0		0.0	2	0.8		0.0		0.0	0.2
11	1	3.7	5	3.3	2	0.8	4	1.8		0.0	1.9
12		0.0	3	2.0	22	8.9	15	6.9	14	7.8	5.1
13	1	3.7	18	12.0	22	8.9	14	6.5	11	6.1	7.4
14		0.0		0.0	2	0.8	2	0.9	1	0.6	0.5
15		0.0		0.0	3	1.2	3	1.4	4	2.2	1.0
16		0.0	9	6.0	26	10.5	26	12.0	21	11.7	8.0
17		0.0	7	4.7	1	0.4	4	1.8	1	0.6	1.5
18		0.0		0.0		0.0		0.0	3	1.7	0.3
19		0.0		0.0	5	2.0	5	2.3	8	4.4	1.8
20	11	40.7	48	32.0	89	35.9	89	41.0	101	56.1	41.2
Total	531		796		733		550		393		
Missing	386		121		184		367		524		
Grand total	917		917		917		917		917		

[a] The average percentage was calculated over all 5 time points for those SCI subjects with a WISCI II score >0 (some ability to stand or walk).

Abbreviations: n, number; %, the percentage of SCI subjects that have a WISCI II score >0.

Relationship between TUG and 10MWT

The relationships between the TUG and the 10MWT are shown in Figure 5.3. The non-parametric correlations (chosen to adjust for outliers) varied between 0.81 and 0.96. At 2 weeks after SCI (Fig. 5.3a), according to the linear regression model, 96% of the variation in TUG could be explained by knowing the variation in the 10MWT results (this is the explained variance; Fig. 5.3f). However, as the number of observations was small, the non-parametric correlation might be more applicable. At 1 month after SCI (Fig. 5.3b), the linear regression model showed the poorest explained variance. Over half of the variation in TUG could be explained by knowing the 10MWT results. The equation (Fig. 5.3b) showed that considerably more time was needed to perform the TUG compared to the 10MWT (11.6 seconds+0.68 times the time needed to perform the 10MWT).



f

	N	R^2adj.	95%CI b_0		95%CI b_1	
			lower	upper	lower	upper
2 weeks	6	0.96	-19.4	-3.0	2.03	3.47
1 month	74	0.57	6.7	16.6	0.55	0.82
3 months	136	0.75	3.0	11.3	0.80	0.97
6 months	131	0.76	1.8	9.9	0.79	0.96
12 months	127	0.78	-3.5	3.2	1.13	1.37

Figure 5.3 Relationships between TUG and 10MWT. Scatter-plots showing the relationships between the Timed Up and Go (TUG) and 10 Meter Walk tests (10MWT) 2 weeks (a), 1 month (b), 3 months (c), 6 months (d) and 12 months (e) after spinal cord injury. Please note the logarithmical scale and the differences in scales between the figures. More detailed information about the regression analysis is provided in f.

Abbreviations: ρ, Spearman's non-parametric correlation coefficient; *, $P<0.05$; ***, $P<0.001$; N, number of observations; R^2adj., adjusted explained variance; lower and upper limits of the 95% confidence interval (95%CI) are presented for the constant b_0 and the regression coefficient b_1 of the regression equation $y = b_0 + b1 \times x$.

At 3 and 6 months after SCI (Fig. 5.3c, d), similar results were obtained. The explained variance was about 75% and the time needed to perform the TUG was still longer compared to the 10MWT. However, it decreased about 2seconds from 3 to 6 months after SCI. Finally, at 12 months after SCI (Fig. 5.3e), the TUG was found to take 1.25 times longer than the 10MWT.

DISCUSSION

The main findings of this study were the following: (1) Many EM-SCI subjects were categorized in a limited number of WISCI II items, while half of the WISCI II categories applied to a small number of subjects. (2) In general, the TUG correlated excellently with the 10MWT, but the relationship changed over time.

As the rehabilitation process continued the number of SCI subjects with a low WISCI II score tended to decrease, while higher WISCI II scores applied more frequently to the EM-SCI subjects. The items 1, 8, 13, 16 and 20 applied frequently to SCI subjects with walking ability. These findings are in line with those from Morganti et al. [12], who found that most walking SCI subjects could be scored 13, 16 or 20 after rehabilitation.

In contrast, about half of the WISCI II categories applied to 11% of the EM-SCI subjects. Redundancy of the WISCI II has already been previously addressed [12], as the WISCI II correlated excellently with the SCIM II mobility category for short distances. The high correlation of 0.97 [12] indicated that 94% of the variation of the WISCI II (which has 21 items) could be explained by the SCIM II (which has 9 items). The present results indicate that if a shorter version of the WISCI II would be desired, the categories 1, 4, 5, 8, 9, 12, 13, 16 and 20 (see Fig. 5.1) could describe the appropriate need of physical assistance and/or walking aids in 80.9% of the EM-SCI subjects with some walking ability.

Relationship between TUG and 10MWT

Although the TUG and the 10MWT correlated excellently with each other, the relationship was not fixed, but changed over time. The time needed to perform the TUG (compared to the 10MWT) decreases over time. Especially at 1 month after SCI, the TUG might provide additional information, as only half of the variation in the 10MWT could explain the variation of the TUG. This difference might be related to an impaired balance, which is suggested to be related to the TUG [10]. However, over time, the TUG might become redundant as at least 75% of the variation in the TUG is covered by the 10MWT results. In the chronic stage (1 year), the TUG can be estimated by multiplying the time needed for the 10MWT by 1.25.

Aspects of walking capacity

In SCI subjects, the assessment of walking capacity is relatively new and information is lacking. For example, maximum walking speed has rarely been tested in SCI subjects [14, 83]. The preferred walking speed of SCI subjects may only partially reflect the potential to participate in the community. Maximum walking speed, for example, which may be needed to catch a bus or cross a street, might be a better measure of daily life ambulatory capacity. Furthermore, walking capacity is tested in a simplified environment (i.e. a well-lit corridor, straight path, no disturbing factors etc.), which might be less applicable to daily life. New tests might assess the capacity to adapt walking to external demands (walk over uneven floors, ascend or descend slopes, avoid obstacles) or evaluate the influence of attention [84] on walking, by applying the dual task approach.

Furthermore, depending on the research question, different aspects of walking capacity might be relevant. For example, the application of functional electrical stimulation (FES) to improve walking ability is still controversially discussed [85]. However, FES systems are improving and might allow independent walking for subjects who are normally wheelchair bound [86]. One goal could be to increase the maximal non-stop covered walking distance for SCI subjects (unrestricted for time). However, at present, we are unfamiliar with an appropriate standardized test protocol.

Standardization of walking tests

To ensure comparability of results (especially in multi-center trials), rigorously standardized assessment protocols are needed. We therefore propose instructions for the walking capacity tests discussed in this study and hope these proposals might initiate a discussion concerning the standardized assessment of walking tests in the field of SCI and perhaps even in rehabilitation in general.

WISCI II

While at present different instructions are available for the use of timed walking tests, there are clear guidelines available for the WISCI II at: http://www.spinalcordcenter.org/research/wisci/resources/wisci-guide.pdf. The scoring form and descriptors are available at: http://www.spinalcordcenter.org/research/wisci/resources/-wisci-scoring-form.pdf.

Timed walking tests

If more than one test is applied during a single session, we propose to perform the less fatiguing test first (e.g. preferred walking speed test before maximum speed

test, or the 10MWT before the 6MinWT). Sufficiently long rest periods between each test should be taken and dress shoes should not be allowed [87]. We suggest that the patient initiates the test and not that he/she should react on a "go" signal, as we do not intend to measure reaction time. A stopwatch with an accuracy of 1/10 seconds is required. In addition to the timed tests, the WISCI II can be used to score the need for walking aids and assistance. For all tests, the investigator should be positioned next to the patient. In this way, the beginning and end point of the timed pathway can be better determined and assistance can be provided if required.

6MinWT

The environment for 6MinWT might be difficult to standardize. A flat, smooth, non-slippery surface, with no disturbing factors is required and the pathway should contain as few turns as possible (preferably a large round or oval shaped path). Distances should be marked at least every 5meters. The total distance should be written down in meters.

Subjects are instructed to walk at their preferred (or maximum) walking speed (Fig. 5.4a). The subject initiates the start of the test. After each minute, the subject should be informed about the time left and should be encouraged to continue his/her performance (Fig. 5.4a).

Remarks: (1) If subjects are unable to walk for 6minutes, rest breaks are allowed. After resting, the subject might continue with the test and the final distance is determined after 6minutes. In such a case, a remark about the rest period should be written down. (2) It will be difficult to assess a 6MinWT in subjects who are categorized to WISCI II scores of 2 to 5, as these subjects depend on parallel bars.

10MWT

The environment should be similar to that for the 6MinWT. The subjects are instructed to walk 14meters, while the intermediate 10meters should be marked on the floor. The measurement starts when the patient crosses a mark on the floor that indicates the onset of the 10meter pathway ("flying start"). After 10meters (32.8feet), the timer is stopped, but the patient continues until he or she has reached the end of the 14meter track. The time is written down to an accuracy of 1/10 seconds. Subjects are instructed to walk at their preferred (or maximum) walking speed (see Fig. 5.4b).

Remarks: (1) A special condition occurs when the patient requires the use of parallel bars, as these are rarely 14meters long. We suggest recording the middle 5meters between the parallel bars twice. The time of the first and second 5meter distances are summed and written down.

(2) This test application is comparable to the 50feet test that has sometimes been used in SCI patients [37], although time is only recorded for 10meters.

TUG

In general, we would suggest to use most of the instructions of the modified TUG test as proposed by Podsiadlo and Richardson [10]. However, we propose that the subject should initiate the test (Fig. 5.4c). Comparable to the 10MWT, a similar environment of at least 4meters long is required. The chair should have a seat height of 46cm and armrests (67cm). The patient sits with his or her back against the chair, arms resting on the chair's arm. As soon as the subject lifts up from the chair (buttocks), the time recording starts. The subject may use the armrests of the chair for support. After 3meters (9.8feet), the subject turns and walks back to the chair. The timer is stopped as soon as the buttocks touch the chair again. The time is recorded and written down at 1/10 second accuracy.

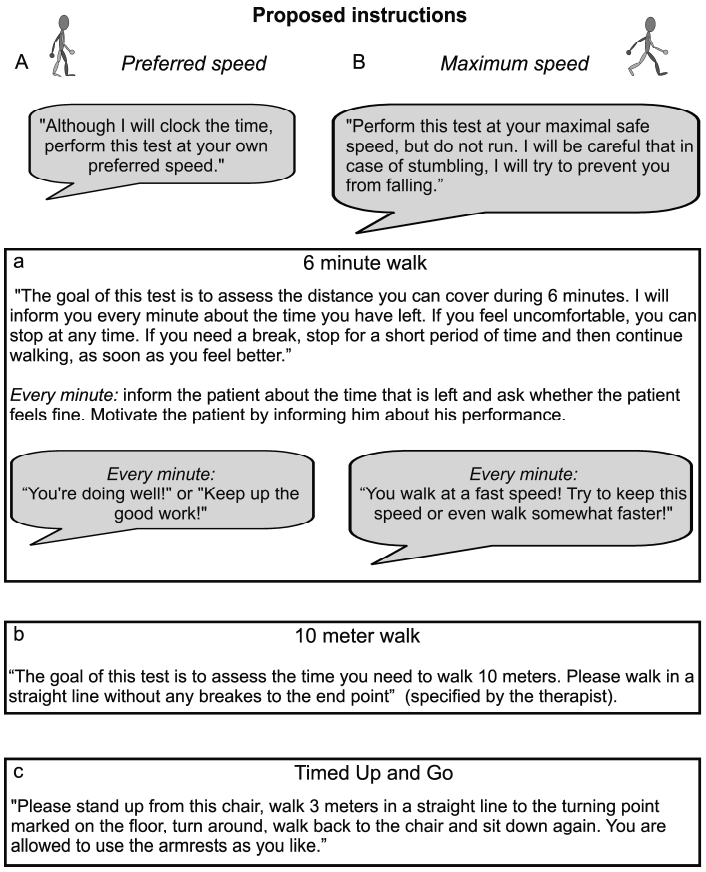


Figure 5.4 Proposals for standardization of the timed walking tests. Proposed instructions for the (a) 6 minute walk, (b) 10 meter walk and (c) Timed Up and Go tests performed at (A) preferred and (B) maximum walking speed.

CONCLUSIONS

There is a need for valid, reliable and responsive tests to assess walking capacity in SCI subjects. Clinically relevant changes in walking ability are important for the individual patient, while sub-clinical changes (on the population and individual level) become important when evaluating new treatments for efficacy and safety. We presented four walking tests that are applied in the EM-SCI. We presented their positive and negative aspects, as well as new results showing that most SCI subjects could be categorized into a limited number of WISCI II items and that the TUG correlated well with the 10MWT, but that this relationship changed over time. We suggest that, at present, the 10MWT might be the best choice for assessing walking capacity in SCI subjects. Furthermore, we recommend the additional assessment of the dependence of the SCI subjects on walking aids or personal assistance.

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CHAPTER 6

Falls in persons with spinal cord injury:
Validity and reliability of the Berg Balance Scale

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ABSTRACT

Background. Persons with spinal cord injury who are able to walk are at risk for falls. *Objective*. The objectives were to investigate if the Berg Balance Scale (BBS) can discriminate those with a propensity to fall; to determine whether the BBS is associated with mobility measures, fear of falling, and muscle strength; and to assess interobserver reliability. *Methods*. The measurement tools used were the BBS, the Spinal Cord Independence Measure, the Falls Efficacy Scale (FES-I), the Walking Index for Spinal Cord Injury, the 10-m walk test, and the standard neurological classification including motor scores (MS). Falls were recorded retrospectively for the previous month and prospectively for the subsequent 4 months. To determine interobserver reliability, BBS performance was videotaped and analyzed by additional physical therapists. Associations between BBS and the number of falls, measures of mobility, FES-I, and MS were calculated using Spearman correlations. The interobserver reliability was quantified using Kendall's coefficient of concordance and intraclass correlation coefficients (ICCs). *Results*. Forty-two participants were included of whom 26 sustained 1 or more falls. BBS performance correlated with measures of mobility, FES-I, and MS (rs = -.83 to .93; P < .001) but not with the number of falls (rs = -.17; P = .28). The interobserver reliability was excellent, both for single items (.84-.98, P < .001) and for the total score (ICC = .95; 95% confidence interval = 0.910-0.975). *Conclusions*. The BBS proved to be reliable and to relate well with other mobility measures, fear of falling, and muscle strength. However, it was unable discriminate between people who did fall and people who did not fall.

Keywords. Spinal cord injuries, Risk assessment, Accidental falls

INTRODUCTION

It is estimated that 10 to 83 persons out of every 1 million experience a spinal cord injury (SCI) every year and that 223 to 755 per million people live with a SCI1. Approximately 50% of these patients suffer an incomplete lesion, meaning that sensory and/or motor function is partially preserved below the level of the lesion [1, 2]. The prognosis for regaining ambulatory function among initially incomplete SCI patients ranges from 50% to 95%, depending on the extent of the lesion [3]. From a European cohort of 178 patients with complete and incomplete SCI about one third regained ambulatory function within six months after the SCI onset [4].

As a result of the motor and sensory impairment with incomplete SCI, balance can be affected. Partial loss of the ability to balance can result in falls and fall-related injuries. Brotherton and colleagues reported that 75% of 119 patients with incomplete SCI sustained at least one fall within one year [5]. As a consequence of the falls, 45% of these patients were restricted in their ability to go out into the community, and in 18% of the patients, a fracture resulted from the fall. The authors pointed out that the incidence of falls is markedly higher in this population than in elderly healthy individuals (75% vs. 25-35%, respectively) [5]. In SCI rehabilitation there are clinical assessments for sensory and motor function [6], independence [7] and walking ability [8, 9] but there is no validated test to assess balance and future propensity to fall. In order to identify patients who are prone to falls and intervene with fall prevention programs for patients at risk, a valid test is required.

For the elderly, the Berg Balance Scale (BBS) was developed to assess balance ability and to monitor changes in this ability over time [10]. It comprises 14 tasks testing postural stability, including static balance (e.g. standing unsupported with feet together) and dynamic balance (e.g. placing alternate foot on a step while standing unsupported). Depending on the performance, each task is rated with zero (unable to perform the task) to four points (best performance) with a total score ranging from zero to 56 points. It has been shown that lower scores on the balance scale are associated with a past history of falls [11]. The BBS proved to be a valid assessment tool when compared to laboratory measures of postural control, and clinical measures of balance and mobility [11]. Since its development, it has been validated for patients with stroke [12-14], brain injury [15], Parkinson's disease [16, 17], multiple sclerosis [18] and learning disabilities [19].

The primary aim of this study was to assess criterion-related concurrent validity and inter-observer-reliability of the BBS. In order to compare the risk of falling as measured using the BBS, the number of falls experienced within the study period was adopted as the external criterion. In addition the BBS scores were compared to measures of mobility, motor scores and fall related self-efficacy. It is hypothesized that fewer falls, higher grades of mobility, higher motor scores and higher self-efficacy are associated with higher scores on the BBS. Specifically, the objectives

were: 1. to determine to what extent the performance on the BBS was associated with the number of falls experienced over a period of five months; 2. to determine the degree of association between the BBS and the Walking Index for Spinal Cord Injury, gait speed, Spinal Cord Independence Measure-domain mobility and the motor scores (MS) test; 3. to assess the association between the BBS and the Falls Efficacy Scale-International Version (FES-I); 4. to explore which cut-off score on the BBS is critical for discriminating people with a risk of falling; and finally 5. to assess the inter-observer reliability when four physical therapists (PT) rate the videotaped BBS.

METHODS

This study was approved by the local Ethics Committee and all subjects gave written, informed consent before participation.

Participants

Participants were selected based on records of the physical therapy ward from the Spinal Cord Injury Center of the Balgrist University Hospital Zurich, Switzerland. All participants received either inpatient rehabilitation or outpatient physiotherapy between January 1998 and September 2007. All patients who experienced a spinal cord injury (SCI) at least one year prior to enrollment and who were able to walk for a minimum distance of 15m were eligible to participate in the study. Exclusion criteria included subjects with known problems of the vestibular system, severely impaired vision or non-SCI-related impairments affecting standing or walking function (e.g. joint replacement surgery of the lower limbs, severe lower back pain or diabetes) and patients younger than 18 years or older than 65 years of age.

Within the time frame of January 1998 to September 2007, 99 persons were identified as potential participants in the study. Of these subjects, 20 could not be contacted, 20 were excluded and 17 refused to participate. The primary reasons given for non-participation were lack of time and distance to travel for the measurement session. There was no difference in age, etiology, injury level, American Spinal Injury Association (ASIA) Impairment Scale, time since injury and sex between participants and those who declined to participate or could not be contacted. Each participant received a small monetary compensation for travel expenses.

Procedures

The measurements took place between July and November 2007, with 42 participants with SCI.

Participants were invited to one measurement session at the rehabilitation center where the BBS, the Spinal Cord Independence Measure II (SCIM II), the Falls Efficacy Scale-International Version (FES-I), the Walking Index for Spinal Cord Injury II (WISCI), the ten-meter walk test (10MWT), and the ASIA standard classification including the motor score (MS) were performed. During that visit, the number of falls the patient had experienced during the previous one month was recorded by interview. From that visit onwards, a four months prospective recording of the number of falls started using a specifically designed assessment calendar.

Instruments

The 14 tasks of the BBS were assessed by a physical therapist (PT) and simultaneously videotaped. To assess inter-observer reliability, three additional PTs working in the same institution rated the videotaped BBS performance of all subjects independently. Contrary to the first rater, these raters were blinded regarding the falls history of the person. Since the BBS was developed for a different population, some criteria have the potential for misinterpretation when the test is applied in patients with SCI. For this study, the use of walking aids e.g. crutches or walking frames was considered as external help. This was done after consultation with Dr. Katherine Berg. Prior to the reliability study the participating PTs were instructed how to assign the ratings. The recordings of all raters (ie. the PT who initially rated the patients as well as those PTs who subsequently rated the patients on the video recordings) were included in the analysis.

The SCIM II is an instrument to assess SCI-related disability [7]. Its items are subdivided into three parts, i.e. self-care (subscore 0-20), respiration and sphincter management (0-40), and mobility (0-40). For this study, the SCIM II mobility domain was obtained by interview and used for further analyses.

The FES-I is a self-reported measure of fall-related self-efficacy developed for elderly persons [20]. Subjects are asked to rate their self-perceived fear of falling when carrying out each of 16 activities on a four-point scale (1=not at all concerned, 4=very concerned). The total score ranges from 16 to 64 points. After a short introduction, patients completed the FES-I on their own while the examiner left the room.

The WISCI II is an instrument to assess a patient's ability to walk using 20 ordinal categories [8]. The rank order of the categories is based on the requirement of personal assistance and/or walking aids or braces. Zero represents no and 20 unrestricted walking function.

For the 10MWT [9] participants were asked to walk at their preferred comfortable and safe pace. The distance was marked on the wall of a straight walk-way. Subjects started approximately two meters before the 10 meter distance and

stopped again two meters after the 10 meter mark. Time was taken using a manual stop watch. The mean of two trials was the score.

An experienced physician examined the participant to determine the actual ASIA motor score and impairment rating according to the standard procedure [6].

In order to assess the current fall status of the participants, falls were recorded one month retrospectively and four months prospectively. For the recording of the latter, patients were instructed about the definition of a fall and how to keep records of falls sustained. According to The Prevention of Falls Network Europe Consensus a fall was defined as an unexpected event in which the participants come to rest on the ground, floor, or lower level [21]. Participants received a monthly calendar containing the definition of a fall, and examples of how to record a fall. Falls were marked either as a fall without injury, or a fall with an injury to the skin, joint or bone. Additionally the mode of treatment (either by a physician or at a hospital) was recorded. At the end of every month a letter was sent to the subjects containing the calendar for the new month and an envelope to return the calendar for the previous month. A reminder phone call was made when a calendar was not returned within one week.

Analysis

Spearman's rank correlations were calculated for the analysis of the relationships between the BBS and the number of falls, SCIM mobility score, FES-I, WISCI, gait speed and MS, respectively. Scatter plots were used to visualize these relationships.

In order to find an optimal cut-off value of the BBS, which differentiated between fallers and non-fallers, a receiver-operating characteristic (ROC) curve was applied and the area under the curve was calculated. An optimal cut-off value would identify fallers with the highest accuracy (i.e. with high sensitivity (true fallers) and specificity (true non-fallers)). For this analysis, subjects were categorized as fallers if they sustained one or more falls within the observation period. Subjects who had experienced no falls within the same period were considered as non-fallers.

Finally, for inter-observer reliability of the individual items of the BBS the Kendall coefficient of concordance was calculated, whereas for the total score the intra-class correlation coefficient using the two-way random effects model type absolute agreement was calculated. The level for statistical significance was set at 0.05. Microsoft Excel 2002 (Microsoft, Redmont, Washington) and SPSS for Windows 12.0.1 (SPSS Inc, Chigaco, Illinois) were used for the analysis.

RESULTS

For detailed characteristics of the 42 included subjects, see Table 6.1. About one third of the participants achieved maximum scores on the BBS, SCIM, FES-I, WISCI and MS. Thirty-one subjects were ambulatory for distances beyond 100m outdoors, while 11 subjects required a wheelchair for this task and were only capable of walking indoors for short distances using assistive devices. Twenty-six participants experienced one or more falls over the study period of five months. The total number of falls was 270. Seventeen falls sustained by eleven subjects resulted in injury (Table 6.2). Among the participants there were eight subjects who fell more than ten times, with one participant reporting 52 falls. Four participants sought a general practitioner or a hospital for treatment of fall-related injuries.

Table 6.1 Characteristics of the subjects included in the study (n=42)

	Frequency (%)	Mean (±SD)	Median (Range)	Lower Quartile	Upper Quartile
Age (years)		49.3 (11.5)	51.1 (24-65)	41.3	60.3
Gender					
female	9 (21.4)				
male	33 (78.6)				
Level					
cervical	16 (38.1)				
thoracic	9 (21.4)				
lumbar	17 (40.5)				
ASIA impairment scale					
A	2 (4.8)				
C	2 (4.8)				
D	35 (83.3)				
E	3 (7.1)				
UEMS		49.1 (2.0)	50 (41-50)	50	50
LEMS		40.5 (11.4)	46.5 (16-50)	30	50
Etiology					
traumatic	33 (78.6)				
ischemic	6 (14.3)				
hemorrhagic	3 (7.1)				
Time since SCI (months)		66.5 (66.2)	62.7 (12-426)	21.4	86.3

Abbreviations: ASIA: American Spinal injury Association; SCI: spinal cord injury; UEMS: Upper extremity motor score; LEMS: Lower extremity motor score; SD: standard deviation

Table 6.2 Berg Balance Scale, mobility scores and falls data

	Frequency (%)	Mean (±SD)	Median (Range)	Lower Quartile	Upper Quartile
Berg Balance Scale		41.1 (15.2)	44 (11-56)	30	55
SCIM total score		90.7 (8.9)	92.5 (69-100)	83	99
SCIM mobility score		32.3 (7.8)	35 (17-40)	26	40
Falls Efficacy Scale[a]		30.7 (12.1)	30.5 (15*--55)	19	38
WISCI		16.9 (3.4)	18.5 (11-20)	13	20
Walking speed (m/s)		0.93 (0.48)	0.87 (0.12-1.67)	0.56	1.43
Falls without lesion	253 (93.7)				
Falls with lesion	17 (6.3)				
Skin abrasion	8 (3)				
Joint sprain	7 (2.6)				
Bone fracture	2 (0.7)				

Abbreviations: SCIM, Spinal Cord Independence Measure; SD, standard deviation; WISCI, Walking Index for Spinal Cord Injury.
[a]Missing one item in one patient.

Berg Balance Scale and falls

There was no relevant association between the number of falls and the score on the BBS (Fig. 6.1). This holds true for both falls without and falls with injury (Table 6.3).

A post hoc analysis including only those participants who achieved less than the maximum score on the BBS, or only restricted walking function (i.e. a WISCI score less than 20), still revealed that there was no association between the BBS and the number of falls.

Berg Balance Scale and mobility measures

The BBS correlated strongly and significantly with the SCIM mobility score, WISCI and with the 10MWT (Table 6.3). The results indicate that higher scores on the BBS were associated with a higher grade of mobility in terms of independence of walking aids and walking speed.

Berg Balance Scale and motor score

Participants with high values on the BBS also rated significantly higher on the MS.

Berg Balance Scale and Falls Efficacy Scale International-Version

Higher scores on the BBS were significantly associated with lower scores on the FES-I. This correlation suggests that patients who had a better ability to balance showed less fear of falling and hence were able to make a realistic self-assessment (Table 6.3)

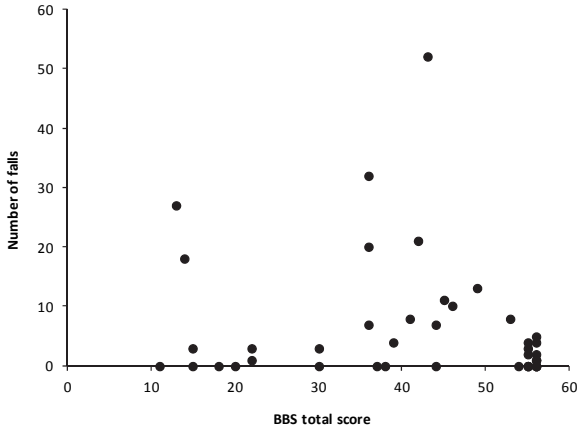

Figure 6.1 Relationship between total Berg Balance Scale (BBS) score and the number of falls sustained over a period of 5 months. The maximum score of the BBS is 56 (note that there are data points which represent more than one subject and are superimposed: 4 participants with BBS=56, and no falls, 2 with BBS=56 and one fall and 3 with BBS=55 and no falls).

Table 6.3 Correlation matrix expressing the relationship between Berg Balance Scale and falls, the fall related self-efficacy, mobility- and motor scores[a]

	Falls total	Falls without lesion	Falls with lesion	SCIM mobility score	WISCI	Walking speed	FES-I	MS
BBS	-0.17 (0.28)	-0.17 (0.28)	-0.16 (0.32)	0.89 (<0.001)	0.82 (<0.001)	0.93 (<0.001)	-0.81 (<0.001)	0.62 (<0.001)
Falls total		0.96 (<0.001)	0.52 (<0.001)	-0.14 (0.38)	-0.03 (0.84)	-0.10 (0.52)	0.28 (0.07)	-0.17 (<0.001)
Falls without lesion			0.42 (<0.001)	-0.14 (0.38)	-0.06 (0.73)	-0.10 (0.54)	0.25 (0.1)	-0.10 (0.54)
Falls with lesion				-0.10 (0.52)	0.10 (0.52)	-0.13 (0.4)	0.31 (0.04)	-0.16 (0.31)
SCIM mobility score					0.81 (<0.001)	0.89 (<0.001)	-0.78 (<0.001)	0.59 (<0.001)
WISCI						0.81 (<0.001)	-0.71 (<0.001)	0.66 (<0.001)
Walking speed							-0.83 (<0.001)	0.60 (<0.001)
FES-I								-0.74 (<0.001)

Abbreviations: BBS, Berg Balance Scale; SCIM, Spinal Cord Independence Measure; WISCI, Walking Index for Spinal Cord Injury; FES-I, Falls Efficacy Scale International Version; MS, Motor Scores.
[a]Spearman correlation coefficients are presented with corresponding p-values in parentheses.

Berg Balance cut-off score

In order to determine an optimal value that discriminated fallers from non-fallers, the ROC procedure was applied. The area under the curve was 0.48 (95%CI=0.29-0.67). This means that the BBS cannot discriminate beyond the chance of coincidence between participants who fall and those who do not. Therefore determination of a cut-off score to optimize sensitivity and specificity was irrelevant.

Inter-observer reliability

In addition to the rater (first author) who obtained the BBS directly from the patients, three additional physical therapists rated the BBS independently, based on video recordings. Of the 42 recordings, two could not be included in the analysis due to technical problems. Since all participants achieved the maximum score on item three, hence there was no variance, and this item was excluded from the analysis. The average professional experience of the physical therapists at the time of the study was 12.5±6.6 years, ranging from 5 to 19 years. Their experience with individuals with spinal cord injuries was 10.8±7.2 years (range: 4 to 17years). The agreement among the raters, relating the items as calculated using Kendall's coefficient of concordance, ranged between 0.838 and 0.979 ($p<0.001$). For the total score, the ICC was 0.953 (95%CI: 0.910-0.975). Both results indicate excellent inter-observer agreement.

DISCUSSION

The aim of this study was to examine whether the BBS score is associated with the risk for falls and the level of mobility in persons with SCI who are able to walk, as well as to assess the inter-observer reliability of the BBS.

Berg Balance Scale and falls

Our data show no significant association between the number of falls and the scores achieved on the BBS. In addition, the effort to find a cutoff score which discriminated between fallers and non-fallers revealed that there is no such score and that the discriminative power was not better than chance. The recordings of our study showed that about one third of the included subjects recovered to full mobility, according to the applied assessments. This may have led to a ceiling effect. Nevertheless the same analyses including only those participants who achieved less than the maximum score on the BBS, or WISCI, still revealed that there was no association between the BBS and the number of falls.

Our assumption was that people with a lower BBS score would be at a higher risk of falling. There are two possible explanations why this was not observed. First, participants may be aware of their risk. This is supported by the finding that the FES-I is highly associated with the BBS. Obviously persons with impaired balance have learned to handle their risk for falls. One of the inclusion criteria was that patients had lived with their SCI for more than one year, which we consider a sufficient period of time to find strategies for avoiding falls. The results may differ in a sample of recently injured participants.

Second, the recordings of our study revealed that about one third of the included subjects recovered to full mobility, according to the applied assessments. This may have led to a ceiling effect. Nevertheless the same analyses including only those participants who achieved less than the maximum score on the BBS, or WISCI, still revealed that there was no association between the BBS and the number of falls.

The construct behind falls in patients with SCI seems to differ from that of elderly persons, who were the original target population for the use of the BBS [10]. Balance was considered as an important component of fall risk [10, 22]. In the absence of a gold standard for balance, several ways have been adopted to establish criterion-related validity, (eg. laboratory measures [12, 15, 22, 23], other measures of balance or measures of mobility [13, 16-18, 23-25], measures which assess the impact of a specific disease [16] or length of stay in a hospital and discharge destination [14]). Some of these studies also compared the performance on the BBS with the fall status of the included subjects [11, 17, 18, 22, 24, 25]. These results are somewhat controversial and seem to depend on the included subjects. Some studies found that the BBS was able to discriminate fallers from non-fallers. Those studies included mostly elderly persons [11, 22, 25]. A significant difference in the sum scores of the BBS between fallers and non-fallers was also found in a sample of 45 patients with Parkinson's disease [17]. However, in accordance with our results, in two studies that included participants with stroke [24] or multiple sclerosis [18], no clear difference in the performance on the BBS between fallers and non-fallers was found.

Multiple factors have been identified as contributors to fall risk. Brotherton and colleagues performed a mail survey and identified several factors associated with falls in individuals with incomplete SCI [26]. Beside these self-reported factors, additional studies are required that include direct measures of impairment in order to characterize fallers and to find or create useful clinical assessments to identify persons at higher risk for falls.

Berg Balance Scale and mobility

The results show that the sum scores of the BBS correlate highly with measures of mobility (i.e. SCIM sub score mobility, WISCI and gait speed). The BBS has been used as a measure of balance along with other assessments in the Spinal Cord Injury Locomotor Trial (SCILT), which included 146 patients with incomplete SCI [27]. In line with our study, the authors reported significant correlations between the BBS and the WISCI, gait speed and MS, respectively. This association indicates that the BBS tasks seem to measure the construct underlying ambulatory function and that voluntary muscle strength, as measured with the ASIA Motor Score, is an important factor regarding balance.

Fall risk

Sixty-two percent of the included subjects fell once or more during the observation period of five months. Among the fallers, there were 42% who sustained an injury as a consequence of a fall.

Brotherton and colleagues found a fall incidence of 75% within one year for persons with an incomplete SCI [5]. Compared to the sample of Brotherton et al, our sample was slightly younger (49.3y vs. 51.6y) and the time since injury was shorter (5.5y vs. 13.6y). Besides the shorter observation period, the smaller risk for falls in our sample corresponded with a greater amount of persons able to walk outdoors (74% vs. 70%). In spite of these differences, the increased risk for falls within the population of patients with SCI who are able to walk was confirmed.

Inter-observer reliability

Similar to the results of previous studies [10, 18, 19, 28-30], we found excellent inter-observer reliability for the individual items, as well as for the total score on the BBS. A number of participants in our study used a walking aid (crutch or walking frame) to perform the BBS. After consulting with the developer of the BBS, the use of such assistive devices was considered as an external help and was rated accordingly.

Methodological issues

In our study, the recording of falls was initially retrospective for one month, followed by prospective collection for an additional four months. The retrospective survey, even though widely used, may be inaccurate due to recall bias [31, 32]. We performed a comparison of the means of month one with the means of months two to four. This analysis showed no significant difference, indicating that the fall re-

cords as a whole can be considered as consistent. The true risk for injurious falls may be underestimated by the fact that the records were based on self-report only.

The circumstances of falls (e.g. time of the day, environment, and activity) were not recorded. This information would have allowed an insight into the mechanisms and circumstances of the fall events. The months where falls have been collected ranged from summer to spring. Weather and seasonal influences may have affected the mobility behavior of the participants. However, there was no correlation between the number of falls and the order of inclusion as a measure of a chronological order.

Bias may have arisen from the fact that we included a convenience sample from a single rehabilitation center rather than a random sample from multiple centers. In addition, the number of participants may be too small since approximately one third achieved maximum scores on the BBS, and hence, the central and lower range of the scale may be underrepresented.

For the reliability analysis there was concern as to whether video recordings would be sufficient for rating all items of the BBS, especially those items where standby support could influence the judging. A review of the results showed that there was a similar concordance among the ratings in all items.

Finally, concern may arise that the measurements were influenced by the fact that the same assessor was engaged in the administration of the test and measures. The lack of blinding pertaining to the fall status could have influenced the administration of the BBS. Patients with a history of falls would likely be scored lower than those who reported no falls.

CONCLUSIONS

The BBS as a measure for mobility in persons with chronic SCI who are able to walk demonstrated excellent inter-rater reliability and correlations with other mobility measures. However, the BBS score was not associated with the number of falls and was not able to discriminate fallers from non-fallers. Nevertheless, this study has revealed that persons with chronic SCI who have the ability to ambulate have a markedly increased incidence for falls and fall-related injuries. For the population with SCI able to walk, further studies are required to identify factors contributing to falls and to analyze the circumstances surrounding the occurrence of falls. These studies will help to create assessments that are able to estimate the risk for falls and to develop preventative measures to reduce this risk.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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CHAPTER 7
Application issues for robotics

Wirz M
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ABSTRACT

This chapter covers the various aspects related to the application of rehabilitation robots. The starting point for developing any novel therapeutic device should be the specific requirements of the users. Users in this case are patients with neurological conditions, but also therapists. Both claim different requirements, which need to be united. Modern neurorehabilitation is grounded in the premise that activity is beneficial. Robots are valuable tools to apply intensive active training in terms of the number of repetitions and task specificity-. The complexity of robotic devices is mainly determined by the residual functions of the patient. In patients with muscular weakness a simple weight support system might be sufficient, whereas in patients with severe paralysis actively driven exoskeletons with multiple degrees of freedom are necessary. Robots must comply with general regulatory and safety standards. Robotic devices have to be adjustable to a wide range of anthropometric properties and to the amount and the characteristics of their impairment. The user-friendliness of the robot's human-machine interface consisting of the mechanical, the control and the feedback interfaces determines whether a device becomes integrated in the rehabilitation program or not. An inherent advantage of the more complex rehabilitation robots is their ability to use angular and force sensor signals for assessment and documentation. These are important to objectively control the course of the training, to legitimate and shape the training and to document progresses or deteriorations. In the future devices which allow the continuation of a robotic therapy at home will further enlarge the range of applications.

INTRODUCTION

This chapter focuses on aspects which need to be considered when technologies are applied to subjects. Technical devices are developed in order to support humans in many ways. Tower cranes are able to lift and manipulate heavy loads. Submarine robots work in an environment which is not compatible with human life. Smart controllers inflate airbags within split seconds in order to protect the driver of a car. There is also a long list of technical devices which have been applied in medicine e.g. infusion pumps, blood pressure measuring devices or electric stimulators for the treatment of pain. One kind of machines is driven by the force of the person using it e.g. strengthening apparatus. These are considered as passive devices. Other systems include electric drives or other actuators e.g. pneumatic devices and can apply supporting, assisting or resistance forces. Such actuated devices are referred to as active systems. Devices can act on their own by means of a controller which follows predefined algorithms e.g. for the surveillance of vital functions such as heart rate monitors. Not only in daily life the technology becomes smarter but also in the field of treatment and rehabilitation. After an accident or a disease highly sophisticated devices are applied. These devices help the human physician to draw meaningful conclusions out of a number of figures or to eliminate muscle trembling during a subtle surgical intervention. The focus of this chapter is set on rehabilitation technologies including robotic devices which became established within the last decade for patients with neurological conditions e.g. spinal cord injury or stroke. These robotic assistive devices enable to start a functional and goal oriented training earlier as compared to the conventional approaches. In addition an intensive application of adequate afferent feedback and a high number of repetitions of functional movements support the rehabilitation of function such as walking or arm use. Robots not just perform movements repeatedly, but they allow the introduction of task variation and provide feedback in order to maintain an adequate level of challenge for the patient. The issues discussed may partially also be valid for other types of rehabilitation and assistive technologies.

The starting point for developing any new device should be the specific requirements of subjects. Subjects in this case are patients with neurological conditions and it is intended that they will profit from a more effective way of training meaning that they achieve their individual goals within a shorter period of time. Subjects are also therapists who, by using robotic devices, experience physical relief and can use assessment systems for quantification of functional improvements which are less prone to subjective influence. Patients and therapists claim different requirements which need to be united in a meaningful way. Those requirements should be in the focus as opposed to technical feasibility which does not always comply with a rehabilitative demand. This may be different if robots are in the de-

velopmental stage. However, the potential clinical application has to be borne in mind throughout the whole developmental process.

Beside the specifications which are framed by patients and therapists there are several technological issues and principles regarding the clinical application of therapeutic robots. Both aspects will be covered in the next sections.

HUMAN ISSUES

Patient

The clinical presentation of a spinal cord injury (SCI) or a stroke comprises motor weakness or complete paresis, complete or partial loss of sensory function and a more or less pronounced derailment of the vegetative functions [1-3]. The latter include lack of bladder and bowel voiding function, lack of blood pressure adaptation as a response to upright position (orthostatic hypotension) etc. Patients in the early stage after such an event generally have a poor condition which needs to recover to a certain extent before intensive rehabilitation can be initiated. Beside the vegetative symptoms patients have a reduced vital capacity which may become evident in upright standing and during exercise. Also in the acute phase after stroke patients stability in terms of circulation, mood and motivation is impaired. Robotic devices should account for those instable situations in such a way that subjects can be evacuated from the device within a short period of time. Fittings must be designed that they can be removed quickly and the whole device must be removable in order to get access to the patient or to transport an unconscious patient from the device without constraints. Patients with SCI have a marked propensity to faint once they are elevated in an upright position. The possibility to position patients horizontally when the blood pressure starts to drop is therefore crucial. After a traumatic SCI the spine becomes instable in most cases. In addition extremity fractures can occur. Rehabilitation therapists have to make sure that the musculoskeletal system is stable enough to tolerate the applied load and forces as it is the case in robotic devices which are used to train walking function. This holds also true in cases where fractures and instabilities have been treated surgically. The partial lack of sensibility has to be taken into account when a patient with a neurological condition is trained. After every training session the spots where forces are exchanged between the robotic device and the patient have to be inspected visually. Any sign of strain must be documented and carefully controlled. Robotic devices enable intensive and long training sessions with a large number of repetitions. Some patients may react to that amount of workload with signs of overload e.g. joint swelling, increased spasticity or pain. In older patients with a known history of osteoporosis the training

intensity has to be set carefully. The repeated stress on bony structures may result in a fatigue fracture.

Patients who experience an impairment of their cognitive function e.g. distorted self-perception might not be able to cooperate with a robotic device. Even though some devices use virtual environments which are very alike the real world and the control of these environments is intuitively patients still require the ability to abstract. In order to completely cope with robotic devices and to make use of the numerous ways of training modalities patients need to have only mild cognitive deficits.

The population experiencing a SCI is becoming older [4]. Patients with stroke are typically of advanced age. These subjects are generally not used to work with new information technologies and may be reluctant to train in a robotic device. Without complete confidence in a training device the success of the intervention gets endangered. It is therefore important that patients are able to acknowledge robotic training as an important component on the way to their maximum possible independence. For future generations who are much more used to computers and robots from their lives before the neurological incident this item might be less an issue.

Therapist

Usually the usage of robotic devices is not a subject in basic physiotherapy training. The reason for that is that the field of rehabilitation robot is growing rapidly and a large number of new devices become developed every year. Different robots are available and to date no standard devices are established. However, the proper use of robotic devices is critical for the success of the training. A sufficient period of time should be scheduled for the instruction of therapists. It is important that every therapist does as many one-to-one trainings under supervision of an expert user as needed until she or he is able to apply the device accurately and safely. It is recommended that in a given institution special safety procedures become defined. It must be ensured that every person who trains with a robotic device has been instructed properly beforehand. The emergency procedures should be trained practically. Liability issues for the case of an accident must be clarified. Some devices are easy to use and a basic instruction is sufficient. However, other devices require extensive training and experience in order to respond to variations and irregularities. It must be evaluated if multiple or only few therapists are assigned to use a device. In the case of a large number of users a single therapist will never become confident with the device. On the other hand when only few staff members know how to run the device experience can be cumulated in a shorter period of time. Additionally knowledge exchange is easier among a smaller group of users. There are also mixed models where an experienced user does the setup for a given patient

during an initial training session. The subsequent trainings will then be performed by a therapist with less specific knowledge, usually the therapist who trains the patient with non-robotic interventions. If required the more experienced colleague provides supervision in that phase. The advantage of such a model is that a therapist who knows a patient from the "conventional" therapy can also perform the robotic training as opposed to a therapist who is skilled using the robot but doesn't know the peculiarity of the patient.

Principles of robotic training

At the current stage robots do not introduce completely new rehabilitation strategies [5]. Robotic devices rather enhance and amend existing approaches. Electromechanical devices can generate and apply greater forces for a longer period of time and follow more precisely predefined trajectories. In addition robots can measure far more accurately and free from subjective perception than human therapists. However, robotic devices usually measure forces only in one plane or degree of freedom. A human therapist is able to perceive forces in acting in multiple directions, in particular rotational forces. There are also approaches where a patient can train on a robotic device at his home without direct supervision of a therapist. In that case patient and therapist are connected through the internet where the therapist can monitor the progress of his patient and adapt the training protocol [6].

The question pertaining to the principles behind robotic training is the question regarding the principles of neurological rehabilitation. In recent years there have been many reports on the principles and strategies on which neurological rehabilitation is based [7-13]. Most reports which have been published regarding this topic relate to the stroke population since this is one of the most common conditions for acquired neurological disability. Nevertheless, from an empiric point of view most of the described principles can be transferred to other groups of patients e.g. SCI, multiple sclerosis or M. Parkinson. One major and persistent principle of neurological rehabilitation is that of Motor Learning [11, 12, 14]. During rehabilitation patients have to relearn motor tasks in order to overcome disability and limitations in the completion of daily activities. These processes are initiated by task specific training which support either true recovery of lesioned areas within damaged neural structures or compensation [11, 15]. Regardless the underlying mechanism the principles of motor learning apply in both cases [12, 16]. These principles comprise among others: task specificity, goal orientation, meaningfulness and most importantly a high amount of practice. Rehabilitation robots allow task specific training early after a neurological incident. For the training of gait function robotic devices are applied which support the patient to perform leg movements during walking. At such an early stage patients cannot stand up independently and are not or only partially able to perform leg movements on their own. Studies have shown that

adequate proprioceptive afferent input is critical for training functional tasks e.g. walking in patients with SCI [17-20]. The reciprocal unloading and loading of the legs as well as hip extension seem to be task specific afferents for the appropriate facilitation of neural structures which are involved in the control of walking.

Also, devices for the training of upper limb functions are most valuable for the rehabilitation. These robots assist patients to follow task specific trajectories. There are upper extremity robots which are designed for the use in a very early stage when the patient still lies in his bed for most of the time [21]. A number of devices work in conjunction with a display on which the patient completes meaningful tasks of daily living within a virtual environment [22]. An advantage of such a training using virtual environment is that patients do not focus on the learning of specific movements itself but on the effects of these movements. This so called external focus is beneficial for the learning of task automatism [23, 24]. Other approaches aim at minimizing the lack of coordination between shoulder and elbow joint during reaching movements [25].

Without the support of electromechanical devices patients won't be able to start these exercises at an early stage or may get exhausted after a short while and little number of repetitions. Compared to the human therapist who might get tired while providing extensive amount of support to patients who are dependent on help for completing task oriented exercises robotic devices allow longer training durations and a higher number of repetitions. Studies have shown that augmented exercise results in an improved outcome [26]. However, it seems not sufficient just to repeat a specific movement or completion of a task. Task variability improves the acquisition of that task [14]. Robotic devices which have been developed so far offer numerous ways to adapt and vary training. The introduction of virtual environments wherein the patients take over control enables multiple ways of tasks and task variation within the same robotic setup. Further possibilities to adapt tasks are the number of degrees of freedom which are under control of the patient. The amount of support to control a given degree of freedom e.g. hip flexion or extension could be adapted according to the patient's abilities. Robots may not only provide assisting forces but in later stages also resisting forces. Increased resistance perpendicular to a defined trajectory help to guide a patient through a desired movement path. The changes of movement velocity entail a different level of challenge. Walking within a robotic device allow dynamic walking at a nearly normal walking speed as opposed to walking within parallel bars or other walking aids where speed is markedly slowed down. Walking speed during training is considered important to warrant further improvements [27].

In order to control movements and for safety reasons robots are equipped with sensors. These sensors measure positions, velocities and accelerations on one hand and torques and forces on the other hand. These signals can be used for a specific feedback for both, patients and therapists. Feedback can be provided using various

cues such as auditory, visual or haptic. Based on the forces patients exert on the machine selected actions occur in the virtual environment e.g. an avatar walks left or right or a virtual hand grasps an object. In such a way robotic devices act as an interface between the real and a virtual world. The raw signals however serve the therapist to survey the level of activity of the patient and to document the progression within a training series. However, to date only little is known how these figures translate to unsupported activities without a robot.

After all it is the skill of the human therapist to integrate various signals and expressions and hence to perceive the actual state of the patient. Based on those findings therapists will shape exercises and set up conditions in a way that patients are challenged and motivated without being overstrained. For therapists and patients robotic devices offer a useful tool to implement the principles of neurological rehabilitation from the very beginning of rehabilitation and to measure and control the progresses.

TECHNICAL ISSUES

Complexity of robotic devices

The main goal of a task-oriented neurorehabilitative training is to enhance neuroplasticity by enabling patients with neurological impairments to perform movements of activities of daily living. A key factor for the success of the training is the number of repetitions and the generation of physiological afferent stimuli [28]. For achieving a meaningful improvement of motor functions by mass practice therapy regimes supportive devices are beneficial and valuable tools. The complexity of these devices is mainly determined by the residual functions of the patient group in the focus. In patients with minor to moderate impairments passive devices may be sufficient to enable the execution of relevant tasks. This is especially true for the upper extremity, where passive devices like the Swedish help arm (also known as Helparm, Swedish Sling, Deltoid Aide or OB Helparm), the Freebal device or the recently commercialized ARMON orthosis (Mircogravity Products BV, Rotterdam, Netherlands) are used to reduce or eliminate the effects of gravity and thereby allowing the user to effectively use his weak muscles for performing functional tasks like eating, drinking or grooming. These devices may also help the patient retain or reestablish important proprioceptive information about the achievable workspace that the impaired limb should be able to reach as recovery progresses. Since the purely passive devices are relatively simple in their construction they are affordable also from the patient her/himself and are easy to use. The main disadvantage of these simple passive devices, which are mainly based on springs or counterweights, is that they basically provide a constant amount of weight reduction regardless of

the position of the extremity. Even in positions of the arm, where less or no support is necessary, the patient is supported. Additionally, the desired movement trajectory cannot be predefined and therefore the user may train a wrong, unphysiological movement pattern. In the worst case the patient cannot complete a desired movement at all. To overcome this limitation passive devices are often used during occupational therapy sessions under supervision of a therapist, who actively support the movements to ensure that a physiological movement trajectory is achieved.

To free therapist from this physically exhausting and mechanistic work of manually guiding the movements and to perform a therapy in a more standardized way active robotic devices with integrated actuators have been introduced. The active components of the robots consist nowadays mainly of electric motors or pneumatically driven actuators in combination with spindles, gears or bowden cables. Within the class of active devices there are technically more simple devices, which are mainly based on an end-effector approach, and complex devices, in which several degrees of freedom (DOF) of several joints are actively driven independently.

The end-effector based systems use dedicated hand grips or footplates and guide the movements of the hand or foot in space [29-31] (Fig. 7.1). Their main advantage is their easy setup since no technical joints of the device has to be aligned with the anatomical joints of the human body. Furthermore they only use one or two drives per extremity to generate a 2D-planar motion. However, the movements originate from the most distal segment of the extremity and therefore – though the kinematic movement pattern looks similar to the physiological situation – the kinetics of the generated movements may not be perfectly physiological [32]. However, this seems to be crucial for the success of the therapy [20]. Additionally, only information about forces and / or position of the most distal part of the Examples of machines based on the end-effector approach for the upper extremity are the MIT Manus [33] approach and for the lower extremity the gait trainer [34] (Fig. 7.1).

A physiological movement of all joints of an extremity can only be achieved by the use of active drives, which support the movements of every DOF of a dedicated joint. Additionally an individualized setup of a joint and movement phase related resistance is only possible with actively driven exoskeletons. Locomotion robots are often constructed as actuated exoskeletons which operate in conjunction with a system for partial body weight unloading and a moving treadmill [35-38]. Since active components form the most expensive parts of a robotic device usually a compromise between costs and functionality in terms of perfectly following a given trajectory has to be made. Therefore robotic locomotion training machines are mainly generating movements in the sagittal plane whereas movements in the frontal or transversal plane are restricted to passive movements.

Figure 7.1 The Gait Trainer GT I assists the patient during gait training using an end-effector-based approach combined with a system for partial unloading of the body weight.

A general challenge of the application of exoskeletons is their proper adjustment and alignment to the anatomical constraints of the different types of joints. Due to their mechanical complexity the exoskeletons are often time-consuming in their initial setup and in everyday applications. Examples for actively driven exoskeletons are the Lokomat and Lopes devices for the lower extremity [18, 19] and the ARMIN and RUPERT device for the upper extremity [39, 40].

Though actively driven exoskeletons represent the state of the art of robotics technology they still leave room for improvement. Most of the systems are operating in an open-loop position control mode, which means that the actively driven joints follow predefined reference trajectories. Hence the patients' movements are supported even during phases where the voluntary force of the patient would be sufficient. In these cases the robotic device does not help, but hinders a patient to perform a movement task. Therefore a closed loop "assist-as-needed" control scheme should be implemented into the active devices to challenge the patient as much as possible and to provide support, when and where it is needed [41]. Special focus should be put on the fact that a physiological movement does not consist of a highly reproductive movement pattern, but contain some variability [42]. Therefore also robotic devices should incorporate a control scheme that does allow for small deviations from the reference trajectory, e.g. like the nonlinear control scheme of the "force fields" implemented in the T-/Pneu-WREX device [43] or an impedance control scheme of the Lokomat [44]. In this way a true cooperative robot-assisted therapy will become reality.

Nevertheless all motor-driven orthotic devices only generate muscle movements in a passive way. However, from the results of pilot studies it may be con-

cluded that an additional activation of muscles by externally applied electrical currents lead to a better outcome [45, 46]. Therefore the combination of Functional Electrical Stimulation and an actively driven exoskeleton may enhance neurorehabilitation in the future. From a technical viewpoint this combinatorial approach causes additional problems since two force generating systems – the muscles and the external drives – contribute to the same movement and appropriate, robust control schemes have to be developed and tested.

However such hybrid systems offer the possibility that not only a training of restricted or lost motor function can be performed, but that the same system can also be used for substitution of permanently lost motor functions [47]. To achieve this functionality novel light-weight drives and multichannel, dry electrode concepts have to be introduced.

Regulatory and safety issues

Robotic training devices and all of their subsystems including software are medical products and therefore have to comply with the International Standard IEC 60601-1, which has become the global benchmark for medical electrical equipment. Compliance with the IEC 60601-1 International Standard and/or the relevant national versions does not equal medical device approval. However, it is a recognized step towards medical device approval in nearly all markets across the world. As a result, many companies view compliance with IEC 60601-1 as a de facto requirement in most markets for product registration, “CE” “UL” “CSA” marking, contract tenders and defense against claims in the event of problems etc. The biggest upgrade in the 3rd edition of the standard published in 2005 [48] is that it requires a manufacturer to have a formal risk management process in place which complies with ISO 14971. The following, not exhaustive list summarizes the most important standards that apply in particular to therapeutic robotic systems.

1. IEC 60601-1-1: Medical electrical equipment, General requirements for basic safety and essential performance;
2. IEC 60601-1-2: Medical electrical equipment, Electromagnetic compatibility;
3. IEC 60601-1-4: Medical electrical equipment; Programmable electrical medical systems;
4. IEC 60601-1-6: Medical electrical equipment, Usability;
5. ISO 13485: Medical devices, quality management system;
6. ISO 14971: Medical devices- application of risk management to medical devices.

In parts also the “ISO 9241: Ergonomics of human-system interaction”, which contains substandards for user-centered design, applies to the design of robotic devices. It has to be emphasized that devices used in clinical applications have not necessarily to be certified. However, if these not certified machines are intended to

be used in human applications then additionally to the application to an ethical committee a special insurance has to be procured, which covers the risks of adverse events caused by the application. By all means a risk analysis according to ISO 14971 is mandatory to obtain ethical approval. Additionally to the safety manufacturers have to prove in a clinical testing that the device is efficient in order to introduce the device in the European and US market. Since therapeutic robots are highly innovative products in most cases no data can be taken from literature, which prove their efficiency. Therefore clinical trials, preferably with a controlled and randomized study design, have to be performed. This fact has to be considered especially by small or medium sized companies, because a proper efficacy study may cause additional costs in the range of the device development before the introduction of the novel device to the market.

Within the framework of the IEC 60601 no dedicated substandard for robotic training devices has yet been introduced. Thus, the potential risks of harming the patient by the robotic training or the device itself has carefully to be considered. In general active orthotic devices inherently bury the risk of causing severe injuries to the musculoskeletal system, e.g. bone fractures, capsule injuries, ruptures of muscle fibers etc. This risk has to be minimized by a joint-related limitation of the maximum torque, which may be generated by the drives. Since a model based estimation of the drives' torques is often not precise enough redundant force or torque sensors have to be foreseen to ensure that the applied forces in every DOF stay in a safe range. In case the reference trajectory cannot be followed with maximum torque the robot may either switch off, halt the movement or limit the applied torque to a safe amount. In case of end-effector based robotic systems only the net force of several joints can be measured, which may lead to false switch off episodes of the machine or in the worst case to a exceeding of safe torque limits.

The most apparent adverse events of robotic devices in particular of active exoskeletons for locomotion training are skin erythema [49]. Though skin erythema are not a life-threatening condition they may severely affect the compliance of the patient since the training may be interrupted a few days to allow for healing. Therefore the main focus of the mechanical design of robotic devices has to be put on the parts that are in direct contact with the patient. It is highly recommendable to avoid the occurrence of shear forces in the orthotic components with direct skin contact by design, in order to minimize the risk for skin erythema in case of misalignment of the human and the machines joint centers.

Depending on the onset of training after a CNS lesion and the cardiovascular status of the patient episodes of presyncopes or syncopes may occur during verticalization for locomotor training. For adequate handling of a patient in this case of a medical emergency safety mechanisms for quick evacuation of an uncooperative patient are necessary.

Despite the automatic deactivation of the device in case of excessive torques several emergency stops or enabling mechanisms have to be foreseen [50]. This will allow to check for attendance of the therapist or to give the patient the opportunity to stop the training on his own will. The latter is especially important if the patient performs the training on his own without supervision of a therapist.

In summary, the best safety concept of a machine is useless, if it does not work properly due to defective mechanical or electrical components. Thus, a highly qualified technical support has to be available to perform regular check-ups and maintenance of the device.

Customization

Human beings vary to a great degree in their anthropometric data like size, weight and body proportions like length or widths of extremities. In order to perform the training in 95% of the population with one device the machine has to be adjustable to a large degree and in many ways. This means that e.g. in a locomotion exoskeleton the length of the shank and thigh, the width of the pelvis and the position of the trunk in all three directions must be adaptable to the individual patient. Also the continuous increase of the Body Mass Index of the population of industrial countries represents a challenge for the level of adaptability of orthotic and robotic devices.

Additionally to the differences in the properties of the body segments the amount of impairment of neurological patients vary to a high degree. This applies not only to individuals within the same patient group but also between different patient groups. For example in incomplete spinal cord injured persons the individual motor deficits may vary between subjects to a high degree ranging from an isolated drop foot on one side to an almost complete loss of motor function in both legs. In stroke survivors an increased spastic muscle tone may restrict the successful application of a robotic training. In traumatic brain injury cognitive restrictions may occur additionally to the physical impairments, which reduce the cooperativeness of the patient to a minimum. All these patient related factors lead to an individualized setup of either the mechanical components of the machine or the training paradigms including feedback modalities. Since a regular therapy session is for personnel resources reasons limited to 45-60minutes every effort has to be made to keep the changeover time at a minimum. In reality it takes one therapist about 5minutes to prepare an end effector-based robotic system to a patient and about 10-15minutes in case of an exoskeleton. A much higher amount of time has to be reserved, when the system is initially been setup.

Ideally a machine would automatically adapt to different patients or does not need any type of adjustment, since technically solutions have been provided which do not need manual interventions. Surprisingly, up to now not a lot of efforts have been made into this direction.

Also the machine has to provide the possibility for setup of a large variety of training paradigms in order to broaden its fields of application. Most importantly the function that is trained has to be the same as the one which should be improved. Recent developments in robotics for the lower extremities take this prerequisite into account and offer the possibility for training of stair climbing [22].

Nevertheless, it has to be kept in mind that practically none of the robotic device is able to generate a fully physiological movement since not every DOF is equipped with an actuator and therefore cannot be controlled independently.

HUMAN-MACHINE INTERFACE

The user interface is a crucial part of a robotic therapy system since it determines to a large degree whether a device is regularly integrated in the rehabilitation program of neurological patients or not. Since the robotic systems are designed by research and development engineers the user interfaces they design tend to be complicated and are not intuitive to understand. This is a general problem of the human machine interface in almost every technical product intended to be operated by users with different technical expertise and non-technical professional background. Therefore the ISO 9241-210 standard, which refers to “Ergonomics of human-system interaction -- Part 210: Human-centered design for interactive systems” may be a good starting point to continuously improve the human-machine interface of a technical system. The ISO 9241-210 standard defines the framework of an iterative approach to involve end users during all stages of development of a product and explicitly includes parts which are important for any type of assistive technology.

It has to be emphasized that in rehabilitation robotics the term “end user” includes therapists as well as patients. Therefore their feedback should be addressed very carefully by developers and implemented into novel designs for increasing the acceptance.

Mechanical interfaces

Special attention must be paid to the mechanical interfaces between robot and patient. At the points where the robot is attached to the patient high forces are transmitted depending on the mode of operation i.e. either a robot assists the performance of movements or applies resistance forces. Force vectors have to be in accordance to the joint axes to allow pure rotational moments. The fixations of the robot have to be soft and mold to fit the respective part of the body in order to prevent the occurrence of pressure lesions or abrasions of the skin. In contrast to that requirement the interfaces must transmit the forces without loss e.g. by deformation or loose fit. This will ensure appropriate monitoring and modeling of the

forces which exert on the patient. This is especially important pertaining to the assessment features of robotic devices. Fixations have to be adaptable to a wide range of anthropometrics. The usage has to be unambiguous and easy. This is of importance in the case when a patient has to be removed from the device quickly.

Control and feedback interfaces

An important component of the robotic system is the control interface, which is used by the therapist to set and adapt the most important therapy parameters like speed, amount of support or range of motion, and the feedback interface, which is used to provide the patient with information about the current status and the progress of the training. The control interface has to provide a very intuitive graphical user interface, which can be handled by an operator during the therapy. Special focus has to be put on the limitation of the number and the selection of an appropriate size of the control elements on the screen or on the operator panel to avoid faulty parameter settings. A general requirement of the robotic device often demanded by therapists is a high degree of "transparency", i.e. all of the machine parameter and options are accessible. However, a balance has to be found between maximal adjustability and easy handling. A possible way to meet both claims could be the common implementation of a standard and an expert mode together with the possibility for individualization of the graphical user interface.

Additionally to the graphical user interface the input device is of crucial importance, since keyboards and mice are not easy to handle while having the patient in the focus, which often results in mismatch of parameter settings. Therefore touch panel based interface systems are a proper choice in particular if the system is operated by a patient without supervision.

Since most of the robotic machines are equipped with sensors, which provide feedback about the current state and performance of the patient, the implementation of an automated adaptation scheme would free the therapist from continuously adjusting the relevant parameters of the therapy. In some cases such an adaptation scheme may allow a robotic therapy without the need for continuous supervision by a therapist. However, in this condition an adequate feedback has to be provided to the therapist and the patient, so that both are informed what the machine is doing and to give them the confidence that both have the machine under control and not vice versa.

At the current stage of knowledge the benefit of any neurorehabilitative approach seems to be based on the enhancement of spinal as well as supraspinal neuroplasticity. In order to enhance the supraspinal neuroplasticity the patient has to be provided with an adequate feedback of his current performance in particular in patients with sensory deficits. This is also most important for increasing motivation. Comparable to the situation in the control interface the number of dynamic

feedback parameters presented to a patient at a time have to be carefully chosen, since a patient is only capable to influence one or two parameters simultaneously. The feedback parameters have to individualized chosen according to the main functional deficit and the most severe impairment respectively. In case of the lower extremities this might be a joint angle of a dedicated gait phase like swing or stance phase. The feedback should be provided in an absolute scale so that patients may be able to compare their current status to the status at the end of the last therapy session. Also feedback modalities other than visual may provide a more effective way to enhance the perception of the patient [51].

ASSESSMENT AND DOCUMENTATION

Rehabilitation robots are not only equipped with motors but also with multiple sensors. The signals deriving from these sensors are used to control the operation of the robots but can also serve as feedback and to measure certain biomechanical properties. Angular sensors can measure range of movement, force or torque transducers voluntary strength of muscle groups (Fig. 7.2).

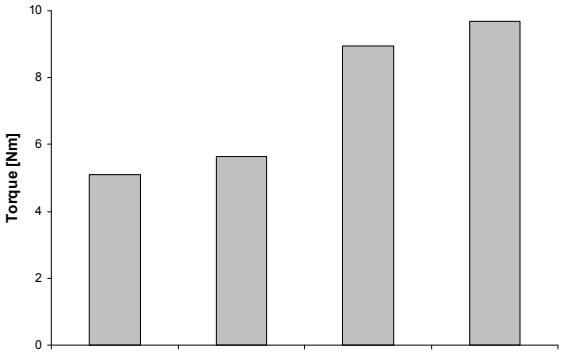

Figure 7.2 Example of a series of force measurements recorded with the Lokomat system. The columns represent the maximum force in direction of unilateral hip flexion during successive sessions from a patient recovering from a Guillain-Barré syndrome (the respective value of healthy volunteer amounts to 74Nm).

Combined signals can assess resistance against passive movements and where in the movement arc resistance occurs. Changes in resistance can be attributed to impaired muscular tone or spasticity. Assessments are important to control the course of the training, to legitimate training and to document progresses or deteriorations. Measurement results can be used to monitor the actual state of the patient and to shape the training accordingly. Some improvements may not be perceived by

the patient but are accessible for the sensors. Prove of gains are important factors to generate motivation [52]. However, for any assessment there are basic requirements which have to be met in order to be useful. Assessments have to be practical, reliable, valid and responsive to changes. The measurement within a robotic device is easy to perform since it can be performed along with training or as a part of the training. Nevertheless the assessment within a robotic device is restricted to that particular situation. E.g. a robot is able to measure the range of motion in the sagittal plane but its mechanical construction does not allow measuring in the other planes. Appropriate software can record and compare the results to previous measurements or normative values. On the first sight it seems obvious that a mechanical sensor has a higher accuracy than a human examiner. A reduction of error leads to increased reliability. Still there are more sources for error e.g. the instruction of the therapist or pain may influence measurements. Few studies pertaining to this issue affirmed feasibility and reliability [53-55]. The concept of validity states that a given testing procedure aims at measuring a specified property. Regarding range of movement and voluntary muscle strength there are no controversies as opposed to the measurement of spasticity. Even widely used tests such as the Manual Ashworth Scale (MAS) are under debate and may be improved if tested using a robot [56].

Although only few studies addressed the issue of the quality of assessment recorded by rehabilitation training robots it can be stated that these devices measure practical and reliable. Appropriate measurements whose results can be transferred into daily functions need to be defined.

CONTINUATION OF A ROBOTIC THERAPY AT HOME

Due to increasing economical restrictions in the health care system the length of primary rehabilitation is getting shorter, i.e. in the US Model Spinal Cord Injury System the mean initial rehabilitation period of incomplete patients was 89 days in 1975, which continuously decreased to 28days in 2005 [57]. It can be expected that this trend will continue in the future and lead to even shorter rehabilitation periods. With the help of robotic locomotion the sufficient intensity of task oriented gait training can be sustained in the clinical setting, whereas a dramatic reduction of the quantity and quality of the training occurs after the discharge from the rehabilitation unit. This is especially true, if patients return to their home in rural areas.

Though systematic experimental investigations are missing, it may be concluded from review of the literature that long-term, mid-intensity locomotion training over several months is more effective than the application of training protocols with high intensity for only a few weeks [58, 59]. However, up to now only a few robotic training devices exist for home based locomotion training. A simple transfer of the existing robotic devices to the patients' homes is not possible since most of them are

mainly restricted to the application in a clinical setting due to their size, weight and price. Furthermore most of the devices have to be operated by skilled therapist.

The main challenges of therapy devices for application in the home environment are safety issues and the self-operation of the device by the users themselves. This is especially true for the use of locomotion training devices. Whereas in the clinical environment the therapy is supervised by trained therapists, in the home environment a safe operation without the need for supervision has to be guaranteed.

Only a few studies exist which describe the development and application of dedicated home based robotic training systems [6, 60]. In locomotion robotics a key method to minimize the risk of injuries is to put the user in a safe training position, like a semi-recumbent position of the body in the MoreGait device (Fig. 7.3).

From the available results of a real home based training it may be concluded that a safe application without a high risk for serious adverse events is feasible and that the outcomes of the training are in the same range than of systems used in clinics.

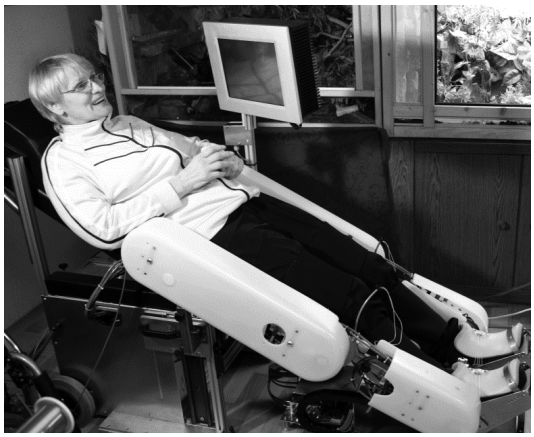

Figure 7.3 The MoreGait is a pneumatically actuated robot for the training of ambulatory function. The device allows the use at the patient's home.

Nevertheless a certain amount of supervision is necessary to assess the current status of the patient, to individually adjust therapy parameters to her/his progress and to help patients in solving small hardware problems. Here internet based telemonitoring methods are a cheap and effective tool for transfer of sensor data and diagnostic trouble codes of the machine to a centralized location e.g. a large rehabilitation center or an outpatient clinic. Personal video conferences between a therapist and users or among different users are very valuable to keep patients motivated and to share experiences.

A very promising way of performing a home based therapy especially in patients with minor motor and cognitive deficits is the use of conventional gaming consoles like Nintendo's Wii or Microsoft's Xbox in particular with the kinect option. The

latter allows for full body movement analysis and therefore a joint specific therapy without the need for dedicated markers or sensor fixed to the body. The main advantage of using such type of technology is the non-limited availability and the low price.

The gaming console based training relies mainly on the feedback principles of the external focus, which beneficial for the learning of task automatism. This form of training is motivating and provides the possibility for giving feedback about the current state of the functional impairment and the improvement over time to the user. However, up to now only a few studies exist, which evaluate the effect of a console-based training [61]. Furthermore it has to be investigated in the future, if the already implemented option for an internet based multiplayer mode may be used for a supervision of a home-based training by a qualified therapist.

Financial aspects

In the long run every novel therapeutic or diagnostic procedure will only become a standard, if a financial benefit for the health care or the welfare system can be achieved. This does not necessarily mean that the novel method has to be inexpensive itself. The maybe most prominent counterexample is MRI, which is a cost intensive diagnostic method, but saves a lot of money by providing the basis for a major improvement in clinical decision making.

The costs for the application of a robotic training are comprised by device's costs, costs for personnel and its training, cost for infrastructural alterations and cost for technical support. The costs of the device are mainly based on its complexity: The more complex, the more expensive. The price of a system is to a large amount dependent on the number of actuators it contains, since not only actuators but also sensors for safety issues have to be foreseen. Most of the people outside the neurorobotics field believe that – like in industrial robots – less personnel is necessary to perform a given therapy regime. This may be true for the lower extremities, where up to three therapists are needed to perform a conventional body weight supported treadmill training. However, this does not apply to upper extremity training settings, where one therapist is necessary to perform a manual training. By any means one therapist is necessary to supervise the robotic training therapy.

The justification for implementing robotic training machines into clinical routine is mainly based on the fact that in the given time frame for primary rehabilitation the patient achieves a higher level of independence by the use of robotic therapies [62], which in turn may save costs for care and prevent secondary complications.

Nevertheless, in most countries the robotic training sessions are not regularly compensated by insurance companies or sickness funds. Here additional efforts are needed in the future from industry as well as from health care providers to give

every patient with a motor disorder the chance to profit from such a type of training.

CONCLUSIONS

For the successful development, application and integration of robotic systems engineers, clinicians and end users have to work closely together. The devices' specifications should be founded on rehabilitative goals and neurophysiological knowledge. The characteristics of robotic devices should comply with the demands of patients and therapists. In order to justify the costs of rehabilitation robots, they should allow the adaptation to a wide range of patients with respect to anthropometrics but also with respect to different grades of capabilities reflecting the actual state of rehabilitation. In the beginning supporting forces are required in later stages a device may apply resisting forces in order to challenge patients appropriately at every level. The setup and operation of robots should fit in a clinical setting. Signals from sensors enable sophisticated feedback modalities and the surveillance of training progression.

Robotic devices are very useful enhancements of rehabilitation interventions by offering additional training as well as measurement options. Studies suggest that an advantage of therapy by robotic devices, compared with conventional therapies, may be an increase in repetitions during training. Robot-assistive training devices therefore allow a massed practice therapy paradigm, which is intensive, frequent and repetitive, and accords with the principles of motor learning. They offer for the first time the possibility to systematically investigate dose-outcome relationships since the variability, the physical constraints of therapists and their limitations in terms of guiding movements of several joints simultaneously can be overcome.

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CHAPTER 8

Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury:

A multicenter trial

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ABSTRACT

*Objective***.** To determine whether automated locomotor training with a driven gait orthosis (DGO) can increase functional mobility in individuals with chronic, motor incomplete spinal cord injury (SCI). *Design*. Repeated assessment of the same patients, or single case experimental design: A-B. *Setting*. Research units of rehabilitation hospitals in Chicago, USA, Heidelberg, Germany, Basel and Zurich, Switzerland. *Participants.* Twenty patients with a chronic (> 2 yrs post injury), motor incomplete SCI, classified by the American Spinal Injury Association (ASIA) Impairment Scale with an ASIA C (n=9) and D (n=11) injury. Most patients were ambulatory prior to locomotor training (n=16). *Intervention.* Locomotor training was provided using robotic-assisted, body weight supported treadmill training (BWSTT) 3-5 times per week over a period of 8 weeks. Single training sessions lasted up to 45 minutes of total walking time, with gait speed between 0.42-.69 m/s and body weight unloading as low as possible (mean=37 ± S.D. 17%). *Main Outcome Measures.* Primary outcome measures included the 10-m walk (10 m), the 6-minute walk (6 min), the Timed Up and Go (TUG), and the Walking Index for Spinal Cord Injury –II (WISCI II) tests. Secondary measures included lower extremity motor scores and spastic motor behaviors to assess their potential contribution to changes in locomotor function. All subjects were tested pre-, mid- and post- training. *Results.* Locomotor training using the DGO elicited significant improvements in the subjects' gait velocity, endurance and performance of functional tasks. No significant changes were observed in the requirement of walking aids, orthoses or external physical assistance. There was no correlation between improvements in walking speed and changes in muscle strength or spastic motor behaviors. *Conclusions.* Intensive locomotor training on a treadmill with the assistance of a DGO results in improved overground walking function.

Keywords. Body-weight supported treadmill training, Paralysis, Locomotion, Physical therapy

INTRODUCTION

In the US alone, over 8000 individuals suffer from a traumatic spinal cord injury (SCI) each year [1-3]. Recent statistics indicate that more than 50% of individuals with SCI have motor incomplete lesions. Approximately half of motor recovery occurs within the first 2 months following initial injury [4-6], with a decreasing rate after 3-6 months, and nearly complete recovery evident 2 years post-injury [7-9]. In patients with an initial motor incomplete SCI, over 75% regain some form of ambulatory function [10].

While conventional rehabilitation programs certainly enhance performance of functional tasks [11], the loss of strength and coordination substantially limits the capacity for overground ambulation training [12, 13]. In the past two decades, body weight supported treadmill training (BWSTT) has been proposed as a useful adjunct to enhance locomotor function following motor incomplete SCI [14]. Such training consists of unloading a portion of a patient's weight above a motorized treadmill using a counterweight-harness system, and providing manual facilitation to assist the patient to perform stepping movements on a treadmill. Use of BWSTT has been shown to improve coordination of electromyographic activity in the lower extremities and postural alignment [13], and allows increased practice of stepping behaviors with diminished or absent supraspinal control [15-17]. The benefits of such training in individuals with incomplete SCI have been reported in several studies over the last decade [18,19] (see recent reviews [20-22]). Specifically, on a cohort of individuals with acute and chronic SCI, Wernig and colleagues demonstrated substantial improvements in functional walking ability following task-specific treadmill training as compared to similar groups who received conventional rehabilitation [18]. While the results from a randomized trial comparing the effectiveness of BWSTT vs. conventional therapy are forthcoming [23], anecdotal reports have confirmed the positive benefits of performing such task-specific training [21, 24, 25].

Despite the potentially positive benefits of BWSTT, its practice in a clinical setting is physically demanding and uncomfortable to those providing assistance. Further, BWSTT can require up to three individuals to facilitate upright posture and normal walking patterns [21]. Concerns that traditional rehabilitation approaches are arduous and labor-intensive have caused many researchers and clinicians to search for alternatives. A computer-controlled, driven (i.e., motorized) gait orthosis (DGO) has recently been developed to provide assisted locomotor training (please see Fig. 8.1). In the place of therapists, the exoskeletal apparatus assists individuals' lower extremities through symmetrical, coordinated trajectories that mimic physiological walking patterns. In combination with body-weight support, the DGO may provide some of the critical sensory cues necessary for generating the appropriate locomotor pattern, as suggested by work in experimental animal models of SCI [26]. Use of such a device in the rehabilitation setting could potentially maximize locomo-

tor function following motor incomplete SCI by increasing the total duration of training and reducing the labor-intensive and costly interventions provided by therapists.

The primary aim of this multi-center study was to examine whether locomotor training using the DGO resulted in improved overground walking function and performance of a multi-functional task in patients with chronic, motor incomplete SCI. In a subpopulation of participants in one setting, we further examined whether locomotor training affected lower extremity motor scores and spastic motor behaviors. Changes in locomotor performance in subjects with SCI following intensive, long-duration gait training using the DGO could establish the therapeutic benefits of automated, task-specific therapy following SCI.

METHODS

The study was carried out in five separate SCI rehabilitation units over a period of two years. The protocol of the study was approved by the local ethics committee (i.e., institutional review board) of each training facility, and all participants were informed and gave written consent.

Subjects

Twenty patients (18 men, 2 women), with a motor incomplete SCI with a neurological lesion level of greater L1 or higher, with the primary neurological insult due to trauma or ischemia, participated in this study (please see Table 8.1 for a description of each patient). Mean age at the time of study enrollment was 40years (range: 16-64years, standard deviation: ±14years). The average interval between SCI and the onset of DGO training was 5.9years (2-17years, ±4.9years; please see Table 8.1). Nine subjects were classified by the American Spinal Injury Association (ASIA) as ASIA C and 11 as ASIA D. Eleven of the subjects presented with tetraplegia and 9 with paraplegia. Sixteen subjects were able to ambulate *at least* 10meters overground with various assistive devices and the assistance of one person, although only four individuals used overground ambulation as their primary mode of locomotion in the community.

Specific inclusion criteria included: greater than 2years since initial SCI; not currently enrolled in physical therapy or other training regimens; and, the ability to maintain their current anti-spastic medication dosage throughout training sessions. Under these conditions, the majority of changes in motor behaviors and functional ability were assumed to be due to the locomotor training provided by the DGO. Additional inclusion criteria consisted of the following: between 16 and 65years old, lower extremity weight bearing (standing and/or walking) as part of typical activities

of daily living; and, medical clearance to participate. Exclusion criteria included: presence of concurrent severe medical illness, unhealed decubiti, existing bladder or other infection, thromboembolic disease, significant osteoporosis (as indicated by history of fractures), severe lower extremity contractures or excessive lower extremity spasticity limiting range of motion or normal kinematics during locomotor training, history of significant obstructive and/or restrictive pulmonary disease, and inability to tolerate 45minutes of standing without orthostasis (i.e., decrease in blood pressure by 20mmHg systolic and 10mmHg diastolic). Size limitations for the DGO included femur length less than 35cm or greater than 47cm, and body weight greater than 150kg.

Table 8.1 Description of the 20 study subjects

Patient No	Sex	Lesion Level/ ASIA Grade	Years Post-SCI	Antispastic Medications
1	M	C6/C	2	60 mg baclofen
2	M	C5/C	4	none
3	M	C5/C	13	none
4	M	C6/D	3	none
5	F	T8/D	4	none
6	M	T10/C	17	none
7	M	T9/C	8	none
8	M	C5/C	2	none
9	M	C7/D	4	30 mg baclofen
10	M	C3/D	3	none
11	F	C3/D	6	none
12	M	L1/D	2	none
13	M	L1/C	6	none
14	M	C5/D	16	none
15	M	T10/D	2	none
16	M	L1/D	2	none
17	M	C5/C	3	160 mg baclofen, 20 mg valium
18	M	T7/D	3	25 mg baclofen, 0.5 clonazepam
19	M	T8/D	3	none
20	M	C7/C	10	none

Note. Subjects had a mean age of 40.5 years (range, 22-64y).
Abbreviations: F, female; M, male

Training paradigm

A detailed description of BWSTT has been published previously [18, 27, 28]. Briefly, training involved unloading a subject over a motorized treadmill using a harness and overhead suspension system, with the amount of unloading adjusted to maximize lower extremity weight bearing while ensuring correct limb kinematics through stance and swing (minimizing excessive knee flexion during stance phase/weight acceptance) [21, 29, 30].

To perform stepping patterns on the treadmill, subjects were assisted by the DGO (Lokomat®, Hocoma AG, Zurich, Switzerland; Fig. 8.1). The DGO is composed of bilateral, exoskeletal leg braces secured to the patient at the level of the pelvis and throughout the lower extremities by adjustable size cuffs attached to the exoskeleton (one cuff at the thigh, two at the shank). Leg lengths were adjusted to align each subject's hip and knee joints to the axes of the exoskeleton. The ankle was secured in a neutral (i.e., 90 degree) position by elastic straps fixated around the metatarsal heads and attached. The pelvis and trunk were secured in place by Velcro® straps attached to backrest.

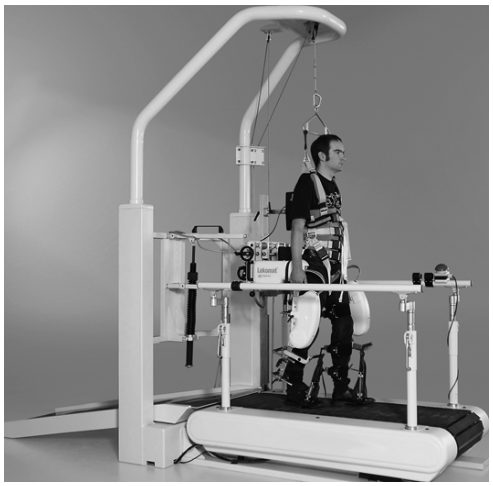

Figure 8.1 The DGO (Lokomat)

The DGO is controlled by computer-programmed DC motors at bilateral hip and knee joints that provide an automated, reciprocal stepping pattern consistent with normal kinematics of human gait [25] and synchronized with the treadmill belt speed [32, 33]. Electromyographic recordings of selected lower extremity muscles measured during DGO-assisted treadmill training are similar to that obtained during manually assisted training in individuals with SCI [34].

Training using the DGO lasted 8weeks, with 3-5training sessions each week as tolerated by the subjects (i.e., subjects typically could not attend >3session/week) . Each training session lasted up to 45minutes of walking time supervised by a licensed therapist or therapist assistant. The amount of body-weight support provided to each patient was adjusted independently, and decreased as tolerated without evidence of excessive knee buckling and toe drag. The speed of training was set at a comfortable level for each subject, and increased as tolerated, up to a maximum of 0.66m/s. The speed of training was limited by the gait pattern of the DGO at higher speeds, by subjective report of fatigue by the subjects, and the comfort level of the subject during training (e.g., increased spastic motor behaviors at higher speeds).

Outcome measures

Primary: Locomotor performance tests were assessed at pre-, mid- and post- training evaluation sessions. All outcome measurements were performed outside of the DGO. The Walking Index for Spinal Cord Injury II (WISCI II) was used to determine subjects' ambulatory capacity by assigning a ordinal measure (range 0-20) with regard to amount of assistance required during ambulation, and use of assistive devices and/or lower extremity bracing [35, 36]. Category 0 indicates that the subject is not able to stand or walk, category 20 indicates that the subject is able to walk at least 10 m without devices, bracing or physical assistance.

Gait speed was assessed using the 10m walk test. Although multiple methods exist to test the 10-m walk test [37-40], walking time was recorded after the subject ambulated 2m, and stopped 2m prior to the finish line to account for potential acceleration and deceleration effects [41]. Subjects were instructed to walk at a comfortable pace over the required distance in a straight line. Patients could use their preferred assistive device including minimal physical assistance as needed. One of the four centers recorded the time required for the subjects to ambulate six meters while the other three centers recorded the time required to walk ten meters. Despite differences in protocol at the separate sites, the measurements remained consistent at each center.

The 6-minute walk test was used to determine gait endurance [42]. Subjects were asked to walk for 6minutes at their self-chosen pace, and were allowed to rest when they felt unable to continue. The total walking distance was recorded. The use of any physical assistance, bracing and/or devices was documented. Each subject used the same assistive device and/or bracing at all evaluation sessions.

The Timed "Up and Go" test (TUG) was performed to assess performance of multiple tasks, including sit to stand transfers, gait speed, and postural stability. In the TUG test, the time required for a subject to rise from a standard height arm chair, walk 3m, return to the chair and sit down has been used as an indicator for individuals at risk for falling [43].

With the exception of the WISCI II, functional ambulation and balance measures are not specific for the population with incomplete SCI. The validity and reliability of these measurements have been assessed in other patient populations, and reflect general measures of ambulatory and functional performance [42-45].

Secondary*:* In a sub-population of the subjects enrolled in the study at one center (n=10; subjects 1-9 and 17 in Table 8.1), we also assessed changes in *lower extremity motor scores* (LEMS) and the magnitude of spastic motor behaviors. For LEMS, manual muscle testing was performed according to the American Spinal Injury Association (ASIA) guidelines [45]. Five key muscle groups of the lower extremities were assessed bilaterally, including the hip flexors, knee extensors, ankle dorsiflexors, great toe extensors, and ankle plantarflexors. Each muscle group was grad-

ed between 0 (no muscle contraction) to 5 (able to withstand maximal resistance) with the maximum score of 50.

For spastic motor behaviors, two types of involuntary movements are often present following SCI. Spasticity, or velocity-dependent resistance to externally imposed, passive muscle stretch, is common in individuals with lesions to descending motor pathways [46]. In distal musculature, this behavior may present as clonus, or periodic (6-8 Hz) muscle bursting with lengthening perturbations [47], although these behaviors can occur in the ankle without substantial changes in the length of the triceps surae [48]. In addition, subjects with SCI often experience "spasms", which are manifested as hyperactive, multi-joint reflexes coexisting with spasticity [49]. In general, spasms are classified as either extensor spasms, distinguished as knee extension with ankle plantarflexion and hip co-contraction [50], or flexor spasms, characterized by ankle and great toe dorsiflexion, with knee and hip flexion [51].

The Ashworth scale was utilized to assess spasticity, in which the involuntary resistance to single-joint passive movement is assigned an ordinal score (0-4) [52] with lower scores representing no spasticity and higher scores indicating increasing resistance to external perturbations. To evaluate spasms and clonus, the recently validated Spinal Cord Assessment Tools for Spasticity (SCATS) [53] was utilized by assigning ordinal score (0-3) describing either the duration or magnitude of spasm activity following specific manual perturbations (Table 8.2). Flexor spasms are elicited by stroking the sole of the foot with the back of reflex hammer (i.e., Babinski test) with a subject in the supine position, and assigning scores according to the degree of great toe/ankle/hip movement observed. Extensor spasms and ankle clonus are determined by spasm duration with subjects in the supine position. Extensor spasms were triggered by passively flexing the knee and hip to 90degrees, then rapidly extending the limb and monitoring the duration of quadriceps contraction. With clonus, the ankle is rapidly dorsiflexed from an initial extended position and held in place, with the therapist determining the duration of clonus bursts. The degree and type of spastic motor behaviors vary across the population of SCI subjects tested, and are not correlated with level, duration or completeness of injury [53]. Scores were determined on each lower extremity with the measurements from the more spastic extremity used for statistical analysis.

Table 8.2 SCATS Rating Scheme

Spasm type	0	1 (Mild)	2 (Moderate)	3 (Severe)
Clonus	NR	1-3 sec	3-10 sec	>10 sec
Extensor	NR	1-3 sec	3-10 sec	>10 sec
Flexor	NR	<10° hip/knee flexion and/or great toe extension	10-30° hip/knee flexion	> 30° hip/knee flexion

Abbreviations: NR, no response

Statistical analysis

Measurements of motor performance and functional abilities were assessed prior to and following 4 and 8weeks of treadmill training. Inclusion of subjects with neurological levels of injury below T11 (3 subjects) and those prescribed anti-spastic medications (4 subjects) presented two potentially confounding factors for enhancing locomotor ability with repeated treadmill training. Statistical analyses were therefore performed using all subjects and following exclusion of the sub-population of subjects described above.

The lack of normally distributed measurements (determined by the Shapiro-Wilk test) required use of non-parametric statistical methods to detect changes in locomotion function and motor impairments throughout training using both ordinal and ratio data. The Friedman ANOVA by ranks and subsequent pair-wise comparisons using the Wilcoxon Signed Ranks tests were performed to assess differences in pre-, mid- and post-training measures, with the family-wise error rate noted at $P<0.017$ to account for multiple comparisons (pre- to mid-, mid- to post-, and pre- to post-training). Statistical analysis was performed for the absolute changes in all clinical measurements. For the 10m, 6min, and TUG tests, the relative changes in performance (percentage change from initial evaluation) were also calculated and reported. Specific relationships between changes observed between the evaluation periods (i.e., between the first 4weeks vs. second 4weeks of training) were determined using the Wilcoxon Ranked Signs Test, with significance also noted at $P<0.05$. Spearman correlation coefficients were calculated to assess for correlations between the initial performance on locomotor and functional assessments vs. changes in performance of these tasks (absolute and relative), and between changes observed in LEMS, Ashworth, and SCATS measurements with functional improvements.

RESULTS

The mean (±S.D) total number of sessions for all subjects was 26±4.3 sessions during the 8weeks (range: 24-37). The average distance ambulated during single training sessions was 1279±282 m (range: 200-1893) at a walking speed of 0.55±0.03 m/s (range: 0.42-0.67). Mean unloading during treadmill training was 37±17% (range: 0-85) of body weight (Fig. 8.2).

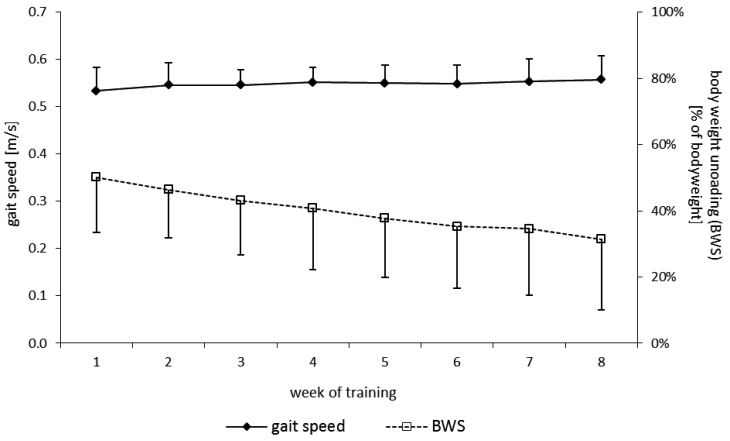

Figure 8.2 Mean training speed and percentage body weight throughout training. Error bars indicate standard error (SE). Abbreviation: BWS, body weight support

Primary outcome measures

Improvements in walking ability as determined by WISCI II scores were observed in only 2 out of 20 subjects. One subject who used two crutches before the training series could walk with only one cane after training, but still required a leg brace (WISCI II score increased from 12 to 15). In another subject, a single straight cane was utilized prior to training, although no assistive devices were required following 8weeks of locomotor therapy (WISCI II score change from 19 to 20). All individuals who were non-ambulatory prior to training did not regain locomotor function. No significant difference was found for the WISCI II (χ^2=3.0; P=0.22) across all ambulatory subjects or following exclusion of subjects prescribed anti-spastic medications or subjects with lesion levels below T11 (all individuals in these latter groups did not change their WISCI II scores).

For overground gait assessments, improvements in speed and endurance were observed in nearly all subjects following locomotor training using the DGO (Fig. 8.3). Using the 10m walk test, there was a significant increase in mean gait speed (0.11±0.10 m/s) following locomotor training (χ^2=20.1; P<0.0001). This change corresponded to a 56±60% improvement over initial, control (pre-training) values. Of the five subjects who, prior to training, were able to walk faster over-ground than the maximal speed of the Lokomat (0.66m/s), three individuals improved in their gait speed post-training. Significant changes across all subjects were observed from pre- to mid-training evaluations (i.e. 0 to 4weeks; P<0.0001), and from mid- to post-training assessments (i.e. 4 to 8weeks; P<0.0001) across the population tested, with no difference observed in the rate of improvement when comparing the initial vs. final 4weeks of training (P=0.79).

Gait speed increased significantly following exclusion of individuals with injury levels below T11 or those prescribed anti-spastic medications. Specifically, the mean increase in gait speed in individuals with lesion levels at or above T11 was .09±0.09 m/s (P<0.001) vs. 0.16±0.12m/s in individuals with lesions below T11. Despite this large relative difference between groups, statistical differences were not calculated due to the small sample size. The average increase in gait speed in individuals not prescribed anti-spastic agents was .09±0.09 m/s (P<0.001), which was also less than in the group of ambulatory subjects prescribed these agents (0.13±0.10 m/s).

Similar results were observed for the 6-min walk test, with 15/16 subjects demonstrating improvements in their walking distance. The mean increase in distance ambulated across the subject population was 32.3m±37.5 (relative increase of 53±50%; χ^2=26.4; P<0.0001). Similar to the 10-m test, significant differences were noted during the initial (P<0.01) and final 4weeks of training (P<0.001), with no difference between the rate of improvements observed during these periods (P=0.46). Significant differences were also noted following exclusion of subjects with lesion levels below T11 (46±39m; P<0.001, vs.37±24 m in subjects with <T11 lesions) and prescribed anti-spastic medications (47±38 m; P<0.001, vs. 30±22m in subjects prescribed agents).

For the TUG test, improvements were observed in all but two of the ambulatory subjects tested. The mean decrease in time to perform the TUG test was 25±30 s (32±19%; χ^2=22.1, P<0.001), with the largest changes observed following the first vs. second 4weeks of training (mean decrease =20±26s, P<0.01 vs. 5±6s, P<0.01, respectively). The difference in the rate of improvements in the performance of the TUG was significantly different (P<0.001), however. Improvements in the TUG were slightly less in individuals with lesion levels >T11 (21±18s) and in those not prescribed anti-spastic medications (24±32s), although the differences were both statistically significant (P<0.001).

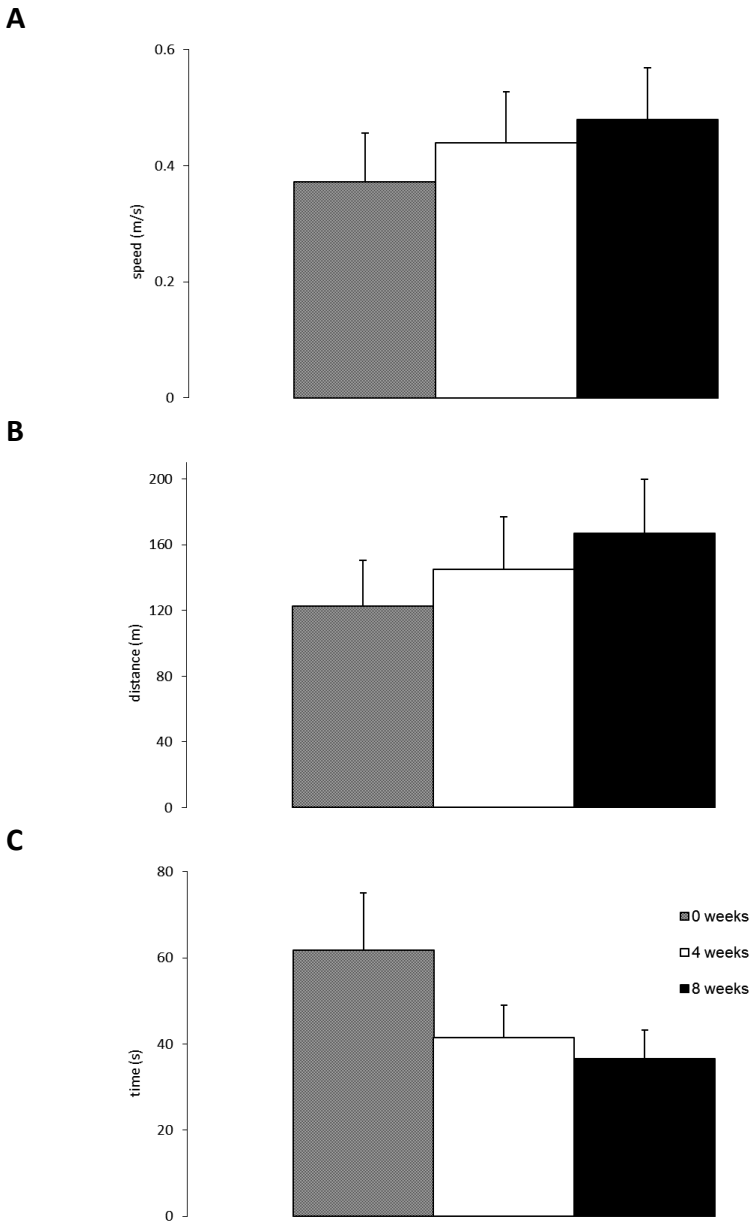

Figure 8.3 Changes in (A) 10MWT, (B) 6MWT, and (C) TUG test before and after 4 and 8 weeks of robotic-assisted locomotor training.
Error bars indicate SE.

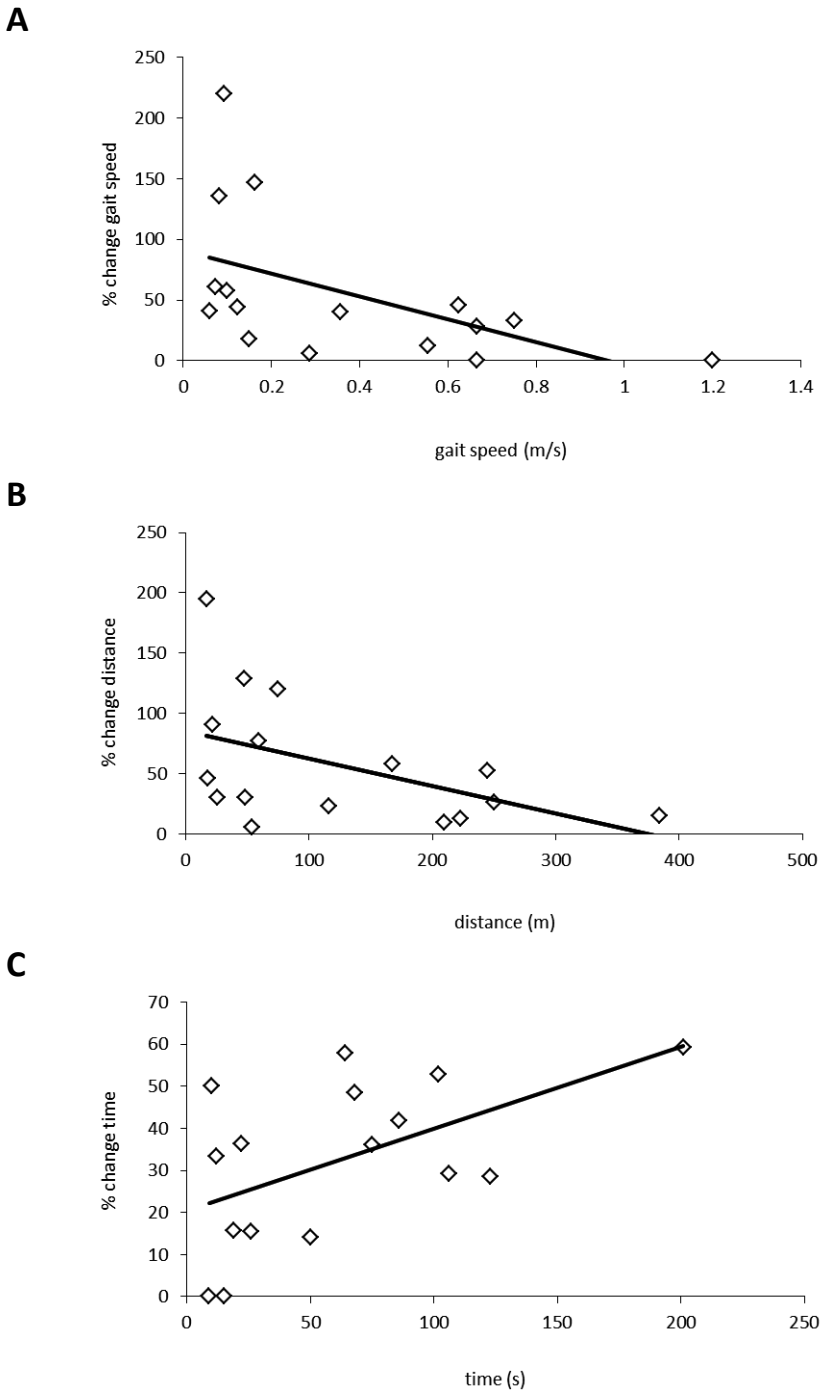

Figure 8.4 Initial versus relative (ie, percentage) changes after locomotor training in (A) 10MWT; (B) 6MWT; and (C) TUG test.

For the observed changes in locomotor ability during the 10-m, 6-min, and TUG tests, significant correlations between the initial pre-training performance and the magnitude of the improvements were observed (Fig. 8.4). As compared to the relative (i.e., percentage) change from the initial value prior to locomotor training, correlation coefficients revealed significant negative relationships for 10m walk (r_s=-0.67, P<0.01) and the 6min walk (r_s=–0.51, P<0.05), indicating that the slower ambulators demonstrated the greatest relative improvement. This was not the case for the TUG as the correlation coefficient only approached significance (r_s=0.44, P=0.08).

Secondary outcome measures

In addition to gait and functional assessments, LEMS and spastic motor behavior tests were performed at only one of the four test centers. For LEMS, the mean improvement in total scores for 10 subjects tested prior to, and the mid-point, and following locomotor training was 2.5 (LEMS initial =32 vs. final =35, n=10; χ^2=13.4, P=0.016), with significant differences observed only between the 4week and 8week assessments. Changes were not specific to any individual muscle groups tested. For nine ambulatory subjects, changes in LEMS were not correlated to the absolute or relative changes in performance on the 10 m walk test, the 6min walk test and TUG, with the lowest coefficient observed for the changes in LEMS vs. relative changes in the 10m walk test (r_s =–0.44, P=0.20). Notably, the correlation is negative, whereas a positive correlation between LEMS and gait speed changes was expected. An example of this relation is shown in Fig. 8.5 for LEMS scores vs. the relative (i.e., percentage) increase in gait speed for the 10-m walk test.

For spastic motor behaviors, we evaluated the involuntary resistance to passive stretch of the quadriceps muscle groups using the Ashworth scale, and assessed clonus, and multi-joint extensor and flexor spasm activity using the SCATS. Averaged scores for each assessment prior to and following 4 and 8weeks of locomotor training are presented in Fig. 8.6. Of these measures, only extensor spasm scores using the SCATS decreased substantially following 8 weeks of training (P<0.01). Changes in all spastic motor assessments were not correlated to changes in relative or absolute measures of the 10-m, 6-min or TUG tests (smallest r_s=0.41; P=0.27).

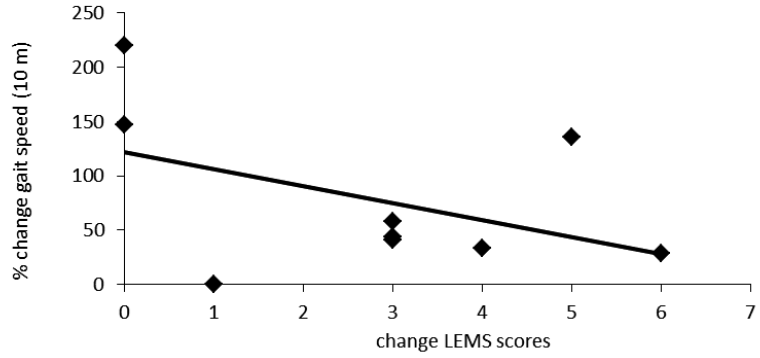

Figure 8.5 Change in LEMS versus change in gait speed after locomotor training.

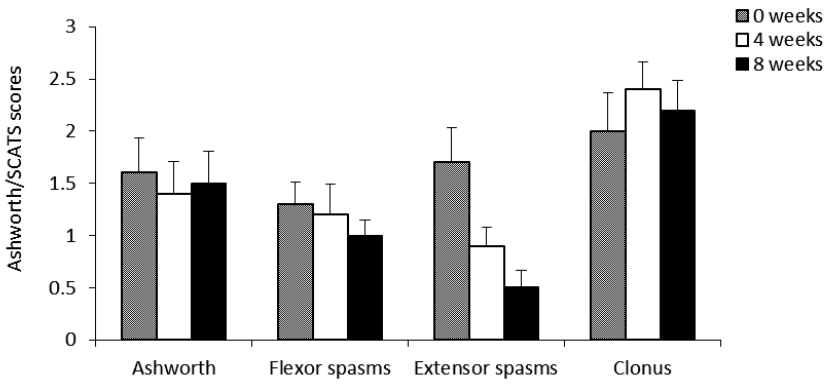

Figure 8.6 Changes in knee extensor Ashworth Scale scores and SCATS scores before and after 4 and 8 weeks of robotic-assisted locomotor training.
Error bars indicate SE.

DISCUSSION

The primary aim of this study was to evaluate whether an intensive locomotor training using a robotic device (DGO) improved ambulatory and functional capabilities of individuals with chronic motor incomplete SCI. The main observations were threefold. First, there were no significant changes in WISCI II scores, indicating the degree of physical assistance, use of assistive devices, and lower extremity bracing. Significant changes were, however, observed in functional limitations, including: a) increased overground gait speed (10-m walk test), b) improved gait endurance (6-min walk test), and, c) decreased time necessary to perform the TUG test. Those ambulatory subjects whose locomotor and functional ability was most impaired experienced the greatest benefit from the training, as demonstrated by higher relative and absolute gains in performance on the standardized assessments. Finally, improvements in LEMS and decreases in specific spastic motor behaviors (i.e., extensor spasms) were observed, but were not correlated to changes observed in walking function. The results of this preliminary assessment of the effects of long-duration, locomotor training using the DGO in combination with BWSTT in subjects with motor incomplete SCI indicate that robotic treadmill training can elicit substantial improvements in overground functional ability.

The role of manual-assisted BWSTT to enhance motor recovery and improve ambulation following neurological injury has been studied intensively for the past 15 years (recently reviewed [54]). Increases in lower extremity motor strength, walking ability and postural stability have been observed in individuals with motor incomplete SCI and stroke in the acute through chronic stages of recovery. Such changes have been compared favorably to conventional rehabilitation [18, 55-57], indicating that task-specific, manual-assisted BWSTT may maximize neurological recovery and gait restoration. One of the primary limitations of such therapy is, however, the labor-intensive efforts required on the part of the therapists. Manual facilitation of the lower extremities and trunk to generate appropriate kinematics associated with stepping behaviors can require substantial effort, especially during training of patients with significant weakness or spastic motor behaviors. As many as three individuals are often required to assist stepping behaviors, thereby limiting the extent to which such therapy can be performed in the clinical setting.

Robotic- and manual-assisted, body weight supported treadmill training are similar in their attempt to practice walking while facilitating kinematically correct stepping patterns. The noted advantage by delivering robotic-assisted training is that specific locomotor interventions can be carried out with the assistance of only one therapist, and can be performed for a longer duration, thereby increasing the amount of practice of stepping behaviors. The results from this study suggest that the improvements in locomotor function in our ambulatory subject population were statistically and functionally significant, with the mean increase in gait speed and

endurance greater than 50% of pre-training values. The improvements in ambulatory subjects were qualitatively similar to those observed in individuals with a similar diagnosis and chronicity of injury whom performed manual-assisted BWSTT [58]. Furthermore, similar to studies investigating the effects of manual-assisted, BWSTT, individuals in the chronic stages of injury who were not ambulatory prior to training did not regain functional, overground ambulation capability after training on the Lokomat® (c.f., [58]). Whether robotic-assisted BWSTT can elicit similar or greater functional improvements as compared to manual-assisted locomotor training or conventional therapy remains to be elucidated in future work.

Five caveats regarding the improvements in locomotor ability following robotic-assisted treadmill training in individuals with chronic SCI should be addressed. First, despite improvements in at least one of the functional gait assessment in all subjects, the extent of recovery was dependent on their initial ambulatory capacity. Specifically, individuals who demonstrated the greatest improvements in gait speed, endurance, and the TUG test were generally most impaired, as determined by the correlation coefficients between initial and relative improvements in functional performance. These results indicate that the locomotor training provided by the DGO may have been insufficient to elicit greater improvements in motor recovery of higher functioning patients, or that recovery in these individuals had maximized their neurological recovery. Indeed, four subjects with SCI ambulated at higher overground gait speeds than the DGO allowed, and demonstrated the smaller relative improvements. Future studies should address the most appropriate selection criteria of subjects for locomotor training using the DGO.

Second, enrollment of subjects with neurological injury levels below T11, or of individuals prescribed anti-spastic medications, presented two confounding factors that may have influenced the results of robotic-assisted training. Damage to lower extremity peripheral nerves (as may occur with lower level injuries) may reduce the conduction of afferent signals to the spinal cord thought to be essential to enhancing spinal plasticity associated with locomotor improvements. Further, various anti-spastic medications have been shown to affect locomotor activity in individuals with SCI [59], and may alter the rate of locomotor recovery with training. The results of this study indicate that the mean improvements in gait speed and endurance or the TUG were not altered considerably following exclusion of subjects with these potentially confounding variables. Indeed, substantial locomotor improvements were demonstrated in all ambulatory subjects with lower level injuries or prescribed anti-spastic agents, although the lower sample size prevents extrapolation to a larger subject population. The rate and extent of improvements in locomotor function in individuals with lower neurological level injuries or prescribed various pharmacological agents that alter motor behaviors certainly requires future investigation.

Third, the assessment of walking ability in the present study demonstrates that the prediction of the improvement in walking capacity in individuals with SCI is lim-

ited if it is only based on the assessment of static motor behaviors, such as voluntary muscle force or spastic motor behaviors, which represent standardized procedure in patients with a SCI [45]. For example, despite previous studies suggesting a relationship between LEMS and overground walking ability [60, 61], there is some evidence to suggest that, following a specific treadmill training intervention, changes in LEMS do not correlate with changes in over-ground walking speed [62], as demonstrated in this study. While the motor score is likely to reflect the spontaneous recovery of corticospinal function [63], the improvement of walking ability also reflects the plasticity of spinal neuronal centers below the level of lesion [15, 16, 64]. Previous evidence suggests enhanced recruitment of lower extremity motor pools during voluntary treadmill stepping or multi-joint movements as compared to voluntary activity generated during single joint movements [64, 65], as assessed during ASIA classification. A comprehensive assessment of SCI patients should include tests which address the functional performance i.e. walking tests, as used in this study.

In addition, spastic motor activity was not significantly altered, except for the observed reduction in multi-joint extensor spasms, characterized by hip co-contraction, knee extension, and ankle plantarflexion to imposed hip and knee extension in the supine position. The changes in functional performance reflect a substantial alteration in voluntary motor activity in the absence of changes in most clinical spasticity measurements. This observation in 10 chronic SCI subjects is inconsistent with data presented in a case report illustrating reduction in spastic motor behaviors in an individual 5years post-injury following patterned neural stimulation, including BWSTT [66].

Further, in the present study, the WISCI II test did not detect changes in ambulatory function, while improvements in other standardized gait or functional assessments demonstrated substantial improvements. The WISCI II test may be less sensitive to changes in specific interventions, or the extent of locomotor training may have been insufficient to generate substantial improvements in the subjects' use of bracing and assistance. The 10-m walk, the 6-min walk and the TUG tests were more sensitive, however, reflecting improvements in nearly all subjects. While these latter tests were primarily developed to assess the mobility of geriatric patients, they nevertheless can reflect the walking and functional ability of ambulatory individuals with SCI. A further study is certainly required to evaluate the validity and reliability of these clinical assessments in patients with incomplete SCI.

Finally, the results of our study indicate that improvements in locomotor ability are evident for a particular subpopulation of subjects tested. While many subjects demonstrate considerable improvements in over-ground walking speed and endurance, the significant correlation between relative changes in ambulation and initial overground walking speed and endurance indicate that the largest gains were observed in the most impaired subjects. Considering the limits of the DGO used in this

study, it is likely that performance of BWSTT without robotic assistance in individuals walking at higher initial over-ground speeds, particularly those who walked at speeds faster than the maximal velocity of the DGO, could elicit greater improvements in speed and endurance. With continued progress in the field of rehabilitation robotics, the development of specific treatment algorithms will be necessary to assist clinicians in deciding which specific physical interventions are most appropriate to help maximize recovery and function in patients with neurological injury.

CONCLUSIONS

The use of task-specific treadmill training with the DGO to improve functional over-ground mobility is promising. Robotic devices that allow practice of BWSTT in the rehabilitation setting may reduce the number of personnel needed to provide such therapy and relieve therapists from the physical demands of the task. Robotic-assisted BWSTT can be further enhanced by increasing the frequency and duration of training. Continued research however, is necessary to advance the development of both specific physical interventions and treatment algorithms to help clinicians decide which physical interventions are most appropriate for patients with specific functional limitations.

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CHAPTER 9

Effectiveness of automated locomotor training in patients with acute incomplete spinal cord injury:

A randomized controlled multicenter trial

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ABSTRACT

Background: A large proportion of patients with spinal cord injury (SCI) regain ambulatory function. However, during the first 3 months most of the patients are not able to walk unsupported. To enable ambulatory training at such an early stage the body weight is partially relieved and the leg movements are assisted by two therapists. A more recent approach is the application of robotic based assistance which allows for longer training duration. From motor learning science and studies including patients with stroke, it is known that training effects depend on the duration of the training. Longer trainings result in a better walking function. The aim of the present study is to evaluate if prolonged robot assisted walking training leads to a better walking outcome in patients with incomplete SCI and whether such training is feasible or has undesirable effects. Methods/Design: Patients from multiple sites with a subacute incomplete SCI and who are not able to walk independently will be randomized to either standard training (3-5 sessions per week, session duration maximum 25 minutes) or an intensive training (3-5 sessions per week, session duration minimum 50 minutes). After 8 weeks of training and 4 months later the walking ability, the occurrence of adverse events and the perceived rate of exertion as well as the patients' impression of change will be compared between groups. Trial registration: This study is registered at clinicaltrials.gov, identifier: NCT01147185.

Keywords. Spinal cord injuries, Walking, Exercise therapy

BACKGROUND

The general prognosis for regaining ambulatory function after a traumatic SCI ranges from 3% in initially complete SCI patients (according to the Standard Classification of the American Spinal Injury Association ASIA A [1]) to 95% in very incomplete lesions (ASIA D) [2]. It is reported that for patients with a motor complete and sensory incomplete SCI (ASIA B) the chance to become ambulatory is 50%. Those subjects with preserved algesia seem to recover to about the same extent as motor incomplete SCI subjects [3].

The basis for locomotor training after acute spinal cord injury (SCI) in humans is provided by animal experiments which showed training induced plasticity of spinal locomotor centers [4]. In humans with a clinically complete spinal injury walking-like EMG activity can be elicited when subjects perform bodyweight supported and assisted stepping on a moving treadmill [5]. In SCI rehabilitation body weight supported treadmill training (BWSTT) has become established within the last 2 decades. In severely affected SCI subjects movements of the patient legs have to be manually assisted by two therapists. In some cases a third therapist might be needed to stabilize the pelvis. The shortcoming of such manual assisted BWSTT is that it is very exhaustive for the therapists and hence only allows for limited training time. In addition the application of movement assistance requires extra skills to maintain coordination between the two legs. In order to provide longer training sessions with a consistent movement pattern robotic gait devices were developed. These driven gait orthoses (DGO) become successively more established to treat individuals with a locomotor dysfunction such as incomplete SCI, stroke or traumatic brain injury [6]. A widely used DGO is the Lokomat (Hocoma AG, Volketswil, Switzerland, Fig. 9.1) [7]. It has been shown that locomotor training with the Lokomat is feasible and that patients with a chronic incomplete SCI could improve gait speed and endurance as a response to an intensive training which lasted 8 weeks [8].

Patients with mild para- or tetraparesis become ambulatory within days or weeks without being trained using special forms of therapy e.g. BWSTT or Lokomat. In contrast, SCI subjects presenting with an incomplete but severe spinal paresis (i.e. ASIA B and C) are referred to an intensive and specific locomotor training by the Lokomat. So far this algorithm is based on expert consensus [9].

The strategy of rehabilitation after SCI or stroke is based on the principles of motor learning. Important characteristics of exercises have been identified. Beside task-specificity, task-variability, feedback or contextual interference the amount of exercise seems to be a key element [10, 11]. The improvement of motor performance within rehabilitation may be due to true recovery or compensation [12]. Nevertheless, the above mentioned principles are valid regardless the underlying mechanism [11].

A meta-analysis including studies of patients with stroke showed that augmented exercise therapy had a favorable effect on activities of daily living [13] and longer training duration was correlated with improved walking performance (positive dose-response relationship) [14]. One of the advantages of robotic devices like the Lokomat is the ability to prolong time for locomotor training compared to manually assisted training [15]. Yet it is not clear whether longer training duration results in an improved outcome or if certain endpoints in terms of walking capacity can be achieved within a shorter period of time.

The aim of the present study is therefore to evaluate whether SCI patients with severe sensory-motor deficit after acute traumatic SCI (ASIA B and C) profit from prolonged Lokomat training compared to patients who undergo the usual training paradigm. The hypothesis is that patients with a severe but incomplete SCI who undergo a prolonged Lokomat training achieve higher grades of walking ability compared to their counterparts who complete the training as suggested by experts. The secondary aim is to evaluate how feasible prolonged locomotor training time is, i.e. whether there is an association between training intensity and adverse events e.g. increased spasticity or pain.

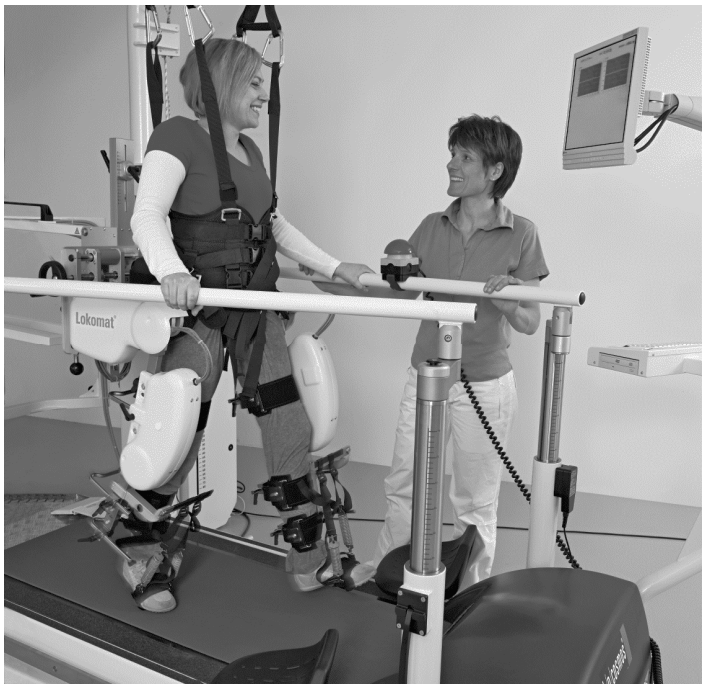

Figure 9.1 The Lokomat is an actuated robotic exoskeleton for the training of ambulatory function on a moving treadmill. The patient is secured by an overhead suspension system which partially reliefs the body weight. Position sensors and force transducers are used to monitor the efforts of the patient (Picture by courtesy of Hocoma AG).

METHODS/DESIGN

The design of the study was developed in accordance with the Consolidated Standards of Reporting Trials (CONSORT statement)[16].

This study will take place at multiple sites (i.e. Zurich/CH (leading center), Barcelona/E, Toledo/E, Heidelberg/D, Murnau/D, Nijmegen/NL and Glasgow/GBR). Local Ethics Committees at each center have approved (Barcelona, Toledo and Zurich) the study. Informed consent will be obtained from all subjects prior to participation. Patients will be included as they are referred to one of the participating centers (consecutive sample).

Subjects

Patients with a subacute traumatic SCI initially categorized as ASIA B or C with a motor level between C4 and T12 and who are only partially able to walk (Walking Index for Spinal Cord Injury-WISCI ≤5 [17]) will be eligible. Subjects should be able to start the training within 60 days after trauma. Patients who do not comply to the requirements of the Lokomat training device (i.e. bodyweight > 130kg, body height > 200cm, leg length diff > 2cm, osteoporosis, instable fracture of lower extremity, restricted range of motion, decubitus ulcer of lower extremity) or with concomitant injury limiting walking ability (e.g. lower extremity fractures, instable spine fractures, Joint instability preventing weight-bearing, severe soft tissue lesion, traumatic brain injury) or with pre-existing medical conditions interfering with unrestricted walking (e.g. total joint replacement, chronic pain, osteoarthritis, polyneuropathy, cardiopulmonary disease) or who are older than 60 years or younger than 18 years will be excluded from participation. Patients who already participate in other rehabilitation or pharmacological study will also not be considered for participation.

In previous studies with stroke subjects [18-23] the mean difference in walking speed amounted to 0.0418m/s. This value was used to calculate the sample size further assuming a standard deviation of 0.05m/s, a statistical power of 0.8 and a significance level of 0.05. The calculation resulted in the requirement of 23 subjects in each group to be able to reject the null hypothesis.

Randomization

Patients will be randomly assigned to either the intervention or the control group using a computer generated 4-block randomization scheme. The allocation will be performed by an independent person not otherwise involved in the study. The responsible researchers at each center request the group allocation by mail.

Intervention

The locomotor training with the Lokomat device should start within approximately 30 days but not later than 60 days after the SCI. The observation period of the training for this study lasts 8 weeks. For the initial 5 trainings there are no defined specifications. These trainings serve to optimize the setup and for the patients to familiarize with the robotic locomotor training device. During subsequent trainings following guideline will be adopted to adjust the training to the actual capacity: body weight unloading will be reduced to the least tolerated amount (no knee buckling or toe dragging). The walking speed will be set within the range of 1.6 to 3.1km/h and the guidance force in the range from 100% (full assistance) to minimum tolerated. The training session will be shaped in the following way: 3 min walking without specification (warm-up period) after that, every 3rd minute either speed, visual feedback or guidance force will be changed. This will avoid that the training becomes monotone and lacks challenge.

Patients who will be assigned to the intervention group receive one or two Lokomat trainings per day on 3-5 days per week. The Lokomat walking time per day should not be shorter than 50min.

Control

Patients of the control group receive one Lokomat training per day on 3-5 days per week. The Lokomat walking time per day should not be longer than 25min.

Outcome

Outcome data will be assessed in the respective centers by therapists and medical doctors. Hereafter the data will be sent anonymously to the PI for analyses. Due to the characteristic of this study neither the therapists nor the assessors nor the patients can reliably be blinded regarding the group allocation. The principal investigator (PI) who is the first author of this report (MW) and will be involved in the analyses will not be aware of the respective intervention.

In order to describe the characteristics of the included subjects, demographic and clinical data will be assessed. The primary outcome is the self selected walking speed using the Ten Meter Walking Test (TMWT) [24]. It will be assessed at baseline, bi-weekly during training, and at the six months follow-up. In addition the following items will be assessed at baseline, bi-weekly during training, and after six months: the Walking index for spinal cord injury -WISCI [17] (an ordinal scaled index for the assessment of walking capabilities with 21 categories. Zero represents that the patient is not able to stand or walk, the maximum of 20 means that the patient can walk without bracing, walking aids or personal assistance), the maximum walking speed, the ASIA classification [1], the detailed Spinal Cord Independence Meas-

ure-SCIM [25], the modified Ashworth scale-MAS [26] of hip and knee joints, and the Penn spasm frequency scale [27]. During the training period the mechanical stiffness and the maximum voluntary torque of the legs as well as the cooperation of the patient during the training will be assessed bi-weekly using the force transducers of the robotic training device. For every training the distance walked, walking speed, walking time and body weight unloading, the rate of perceived exertion as well as the occurrence of any events (e.g. skin breakdown or joint stress or scheduling problems) will be assessed. At the end of the training period, i.e. after 8 weeks the patients subjective impression about the success of the training will be assessed using the Patients' Global Impression of Change Scale-PGIC [28].

Since at the time of the study all patients will undergo a rehabilitation program, they receive along with the Lokomat training the usual rehabilitative therapy (i.e. physio and occupational therapy). In order to assure that the standard rehabilitation program is comparable between the participating centers, therapy schedules of one week will be collected of four patients per center. These schedules should contain the amount of therapy and roughly the content of the therapies (e.g. focus on arm or leg or standing and walking or other activities).

Analyses

All analyses will be performed in the leading center by the PI. He receives the data in form of an electronically completed case record form after completion of the training. For the analyses, the data will then be incorporated into the statistical software (PASW statistics 17.0, IBM-SPSS Inc. Chicago/ IL).

In order to describe the characteristics of the sample, descriptive statistics will be applied.

For the analysis of training induced differences between intervention and control group, T-Test for independent groups or the non-parametric correspondent depending on the outcome variable will be applied. In addition, multilevel models will be used to evaluate potential confounding factors (e.g. center effects, age differences, neurological level of lesion or ASIA) as required.

Competing interests

The authors declare that they have no competing interests.

Authors contribution

MW developed the design of the study and acts as the PI. CB, RdB and VD were all involved in the development of the design. All authors read and approved the final manuscript.

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CHAPTER 10
General discussion

SPINAL CORD INJURY

Heterogeneity

A lesion of the spinal cord results in a complex conglomeration of signs and symptoms. The extent of such a lesion depends on the level of the lesion (it may be of more or less severity and may affect different pathways or structures). Accordingly, patients with an SCI have a wide range of impairment and activity limitations. Additionally, SCIs rarely occur compared to other central nervous system conditions (e.g., stroke). These two factors lead to considerable issues in conducting clinical research studies. The main issue is that an insufficient number of eligible patients can be recruited and included, resulting in underpowered studies. This is of accentuated relevance when certain subgroups of SCI patients should be studied, as we did in our study presented in Chapter 4 [3].

One approach to this problem is to create interventional studies that are not randomized but instead follow a pre-post comparison design. This design may enable the research to show beneficial effects, for example, in our locomotor training study addressed in Chapter 8 [7]. However, this study design does not allow the researcher to attribute the observed changes to a specific intervention since the comparison to a control (unspecific) intervention is lacking.

Another possibility for overcoming a small inclusion rate is to build up networks of rehabilitation centers that treat the same patient groups. Many of the studies included in this thesis [2-4, 8] were or are being conducted within the network of the European Multicenter Study about Spinal Cord Injury (EMSCI). This study follows patients with an SCI over one year. Since its start in 2001, about 1,400 patients have been included and completely documented with comprehensive and valid assessments.

Spontaneous recovery

Within the first six months after an incomplete SCI, patients show marked spontaneous recovery of function [9]. Changes in voluntary motor strength and walking function can be observed [2, 10, 11]. This strong spontaneous recovery influences clinical intervention studies.

The specific effects of a given intervention might be masked because the recovery that is taking place in the sub-acute phase outperforms the changes achieved with a specific training [12]. From a scientific point of view, it would be interesting to deprive a control group of neurorehabilitation since such a design would allow clearer

understanding of a specific rehabilitation measure's effectiveness. However, this sort of study design is impossible for ethical reasons. It is therefore true that clinical studies taking place during primary rehabilitation are diluted not only by spontaneous recovery but also by the routine rehabilitation interventions applied in parallel.

Due to spontaneous recovery, patients with an initially motor incomplete SCI may improve regardless of the rehabilitation measures [13]. Other patients (i.e., those with a complete SCI) experience only limited changes. Further research is needed to discern responders from non-responders to a particular intervention.

AMBULATORY TRAINING

Assisted locomotor training, activation of spinal locomotor centers

Right after the onset of severe forms of incomplete SCI, the neurological deficits are most prominent. This is expressed, for example, by absent or weak voluntary leg muscle activation. During that period, patients are not able to stand and walk without substantial support. Such support is provided in functional training by using body weight unloading systems and the provision of leg movement guidance during the step cycle. As we examined in our study (Chapter 2, [1]), such an assisted locomotor training resulted in coordinated leg muscle EMG activation, even in patients presenting with a clinical and electrophysiological complete SCI (i.e., AIS A). The EMG amplitude increased in response to a series of assisted locomotor trainings. When the training stopped after discharge, the EMG activity decreased in those patients who were not able walk in daily life.

These results support the concept of neural networks within the spinal cord that can be activated by an appropriate proprioceptive sensory afferent input from the periphery, even in the case of a loss of supraspinal input [14]. The background of the concept of spinal locomotor centers derives from numerous animal experiments (for review, see [15]). The modality of the sensory input seems critical for maximally activating the spinal locomotor centers [16]. While the nature of these sensory cues (i.e., loading and hip extension) of the assisted locomotor training are well understood, it is unclear how the intensity of training poses an effect on the outcome. Basic research suggests that higher numbers of repetitions are associated with improved outcome [17-19]. To evaluate the dose-response-relationship of locomotor training, we are conducting the study presented in Chapter 9 [8].

Training-induced neural plasticity

The results of the study from Chapter 2 are in line with the concept of training-induced neural plasticity, which has become a basis for neurorehabilitation (for examples, see [10, 20-23]). This plasticity can exhibit beneficial but also deleterious effects. Learned non-use is a concept introduced in stroke rehabilitation that describes maladaptive neural plasticity as a response to disuse of the affected arm [24]. A similar phenomenon can be observed in patients with SCIs. The non-use of the spinal neural networks involved in locomotion leads to a neural dysfunction expressed by a decreased leg muscle EMG activation (as shown in Chapter 2) and an alteration of the polysynaptic reflex responses [25]. This implies that assisted locomotor training is a useful intervention specifically during the early phase after an SCI and after the resolution of the spinal shock. It is also acknowledged that early after an injury, the central nervous system is in a state of increased plasticity and is therefore more susceptible to targeted rehabilitative interventions [21].

However, in patients with severe incomplete or complete SCIs, the observed leg muscle EMG amplitude during assisted locomotor training cannot be perceived manually and is too weak to lead to a movement. As shown in animal experiments, it is likely that the effects of such training attain a clinically relevant threshold when they are combined with other interventions [21, 26, 27]. An open question remains as to whether an early start of ambulatory training using assisted locomotion results in a better walking-related outcome or whether a certain endpoint is achieved within a shorter rehabilitation period.

Lacking standards

Within the SCI rehabilitation field there is broad acceptance of certain achievable goals [28] and relevant assessments [29]. Surprisingly, there is only limited evidence about how these goals are being achieved. There is no standard content or intensity of rehabilitative measures. Only recently have studies been undertaken to empirically map the currently applied interventions [30, 31]. Further research needs to scrutinize the effect of timing and the intensity of functional training [23].

ROBOTIC DEVICES

Robots have become increasingly common in rehabilitation. The advantages of these technical devices are obvious: robots can assist movements in a controlled way and with a high number of repetitions. The movements resemble everyday activities (e.g., walking) and therefore comply with the premise of task-specificity.

These two characteristics (i.e., high number of repetitions and task-specificity) make robots ideal tools for neurorehabilitation since these elements are recognized to be crucial for achieving improvement of function after CNS damage [19].

Mechanical sensors can measure some features more precisely than humans can and the measured signals serve as a basis for feedback given to the patient and therapist. Virtual reality (e.g., game-like scenarios) can be introduced to keep patients' motivation high. At the same time, parameters and variables related to training and measurement of function can be stored and are available for analysis and documentation.

Finding the correct settings

We are using the Lokomat gait robot (Hocoma Inc., Volketswil/Switzerland) for our research therapy. It was developed at the Laboratory of the Spinal Cord Injury Center of Balgrist University Hospital Zurich/Switzerland. The company was founded as a spin-off and now the device is commercially available. Although the Lokomat can be used in daily clinical routine, it is still at an early stage of development and certain aspects need to be considered for further improvement. The Lokomat is a complex device that requires thorough instruction and experience to apply correctly. Although it is able to measure various parameters, the device itself does not give hints about how to improve the settings.

Control strategy

The movements of the Lokomat are position-controlled (i.e., the joints move through a range of predefined angles). This occurs regardless of whether the patient is active or passive. When patients have impaired proprioception, such a form of imposed walking can help: patients perceive the movement pattern in a tactile-kinesthetic way. However, this control strategy has its limitations in training sessions where the goal is facilitating a patient's activity. When patients feel that their legs are moved for them, they tend to become passive. The Lokomat provides too much assistance. It would be desirable to add a control strategy where the robot supports the patient as needed, meaning that the patient has to perform the initial movement which is then supported by the robot. As soon as the patient became passive, the support would fade away. The result would be that the patient would always be active at a certain level. This level could be set by the patient, the therapist or the controlling computer that constantly determines the optimal level (i.e., a learning system).

No errors

The trajectories of the movements supported by the Lokomat have consistent temporal and spatial characteristics. In the motor control literature (e.g., [32]) it is acknowledged that mastering factors such as gravity, inertial forces or the control of an increasing number of degrees of freedom are critical elements in relearning movement. In general terms, patients need to adapt to errors or the mismatch between intended and performed movement. The robot does not include these elements. Partially this is due to the fact that technical devices used for medical purposes have to comply with strict regulatory and safety requirements. For example, stumbling could certainly encourage the patient to lift his or her foot higher, but it also entails the risk of twisting one's ankle.

Transferring skills

Finally, attention has to be paid to the transfer of skills trained by a robotic device to daily life situations. In our study, which included patients with chronic SCIs [7], we observed two patients who were only able to stand but could not walk, even though the motor scores of their leg muscles were in a range where other patients could walk. We concluded that these patients required extra training to enable them to apply the walking capacity trained by the Lokomat to daily life.

ASSESSMENT

Since traditional SCI rehabilitation is focused mainly on impairment, the clinical measures currently applied include strength and sensitivity [33]. As shown in our study (Chapter 3, [2]), neurological impairment is not in a deterministic relationship with the limitations on performing activities. Thus, all domains (i.e., impairment and activity) must be included in a comprehensive assessment. Tests covering the domain of activities (i.e., the Functional Independence Measure; FIM) are more general and not specific to the SCI population. The spinal cord independence measure (SCIM) [34], introduced in 1997, is an assessment that corresponds to the FIM but is targeted at the particular issues of the SCI population. It also includes a number of items addressing mobility. The description encompasses wheelchair mobility as well as walking mobility. In 2001, the Walking Index for Spinal Cord Injury (WISCI) [35] was published by authors in the USA [35].

Walking Index for Spinal Cord Injury

The WISCI is broadly accepted and increasingly used in the literature. However, we were able to identify some limitations of the measure (Chapter 5, [4]). This study

was possible because it took place within the framework of the EMSCI. With the inclusion of 917 patients in the study, we had a solid basis from which to draw valid conclusions; 71% of the patients could be rated by only five of the 20 WISCI categories.

Timed walking tests

The WISCI scale proved to be less responsive to subtle changes in walking ability [36], so we introduced and validated timed walking tests (i.e., 10meters, 6 minutes walking and timed up-and-go tests) that originated from other patient populations (Chapter 5, [4]). We realized that clear instructions are crucial in maintaining high reliability. This is particularly important within the EMSCI network, where data is collected at multiple sites by many therapists.

The timed walking tests seem to be valid and reliable. However, it is poorly understood how the results of these clinically applied walking tests reflect walking activity during daily life. The environments in the different EMSCI rehabilitation centers are certainly more comparable than the environments in patients' homes. A validation of the tests using activity monitors would add further knowledge.

Identify the fall risk

Studies have shown that patients with SCIs who regain ambulatory function are at a higher risk for falls (Chapter 6, [5]). We intended to validate a widely applied test for fall risk in a sample of SCI patients who were able to ambulate, but the findings showed that the test was not specific for detecting fall risk. Further research is required to find appropriate proxy markers to identify those patients who have an increased risk for falls and fall-related injuries.

CONCLUSIONS

Although SCI is a well-defined disorder, the group of SCI patients is quite heterogeneous. Only the collaboration of several rehabilitation centers enables the performance of valid studies. Ambulatory rehabilitation is an exemplary example of a physiotherapy field that is ripe for a shifting of the underpinning rationale. New knowledge derived from basic research has influenced both interventions and assessments. In the near future, novel strategies aiming to repair human spinal damage will be introduced. It is acknowledged that the effectiveness of these new interventions depends largely on a simultaneously applied functional training. More clinical research is required to more clearly understand how training effects can

further be enhanced. May the combination of training and the application of a new agent lead to improved quality of life for our patients.

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English summary

Deutsche Zusammenfassung

ENGLISH SUMMARY

This dissertation addresses ambulatory rehabilitation in patients with a spinal cord injury (SCI). Topics covered include neurophysiology, assessment of walking capacity and ambulatory training.

Chapter 1 will introduce a background on the spinal cord's anatomy and physiology as well as classification, causes and epidemiological data of SCI. The spinal cord and the brain make up the central nervous system. The spinal cord is involved in the transmission of information between the brain and peripheral organs. In addition, the spinal cord contains its own neural circuitry with the ability to control and generate elementary movements strongly involved in the walking function. These locomotor centers are the focal point of ambulatory training in patients with SCI.

An SCI results in a partial or complete impairment of motor, sensory and autonomic functions. The classification of an SCI is based on a standardized clinical neurological examination (International Standards for Neurological Classification of Spinal Cord Injury- ISNCSCI) and defines the neurological level and the completeness of the SCI. An injury in the cervical spinal cord or the first thoracic segment leads to a *tetraplegia* while lesions below lead to a *paraplegia*. According to the *Impairment Scale* of the American Spinal Injury Association (ASIA) the completeness of the SCI ranges from A (complete SCI) to E (restitution ad integrum). In addition to tetraplegia and paraplegia, special forms of clinical presentations can be found depending on the location and extent of the spinal cord lesion. A SCI can be the result of either a severe trauma or a non-traumatic event. The condition can also be congenital. The most frequent occurring traumatic SCI is an incomplete tetraplegia.

After an acute SCI patients undergo a multidisciplinary rehabilitation whose primary aim is to maximize patients' independence in performing daily life activities and participating in life situations. Lost functions are substituted using compensatory strategies. Preserved functions such as voluntary muscle contraction in the legs are most impaired directly after the onset of the SCI. As a consequence of targeted rehabilitation training and spontaneous recovery processes these deficits become reduced. Ambulatory training is a main focus of physiotherapeutic interventions. With a supported program of ambulatory function training, spinal locomotor centers can be activated even in patients with severe pareses. For this purpose rehabilitation robots are applied. When patients eventually start to regain some voluntary control of their leg movements, the support can gradually be reduced. If during the period of impaired mobility the locomotor system will not be used a secondary worsening by maladaptive plasticity takes place, it may be expressed by a decreased activity of the spinal locomotor centers.

Chapter 2 comprises a study where the long term effects of a locomotor training in patients with incomplete and complete SCI were investigated. Patients underwent a supported ambulatory training on a treadmill. Support consisted of partial body-weight unloading and leg movement assistance. As a result of the training electromyographic (EMG) activity of M. gastrocnemius increased in both groups of patients. In addition, ambulatory capacity was recovered in patients with incomplete SCI. During a period of more than three years after training, the level of leg extensor EMG remained about constant in incomplete SCI in those who regularly maintained locomotor activity. By contrast, the EMG fell in those with complete SCI.

The results suggest a training-induced plasticity of neuronal centers in the isolated spinal cord. Ambulatory training activated these centers. Once the training and non-use of the ambulatory function ceased, activity decreased.

The study in **Chapter 3** includes a longitudinal analysis on the association between neurological deficit (motorscore) and walking function in three patient groups with SCI. Group allocation was based on measurements taken at the beginning of rehabilitation: A, motor complete; B, motor incomplete, non-walking; C, motor incomplete and able to stand. In addition, we performed a cross-sectional analysis evaluating the influence of neurological level of injury on ambulatory capacity in two groups of patients: group 1 with limited walking; and group 2 with unrestricted walking function 6 months after SCI. The analyses revealed that only few patients of group A showed modest recovery of motor and walking function. In contrast we observed in group B that markedly more patients recovered and this to a greater extent. Even more pronounced recovery was observed in all patients of group C. The results showed that in groups B and C, the improvement of walking function was greater than improvements in motor score. The cross-sectional analysis showed that patients with tetraplegia required more muscle strength to achieve an equal walking function compared with patients with paraplegia.

The conclusions of this study are that neurological deficit and walking ability are linearly associated. A combined assessment of both components (i.e. body functions and activities) is important to comprehensively assess the functioning of patients e.g. for the evaluation of the effectiveness of any new interventional therapy.

Chapter 4 contains a retrospective study in which the time-course of neurological deficit (i.e. muscle function); activities (i.e. walking function and daily life activities); impulse conductivity; and rehabilitation length of stay in subjects with central cord syndrome (CCS) and Brown-Séquard syndrome (BSS) were compared. Both syndromes represent a special form of incomplete SCI. In humans the BSS is relatively rare compared to CCS. In basic science, a hemi section of the spinal cord is a frequently used animal model for SCI. In contrast to the assumption of a better out-

come for subjects with BS, no difference was found between the two incomplete SCI groups.

The findings are of interest with respect to the different potential mechanisms leading to a recovery of functions in these two SCI subgroups. This study included two distinct subgroups of SCI patients. The inclusion of a sufficient number of patients was only made possible by the collaboration of multiple SCI rehabilitation centers within the European Multicenter Study about Spinal Cord Injury (EMSCI).

Chapter 5 includes an evaluation of four walking capacity tests for patients with SCI: Walking Index for Spinal Cord Injury (WISCI II), the 6 minute walk test (6MinWT), 10 meter walk test (10MWT) and the timed up and go (TUG) test. We investigated which of the 20 categories of the WISCI II were applied to SCI subjects who participated in the European Multicenter Study of Human Spinal Cord Injury (EM-SCI) and the relationship between the 10MWT and the TUG. The walking tests were applied 2 weeks and 1, 3, 6 and 12 months after SCI. In addition, we compiled positive and negative aspects of the respective walking tests. The analysis showed that only five categories of the WISCI II described 71% of the walking abilities. This indicates that some categories of the WISCI II are redundant, while some discriminate to an insufficient degree. In addition, there appear to be ceiling effects. The 10MWT correlated excellently with the TUG at each time point.

We conclude from this study that the 10MWT appears to be the best tool to assess walking capacity in SCI subjects. Additional valuable information is provided by assessing the needs for walking aids or personal assistance. To ensure that the tests are reliably assessed in the different centers, proposals for standardized instructions are presented.

In **chapter 6** we evaluated a clinical measurement. It assesses the risk for falls in patients with SCI who regained the ability to walk after their rehabilitation. Based on the literature these patients are at an increased risk for falls. If this risk could validly be measured a targeted fall prevention program might reduce future falls. For the study 42 patients were tested using the Berg Balance Scale (BBS). It has been shown that this test is associated with a risk for falls in the elderly. For the evaluation of the validity, the values of the BBS were compared to experienced falls and other variables.

The study revealed that also the included patients experienced an increased number of falls. However, the BBS was unable to discriminate between people who did fall and people who did not fall. Only falls in the past were associated with future falls. The inter-tester reliability which was also addressed in this study proved to be high. The evaluation of the simultaneously assessed fear of falling showed that patients with impaired balance have adapted to their condition and thus behave accordingly.

In **chapter 7** we collected important aspects of the development and implementation of rehabilitation robots. These encompass the needs of patients, users (therapists) and the safe operation. The applications in an institution or at home are discussed. Rehabilitation robots should allow for a targeted training which is based on motor learning principles. Robotic devices have to be adjustable to a wide range of anthropometric properties and to the amount and the characteristics of their impairment. Technical devices allow for longer training sessions. The associated increased training load should not result in adverse events e.g. skin breakdown. The user-friendliness of the robot's human-machine interface consisting of the mechanical, control and feedback interfaces determines whether a device becomes integrated in the rehabilitation program. An inherent advantage of the more complex rehabilitation robots is their ability to use angular and force sensor signals for assessment and documentation. Based on such measurements training parameters can be adjusted to the actual ability of a given patient. In addition these values can be fed back to the patient to encourage his participation.

The collaboration between engineers and experienced clinicians (e.g. physiotherapists) is important for the successful development of rehabilitation robots.

The study presented in **chapter 8** evaluated the effectiveness of a robot assisted ambulatory training in patients with incomplete SCI who were not able or only partially able to walk. Patients were placed in a harness on a treadmill in an upright position with their body weight partially supported. The robot itself comprised an orthosis which was attached to the pelvis and both legs. Drives actuated the hip and knee joints supported leg movements during walking. In this study patients whose SCI occurred at least two years ago were trained. We observed an improved walking ability after eight weeks of training. Patients who were most severely affected profited most.

The study showed that the robot can be used to train and improve walking function even after spontaneous recovery has been completed.

Chapter 9 describes the protocol of a study. Similar to the study in chapter 8 it investigates the effectiveness of a robot assisted ambulatory training. The goal of the study is the evaluation of training intensity in patients with acute incomplete SCI. It is a randomized, controlled, multicenter study design. The trainings of the intervention group last at least 50 minutes while those of the control group last a maximum of 25 minutes. The walking ability after eight weeks of training and the occurrence of adverse events during the training period will be measured and evaluated.

The discussion in **chapter 10** comprises four parts: SCI, ambulatory rehabilitation, rehabilitation robots and assessments. An SCI is a clearly defined syndrome und

occurs rarely. The extent of such a lesion depends on the level of the lesion and may be of more or less severity. Accordingly, patients with an SCI have a wide range of impairment and activity limitations. The collaboration of multiple rehabilitation centers is essential for the conduction of valid studies especially when including certain subgroups. Ambulatory rehabilitation and the application of rehabilitation robots are typical examples of how scientific findings become integrated into clinical applications and, vice versa, physiotherapeutic interventions are subjected to scientific evaluation. The assessment and documentation of functioning and training progress using valid and reliable clinical measurements form the basis of this process.

The results and conclusions arising from the study of the ambulatory rehabilitation may be relevant in the near future when new interventions that elicit (partial) regeneration of damaged nerves are applied in combination with walking training.

DEUTSCHE ZUSAMMENFASSUNG

Diese Dissertation befasst sich mit der Rehabilitation der Gehfähigkeit bei Patienten mit Querschnittlähmung. Sie beinhaltet die Bereiche: neurophysiologischen Grundlagen, das Messen der Gehfähigkeit sowie das Gehtraining selbst.

Kapitel 1 ist die Einführung und vermittelt die Grundlagen für das Thema. Es behandelt Anatomie und Physiologie des Rückenmarks sowie Klassifikation, Ursachen und Epidemiologie der Querschnittlähmung.

Das Rückenmark zählt zusammen mit dem Gehirn zum Zentralnervensystem. Neben der Weiterleitung von Nervenimpulsen zwischen Gehirn und Peripherie können im Rückenmark lokalisierte *Lokomotionszentren*, angeregt durch adäquate afferente Signale, koordinierte Bewegungen erzeugen. Dieses Phänomen ist eine der Grundlagen für das Lokomotionstraining bei Patienten mit inkompletter Querschnittlähmung.

Durch eine Querschnittlähmung werden die Funktionen der Motorik, Sensibilität und des vegetativen Nervensystems teilweise oder vollständig beeinträchtigt. Die Klassifikation der Querschnittlähmung basiert auf einer standardisierten, klinisch-neurologischen Untersuchung (International Standards for Neurological Classfication of Spinal Cord Injury- ISNCSCI) und beinhaltet Ort und Ausmass der Schädigung. Eine Läsion des zervikalen Rückenmarks oder des ersten thorakalen Segments führt zu einer *Tetraplegie*, Verletzungen darunter zu einer *Paraplegie*. Das Ausmass der Rückenmarksverletzung wird gemäss *Impairment Scale* der American Spinal Injury Association (ASIA) unterteilt. Diese Skala reicht von A (komplette Lähmung) bis E (vollständige Erholung). Abhängig vom Ort der Schädigung werden neben Tetraplegie und Paraplegie weitere klinische Syndrome unterschieden. Eine Querschnittlähmung kann durch Unfall oder Krankheit erworben werden, aber auch angeboren sein. Die häufigste Form einer unfallbedingten Querschnittlähmung ist die inkomplette Tetraplegie.

Nach einer Querschnittlähmung werden Patienten einer *multidisziplinären Rehabilitation* zugewiesen. Das Ziel der Rehabilitation ist, dass die Betroffenen ihre möglichst grosse Selbständigkeit und Partizipation wiedererlangen. Verlorene Funktionen werden durch kompensatorische Massnahmen ersetzt. Erhaltene Funktionen, z.B. Willkürmotorik in den Beinen durch gezieltes Training gefördert. Sie sind direkt nach der Querschnittlähmung am stärksten ausgeprägt. Durch Training und spontane Erholungsprozesse bilden sich viele dieser Funktionsdefizite im Verlauf der Rehabilitation wieder zurück. Dabei ist das Training der Gehfähigkeit eines der Schwerpunkte der physiotherapeutischen Interventionen. Die beim Gehen involvierten spinalen Lokomotionszentren können bei Patienten mit ausgeprägten Pare-

sen durch unterstütztes Gehtraining aktiviert werden. Dabei kommen auch Rehabilitationsroboter zum Einsatz. Mit zunehmender Erholung wird die Unterstützung stufenweis abgebaut. Fehlende Reize bzw. fehlendes Training führen im Sinne einer unerwünschten Adaptation zu einer Abnahme der Aktivität dieser Zentren.

In **Kapitel 2** wurden die Langzeiteffekte des Lokomotionstrainings bei Patienten mit inkompletter und kompletter Querschnittlähmung untersucht. Dazu haben die Patienten ein unterstütztes Gehtraining auf einem Laufband durchgeführt und gleichzeitig die Muskelaktivität gemessen. Unterstützt wurde das Training durch teilweise Körpergewichtentlastung und Assistenz der Beinbewegungen. Während des Trainings stieg in beiden Patientengruppen die EMG-Aktivität des M. gastrocnemius medialis an. Patienten mit inkompletter Querschnittlähmung verbesserten gleichzeitig ihre Gehfähigkeit. In den drei Jahren nach Beendigung des Trainings blieb die EMG-Aktivität bei Patienten mit inkompletter Querschnittlähmung, die regelmässig gingen, ungefähr konstant. Im Gegensatz dazu nahm die EMG-Aktivität bei Patienten mit kompletter Querschnittlähmung wieder ab.

Die Resultate deuten auf eine durch das Training ausgelöste Plastizität von neuralen Zentren im isolierten Rückenmark hin. Das Training aktivierte diese Zentren. Nach Beenden des Trainings und Nichtgebrauch der Gehfunktion nahm die Aktivität ab.

Bei der Studie in **Kapitel 3** haben wir mit einem Längsschnitt-Ansatz untersucht, wie neurologisches Defizit (Muskelfunktion) und Gehfähigkeit in drei Gruppen von Patienten mit Querschnittlähmung zusammenhingen. Die Gruppeneinteilung erfolgte aufgrund von Messungen zu Beginn der Rehabilitation. Gruppe A: motorisch komplett; Gruppe B: motorisch inkomplett, nicht stehfähig; Gruppe C: motorisch inkomplett und stehfähig. Zudem untersuchten wir in einer Querschnitt-Analyse den Ein-fluss der neurologischen Läsionshöhe auf die Gehfähigkeit in zwei Patientengruppen: 1. beeinträchtigte- und 2. Nicht beeinträchtigte Gehfähigkeit sechs Monate nach Unfall. Die Resultate der Längsschnitt-Studie zeigten, dass nur wenige Patienten der Gruppe A sich bezogen auf Motorik und Gehfähigkeit gering erholten. Im Gegensatz dazu fanden wir, dass sich in Gruppe B deutlich mehr Patienten und in grösserem Ausmass erholten. Noch deutlichere Erholungen wurden bei allen Patienten der Gruppe C beobachtet. Zudem zeigten die Resultate, dass in den Gruppen B und C die Erholung der Gehfähigkeit grösser war, als die des motorischen Defizits. Die Querschnitt-Analyse zeigte, dass Patienten inkompletter Tetraplegie mehr Kraft in den unteren Extremitäten benötigten, um die gleiche Gehfähigkeit zu erreichen wie Patienten mit Paraplegie.

Die Studie macht deutlich, dass neurologische Defizite und Gehfähigkeit nicht in einer eindeutigen Beziehung zueinander stehen. Die Erfassung beider Komponenten

(d.h. Körperfunktionen und Aktivitäten) ist wichtig, damit die Funktionsfähigkeit, z.B. im Rahmen von Interventionsstudien, ausreichend erfasst wird.

Kapitel 4 beinhaltet eine retrospektive Studie, bei die Verläufe des neurologischen Defizits (Muskelfunktion), der Aktivitäten (Gehfähigkeit und Aktivitäten des täglichen Lebens), der Impulsleitung (somatosensorisch evozierte Potentiale) und der Rehabilitationsdauer zwischen Patienten mit zentromedullärem Syndrom (ZMS) und Brown-Séquard Syndrom (BSS), beides eine Form einer inkompletten Tetraplegie, verglichen wurden. Beim Menschen ist das BSS im Vergleich zum ZMS selten. In der Grundlagenforschung jedoch ist die dem BSS entsprechende spinale Hemisektion ein häufig studiertes Verletzungs-Modell der Querschnittlähmung. Messungen wurden ein und sechs Monate nach dem Ereignis erhoben. Im Widerspruch zur Annahme, dass sich Patienten mit BSS besser erholen würden, unterschied sich keine der gemessenen Variablen zwischen den Gruppen.

Da den beiden Gruppen unterschiedliche Schädigungen zugrunde liegen, ist es wahrscheinlich, dass andere Mechanismen zu den beobachteten Erholungen führten. Diese Studie untersuchte zwei spezifische Patienten-Untergruppen. Eine genügende Anzahl Patienten einschliessen zu können war nur durch die Zusammenarbeit mehrerer Rehabilitationszentren im Rahmen der European Multicenter Study about Spinal Cord Injury (EMSCI) möglich.

Das **Kapitel 5** befasst sich mit den vier klinischen Tests zur Erfassung der Gehfähigkeit von Patienten mit Querschnittlähmung, die im EMSCI Netzwerk standardmässig eingesetzt werden: 1. Walking Index for Spinal Cord Injury II (WISCI II); 2. 6-Minuten Gehtest (6MinWT); 3. 10-Meter Gehtest (10MWT) und 4. Timed-Up-And-Go Test (TUG). Wir untersuchten, welche der 20 Kategorien des WISCI II die Gehfähigkeit der Patienten des EMSCI Netzwerks abbildeten sowie den Zusammenhang zwischen 10MWT und TUG. Die Messungen wurden 2 Wochen sowie 1, 3, 6 und 12 Monate nach Eintritt der Querschnittlähmung erhoben. Zusätzlich wurden positive und kritische Aspekte aller Tests zusammengestellt. Die Analyse zeigte, dass nur fünf Kategorien des WISCI II bereits 71% der Gehfähigkeit beschrieben. Das deutet darauf hin, dass einige der Kategorien redundant sind oder nicht genügend zu unterscheiden vermögen. Ausserdem zeigte sich ein Deckeneffekt. 10MWT und TUG korrelierten zu jedem Zeitpunkt sehr stark. Dieser Zusammenhang änderte sich zwar im Verlauf, blieb aber hoch.

Die Schlussfolgerung dieser Studie ist, dass mit dem 10MWT sowie der Beschreibung der benötigten Gehhilfsmittel und Assistenz durch Hilfspersonen die Gehfähigkeit ausreichend dokumentiert werden kann. Damit die Tests in den verschiedenen Zentren einheitlich durchgeführt werden können, wurde dieses Kapitel mit einer standardisierten Instruktion für die Durchführung ergänzt.

Wie Kapitel 5 befasst sich auch das **Kapitel 6** mit einem klinischen Test. Es ging dabei um die Testung des Sturzrisikos von Patienten mit Querschnittlähmung, die nach Abschluss der Rehabilitation ihre Gehfähigkeit wieder erlangten. Entsprechend anderer Studien haben diese Patienten ein deutlich erhöhtes Sturzrisiko. Wenn dieses gemessen werden könnte, liessen sich künftige Stürze durch geeignete Massnahmen verhindern. Für die Untersuchung wurden 42 Patienten mit der Berg Balance Skala (BBS) getestet. Das ist ein Test, mit dem bei älteren Patienten das Sturzrisiko ermittelt werden kann. Zur Evaluation der Testzuverlässigkeit wurden die BBS-Werte mit den tatsächlichen Stürzen und weiteren Variablen verglichen.

Die Studie zeigte, dass auch die eingeschlossenen Patienten vermehrt stürzten, die BBS dieses Sturzrisiko aber nicht anzuzeigen vermochte. Einzig Stürze in der Vergangenheit waren prädiktiv für künftige Stürze. Die gleichzeitig evaluierte Intertester-Reliabilität war hoch. Messungen der Sturzangst deuteten darauf hin, dass sich Patienten ihres Sturzrisikos bewusst waren und sich entsprechend weniger risiko-reich verhielten.

In **Kapitel 7** werden wichtige Aspekte für die Entwicklung und Einführung von Rehabilitations-Robotern behandelt. Diese betreffen die Bedürfnisse von Patienten und Therapeuten sowie die technische Sicherheit. Es werden Roboter für die Anwendung in einer Institution und zu Hause diskutiert. Rehabilitationsroboter sollen ein gezieltes und den Prinzipien des Motorischen Lernens entsprechendes Training ermöglichen. Dabei müssen die Geräte an die unterschiedlichen Defizite und anthropometrischen Variablen der Patienten angepasst werden können. Das erst durch den Einsatz von Robotern mögliche längere Training darf zu keinen unerwünschten Wirkungen wie z.B. Hautschäden führen. Benutzerfreundlichkeit der mechanischen Elemente und der Steuerungssoftware sind entscheidend dafür, dass die Geräte in die Rehabilitation integriert und regelmässig angewendet werden. Ein Vorteil komplexer Rehabilitationsroboter sind ihre Sensoren, mit denen die Defizite und die Trainingsfortschritte gemessen und dokumentiert werden können. Solche Messungen dienen auch der Anpassung der Trainingsparameter an den jeweils aktuellen Zustand. Zudem können die ermittelten Werte im Sinne eines Feedbacks verwendet werden, um die Motivation fördern.

Die Zusammenarbeit zwischen Ingenieuren und erfahrenen Klinikern (z.B. Physiotherapeuten) ist die Voraussetzung für die erfolgreiche Entwicklung von Rehabilitationsrobotern.

Die Studie in **Kapitel 8** evaluierte die Effektivität eines durch Roboter assistiertes Gehtraining von nicht oder teil-gehfähigen Patienten mit inkompletter Querschnittlähmung. Diese wurden mit Hilfe eines Traggurts in aufrechter Position auf ein Laufband positioniert. Dabei wurde ein Anteil des Körpergewichts entlastet. Der Roboter selbst bestand aus einer Orthese, die an Becken und Beinen des Patienten fixiert

wurde. Motoren an Hüft- und Kniegelenken unterstützten oder übernahmen die Gehbewegungen beim Training. Für die Studie wurden Patienten, deren Querschnittlähmung mindestens zwei Jahre zurücklag, trainiert. Nach acht Wochen Training zeigte sich eine Verbesserung der Gehfähigkeit. Dabei profitierten die Patienten mit den deutlichsten Defiziten am meisten.

Mit der Studie konnte gezeigt werden, dass bei Patienten mit abgeschlossener spontaner Erholung Gehroboter zur Verbesserung einer anfangs stark eingeschränkten Gehfähigkeit eingesetzt werden können.

Das **Kapitel 9** beschreibt das Protokoll einer Studie. Dabei geht es wie in Kapitel 8 um ein durch Roboter unterstütztes Gehtraining für Patienten mit akuter Querschnittlähmung. Das Ziel dieser Untersuchung ist es, den Einfluss der Trainingsintensität bei zu untersuchen. Es handelt sich um eine randomisierte und kontrollierte Multizenter-Studie. Die Patienten der Interventionsgruppe trainieren mindestens 50 Minuten, diejenigen der Kontrollgruppe maximal 25 Minuten. Untersucht wird die Gehfähigkeit nach acht Wochen und das Auftreten von unerwünschten Wirkungen während des Trainings.

Die Diskussion in **Kapitel 10** umfasst vier Teile: Querschnittlähmung, Rehabilitation der Gehfähigkeit, Rehabilitations-Roboter und Assessments. Das Querschnittsyndrom ist eindeutig charakterisiert und kommt selten vor. Neurologische Defizite können in unterschiedlicher Ausprägung auftreten. Entsprechend handelt es sich um eine heterogene Patientengruppe. Für die Durchführung von validen Studien, speziell von Patienten-Untergruppen, hat sich die Zusammenarbeit von mehreren Rehabilitationszentren als unerlässlich herausgestellt. Die Rehabilitation der Gehfähigkeit und die Anwendung von Robotern sind exemplarische Beispiele, wie wissenschaftliche Erkenntnisse in die Therapie einfliessen und umgekehrt physiotherapeutische Interventionen wissenschaftlich evaluiert werden. Die Messung und Dokumentation der Funktionsfähigkeit der Patienten und der Trainingsfortschritte mit validen und reliablen Messinstrumenten ist dabei wichtige Voraussetzung.

Die Erkenntnisse zur Rehabilitation der Gehfähigkeit sind möglicherweise in naher Zukunft relevant, wenn neue Interventionen, die eine (Teil-) Regeneration der Nervenverletzung bewirken, in Kombination mit dem Gehtraining angewendet werden.

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PD. Huub van Hedel PhD, PT used to work as a research physiotherapist and later as the head of 'Paralab' the research department of the spinal cord injury center. We had many common interests and projects and lots of discussions especially on the jogging trails and the following beer with pork knuckle. His direct career showed me that obtaining a PhD was no longer a blurry vision for physiotherapists. Huub I thank you for your inspiring support.

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About the author

CURRICULUM VITAE

Markus Wirz was born in 1967 in Basle, Switzerland. He completed his training as a physiotherapist at the University Hospital Zurich in 1990. In 2008 he gained a Master of Physiotherapy Science at the University of Maastricht/NL.

Markus is appointed head of the physiotherapy ward of the spinal cord injury rehabilitation center 'Zentrum für Paraplegie' at Balgrist University Hospital in Zurich. Beside the clinical work he is involved in research projects focusing on rehabilitative assessments or on evaluating physiotherapeutic interventions e.g. the locomotor training after spinal cord injury.

He was awarded twice with the Sir Ludwig Guttmann prize issued from the 'Deutschsprachige Medizinische Gesellschaft für Paraplegie (DMGP)' in 2002 and 2011. In 2012 he got the PhD-grant of the 'Physiotherapie-Wissenschaften (PTW)' Foundation.

Markus additionally works as a lecturer at the University of Applied Science (zhaw) in Winterthur.

Markus lives with his family close to Zurich.

Memberships

Physioswiss	Schweizer Physiotherapie Verband
ISCoS	International Spinal Cord Society
DMGP	Deutschsprachige Medizinische Gesellschaft für Paraplegie
SAR	Schweizerische Arbeitsgemeinschaft für Rehabilitation
IGPTR-N	Interessengemeinschaft Physiotherapie Neurorehabilitation

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