Rehabilitation of locomotion after spinal cord injury

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Abstract. Advances in our understanding of the control of locomotion enable us to optimize the rehabilitation of patients with a spinal cord injury (SCI). Based on various animal models, it is generally accepted that central pattern generators (CPG) exists for the rhythmic generation of stepping movements, and that this is also the case in humans. However, in humans supraspinal control is also essential for the performance of locomotion. For regaining locomotor function, incomplete SCI subjects strongly depend on visual input to compensate for proprioceptive deficits and impaired balance. In addition, they require additional attentional capacity to stand, walk and handle their walking aids. These factors might contribute to their higher risk of falling. During the last decade, task-specific functional training performed by physiotherapists, combined with manual or robotic assisted bodyweight supported treadmill training have improved the regaining of ambulatory function in patients with incomplete SCI. At present, there is no difference in effectiveness between these three types of training. In the future, rehabilitation programs should be optimized to maximally exploit spontaneous and induced neural plasticity, leading to improved ambulation. To evaluate the efficacy of rehabilitation programs and of experimental treatments that might be translated from bench to bedside within the next few years, several objective assessments such as the 10 meter walk test and Walking Index for Spinal Cord Injury have been successfully introduced in the field of SCI rehabilitation.

Keywords: gait, central pattern generator, motor control, physiotherapy, bodyweight supported treadmill training, gait assessments

1. Introduction

A spinal cord injury (SCI) is a devastating condition that affects motor, sensory and autonomous functions, with the deficits depending on the severity of the injury, the segmental level of the lesion and the sort of nerve fibres that are damaged. Furthermore, the neurological deficit or dysfunction can be temporary or permanent, complete or incomplete. The incidence of SCI is rather small when compared to, for example, stroke (Feigin et al., 2003) and varies between 10.4 (van Asbeck et al., 2000) and 83 (Warren et al., 1995) per million inhabitants per year worldwide (for a review see (Wyndaele and Wyndaele, 2006)). One third of the subjects with SCI suffer from a cervical lesion, i.e. tetraplegia, affecting both upper and lower extremities and about 50% of the subjects are sensory-motor complete (Wyndaele and Wyndaele, 2006). The average age when subjects experience a SCI is 33 years and men are more affected than women (3.8 to 1). Therefore, although incidence is considered low, the personal but also the more general social-economic consequences of spinal cord damage can be severe. In contrast to stroke, where the average age of stroke onset is 70 years in men (Feigin et al., 2003), most of the subjects with SCI are male at the mean productive age and have to work to support their family. They have to increasingly rely on support from the health care system and likely also from social security, perhaps some even for the rest of their lives. Others might have to switch jobs, with or without additional training.

It is therefore an important aim of the health care and research communities to optimize the recovery process of subjects after SCI. The rehabilitation should result

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in a high personal independency and a good quality of life with little socio-economic burden. From the patient’s point of view, the impaired functions that should receive the most attention for becoming restored are bladder and bowel control, and for tetraplegic subjects upper extremity function (Anderson, 2004). Still, independent from the severity of the spinal injury, the time after lesion and age at time of injury, the restoration of walking is given high priority by subjects with SCI (Ditunno et al., 2008b). This already shows that the diversity of problems after a SCI is high and requires a multidisciplinary rehabilitation team that comprises among others of specialized physicians (such as neurologists and neuro-urologists), nurses, occupational and physiotherapists, nutrition specialists and psychologists.

This review provides an overview about the control of locomotion and the mechanisms that underlie improvement in locomotion after a SCI. Furthermore, it presents a short summary of rehabilitation interventions that exploit these mechanisms to improve locomotion, and describes assessments that are used nowadays to evaluate progress in ambulation of subjects with SCI.

### 2. Control of locomotion

The view that a stepping output pattern, whose timing does not depend upon descending or sensory inputs, can be generated in mammals by the intrinsic capability of the spinal cord was first proposed by Thomas Graham Brown (1882–1965) (see Stuart and Hultborn, 2008)). Brown performed experiments in the cat and guinea pig and proposed mutually inhibitory connections between a pair of intrinsically active flexor and extensor “half-centres” on each side of the spinal cord. This rhythmic output is modulated by sensory proprioceptive input, of which especially the information from hip joint and load receptors appears to be important (Dietz et al., 2002; Dietz and Duysens, 2000). Although the models for the central pattern generator (CPG) have become more complex over time, most of them still include a half-centre component.

The CPG is composed of interneuronal circuits (interneurons and possibly motoneurons), whose combined operation produces the fundamental spatio-temporal patterns. These patterns are present at birth and underlie a wide variety of rhythmic movements including various forms of locomotion. Brain centres can initiate CPG activity, which then becomes modulated by sensory input from the periphery. However, these actions do not control the fundamental CPG rhythmicity. In addition, the central nervous system can select/inhibit for a certain task and context the appropriate proprioceptive reflex, as the CPG can open/close reflex pathways in a context and task-dependent manner.

Several observations indicate that the CPG is also involved in locomotion in humans (see e.g. (Dietz et al., 1995; Duysens and Van de Crommert, 1998)). These observations include: (i) neonatal stepping (Forssberg, 1985) and prenatal coordinated whole body movements (Rayburn, 1995), (ii) the similarity in spinal networks underlying locomotion as evoked by the stimulation of flexor reflex afferents in motor complete SCI (Roby-Brami and Bussel, 1987), (iii) rhythmic movements in motor complete SCI subjects, such as observed in sleep related leg movements (e.g. (Lee et al., 1996)) and (iv) coordinated leg movements observed after spinal cord stimulation (Rosenfeld et al., 1995) and vibration-induced air stepping (Selionov et al., 1997) in motor complete SCI subjects.

However, especially in humans, supraspinal input is required for walking. Both the CPG and the reflex mechanisms that mediate afferent input to the spinal cord are under the control of the brainstem (see e.g. (Dietz, 2003)), as specific centres in the brainstem can trigger locomotion. In the cat, it was shown that substances mimicking the action of long descending pathways such as clonidine resulted in distinct and consistent alternating bursts of electromyographic activity inducing spinal stepping (Edgerton et al., 1992). In humans, imaging techniques showed that during locomotion, specific parts of the cortex (bilaterally the medial primary sensory-motor cortices and the supplementary motor areas) become activated (Miyai et al., 2001). The size of the activated areas corresponds to the speed the subjects walk at (Suzuki et al., 2004). Furthermore, for safe locomotion, cortical input might play a more prominent role when adjustments of the locomotor pattern are required to meet certain environmental demands. For example, when stepping over an obstacle, the cortical control of the swing trajectory becomes enlarged as compared to normal stepping (Schubert et al., 1999).

Although human gait for a large part is controlled by supraspinal centres, the amount of descending fibres required to perform simple stepping movements might be as little as 25% of the lateral or ventral white matter, as studied in non-human primates (reviewed in (Dobkin and Havton, 2004)). This finding increases the probability that, in the near future, experimental interventions that might be able to regenerate a (small) propor-
tion of damaged descending axons could result in an improved stepping capacity in SCI subjects (Rossignol et al., 2007).

However, recent studies indicated that in the chronic isolated spinal cord an exhaustion of motoneurons occurs during assisted locomotion (Dietz and Muller, 2004). During automated bodyweight supported treadmill training (BWSTT) in chronic SCI subjects, a strong reduction in electromyographic (EMG) activity, especially in the flexor muscles, can be observed during the first ten minutes of assisted walking. If in the future regeneration of spinal tract fibres becomes feasible in patients with complete SCI, such an approach can only become functionally successful if neuronal activity below the level of the lesion is maintained. Therefore, studies that assess how to prevent or even reverse this situation of degraded motor neuron activation are required.

3. Ambulation after incomplete SCI

The percentage of subjects who regain some walking capacity depends strongly on the extent of the spinal cord lesion. In a previous report, only 3% of those initially diagnosed as having a sensory-motor complete lesion (according to the American Spinal Injury Association (ASIA) classified as ASIA A) regained some ambulatory function. (Consortium for Spinal Cord Medicine, 1999). In patients with a motor complete but sensory incomplete lesion (ASIA B) about 50% regained ambulation and intact pain sensation was a good predictor for achieving ambulatory function. Seventy-five percent of those with a sensory-motor incomplete lesion and little muscle strength (ASIA C) achieved some walking ability (dependent on age), while almost all with little impairment (ASIA D) relearned to walk (95%). In a more recent study, only 35% of the ASIA B, but as much as 92% of the ASIA C subjects and all ASIA D subjects regained walking ability after an 8 week training intervention consisting of BWSTT and/or task-specific physiotherapy (Dobkin, 2006). Apparently, better acute medical care and rehabilitation standards have resulted in improved recovery of ambulatory function. However, only rarely, do these patients achieve a similar level of ambulatory function as healthy subjects. In general, subjects walk slower and many of them depend on the use of walking aids (see Fig. 1; (van Hedel et al., 2007; van Hedel et al., 2005b; van Hedel and Dietz, 2009; van Hedel, 2009); see also Ditunno et al. (Ditunno et al., 2007; Ditunno and Ditunno Jr, 2001; Ditunno et al., 2000)). SCI subjects with walking ability can adapt gait speed, but only within a limited range and they have difficulties in increasing stride frequency (Pepin et al., 2003). Furthermore, they use different kinematic strategies when stepping over obstacles (Ladouceur et al., 2003) or walking uphill (Leroux et al., 1999).

Compared to healthy subjects, subjects with SCI walk with a higher attentional demand (Lajoie et al., 1999), especially when handling walking aids (Wright and Kemp, 1992). Furthermore, they are more dependent on visual input for high-precision adaptive locomotor tasks (van Hedel et al., 2005a), which might be explained by an impaired proprioception in many subjects with SCI. Many of these factors, as well as decreased trunk and leg muscle strength, loss of balance and hazards in the environment are likely to contribute to the increased risk of falling as observed in SCI subjects (i.e. 75%), which is about twice the risk as for healthy elderly subjects (Brotherton et al., 2007).

4. Mechanisms contributing to improved locomotion

After a SCI, and especially after an incomplete SCI, several mechanisms are responsible for the improvement in function observed during (and after) rehabilitation (see also (Curt et al., 2008)). Neural plasticity, a rather broad range of changes in neural connections that can occur either spontaneously and/or be induced after an iSCI, is assumed to play a role in the recovery of locomotion (Barbeau et al., 2002). An example of spontaneous neural plasticity is the cortical reorganization that can be observed after SCI (Ding et al., 2005). This reorganization takes place even for cortical areas reflecting body segments not affected by the SCI (Bruehlmeier et al., 1998) and can continue over the first year after SCI (Jurkiewicz et al., 2007). As well as occurring spontaneously, neural plasticity can also be induced, as is the case for motor learning (see e.g. (Moucha and Kilgard, 2006)). Neural plasticity occurs not only at cortical sites but also at the brainstem and spinal cord sites. The relatively strong improvement in function that can be observed within the first few hours after a SCI could be attributed to neuroplastic phenomena, such as the unmasking of latent synapses (Ding et al., 2005). An improvement in locomotor function, without a corresponding improvement in neurological deficit, might be caused by task-specific training of the CPG within the spinal cord (Curt et al.,
Fig. 1. Recovery of ambulation and mobility after spinal cord injury, adapted from (van Hedel and Dietz, 2009). Box and whisker plots showing the course of A, preferred walking speed (derived from the 10 meter walk test) and B, the outdoor mobility item of the revised Spinal Cord Independence Measure (SCIM II) for ASIA A, B, C and D subjects separately. Outdoor mobility (> 100 meters) is scored as: 0. Requires total assistance; 1. Needs an electric wheelchair or partial assistance to operate manual wheelchair; 2. Moves independently in a manual wheelchair; 3. Requires supervision while walking (with or without devices); 4. Walks with a walking frame or crutches (swing); 5. Walks with crutches or two canes (reciprocal walking); 6. Walks with one cane; 7. Needs leg orthosis only; 8. Walks without aid (see (Catz et al., 2001)). Stars indicate: * $P \leq 0.0125$; ** $P \leq 0.01$; *** $P \leq 0.001$. Please note, significant improvement could be observed without a change in median score, as outliers are not shown in this figure. Abbreviations: ASIA, American Spinal Injury Association; N, number of observations.
Furthermore, peripheral nerve sprouting has been described for partially denervated muscles of the upper extremity (Thomas et al., 1997). If peripheral sprouting occurs also in lower extremity muscles, this might partially explain the improvement in leg muscle strength that occurs within the first year after SCI (van Hedel et al., 2007; van Hedel et al., 2006).

Leg muscle strength of paretic muscles could also increase due to strength training (Hicks et al., 2003) resulting in muscle hypertrophy and an improved coordination between leg muscle groups. However, an improvement in leg muscle strength does not necessarily result in improved locomotion and vice versa (Wirz et al., 2006). Nevertheless, there is a relationship between lower extremity strength and gait capacity (Wirz et al., 2006; Kim et al., 2004).

Compensation refers to a change in function without an accompanying change in the neurological deficit, for example by adapting existing movement strategies or by adopting new strategies, as well as the use of aids. Especially at early phases, walking capacity strongly depends on walking aids for support. While many ASIA D subjects can walk without any aids or assistance after 6 months, ASIA C subjects often depend on walking aids, even in a more chronic phase (van Hedel et al., 2007; van Hedel et al., 2006; van Hedel et al., 2008). Finally, regeneration and neural repair of the central cord system is unlikely to spontaneously occur, as there are no large changes in spinal tract impulse conductivity, as for example assessed by motor evoked potentials (MEPs; Curt et al., 2008; Smith et al., 2000)). However, an increase in MEP amplitude has been observed both in acute incomplete SCI subjects during rehabilitation (Curt et al., 2008; Wirth et al., 2008), as well as in chronic iSCI patients undergoing BWSTT (Thomas and Gorassini, 2005). Although the exact relevance of the MEP amplitude is unclear, it might indicate an improved synchronisation of spinal motoneuron activity, indicating an improved corticospinal control of lower extremity functionality.

5. Training interventions for improving walking

Several interventions aim to exploit the previously described mechanisms to optimize ambulatory function in subjects with SCI. In this paragraph, we briefly describe the most commonly applied interventions such as task-specific physiotherapy and manual or robotic supported BWSTT (Fig. 2). This section does not provide a comprehensive overview. For this, we would like to refer the reader to (Lam et al., 2008b).

In subjects with SCI and some walking ability, the main limitation of over-ground ambulation is usually a reduced coordination, leg paresis, and impaired balance (Dietz et al., 1995). In the early phase of rehabilitation, physiotherapists work on these limitations and provide support in standing (for example, through the use of braces and tilt tables). If leg and trunk strength improves, the physiotherapist(s) apply braces or use parallel bars or other walking aids to improve balance and
weight-bearing during stance. The swing phase can be facilitated manually by the physiotherapist, but also by applying functional electrical stimulation (FES), for example by stimulating the peroneal nerve inducing a flexion withdrawal reflex (e.g. (Popovic and Keller, 2005)). In case of a drop foot, FES can also be usefully applied to activate the tibial anterior muscle during the swing phase, thereby increasing foot clearance and preventing stumbling (Popovic and Keller, 2005).

Currently, there are no generally accepted guidelines concerning the contents of a physiotherapeutic task-specific program aimed at improving gait. In a randomized trial (Dobkin et al., 2006), a therapeutic session consisted of 10 minutes of stretching exercises followed by 30 to 45 minutes of standing for those subjects who could not take steps. For subjects with SCI who could take some steps, walking in parallel bars or over-ground with assistive devices, braces, and physical assistance from one or two therapists was practised.

Besides stepping exercises over-ground, repetitive and intensive stepping can be trained using treadmill training. To enhance the use of weight-bearing muscles, partial weight-bearing support can be provided with an overhead harness using conventional counterweights or high-tech unloading devices (e.g. see (Frey et al., 2006)). This makes it easier for the patient to perform and for the therapist to assist leg movements. Furthermore, the suspension secures the patient by preventing falling. Sometimes a third physiotherapist is required to stabilize the pelvis. However, such trainings involve immense strain for the physiotherapists. Indeed, in cases where patients have little voluntary muscle strength, but high spastic muscle forces, the training duration is often limited by the therapists rather than the patient.

Especially for these more complicated cases, sophisticated robotic devices have been developed such as a robot-driven exoskeleton orthosis (Colombo et al., 2000; Colombo et al., 2001) or an electromechanical device with two driven foot plates that simulate gait phases (Hesse et al., 2004; Schmidt et al., 2003). Another device, a tilt table with a built-in mechanism to apply walking like movements combined with adequate loading of the legs, might even be applicable at an early stage of rehabilitation, as compared to previous devices (Rupp et al., 2002).

The decision to apply a certain therapeutic intervention in a specific patient has been addressed elsewhere (Behrman et al., 2005). Accordingly, decision-making algorithms were proposed, which can be used to standardize task-specific gait therapy. A list of criteria determines when to change from standing to stepping exercises using BWSTT and/or over-ground walking in a specific patient. The decision algorithms also contain aspects such as when to apply verbal or manual facilitation (Behrman et al., 2005). Although such decision algorithms have not been investigated thoroughly for their applicability and effectiveness, this could be an appropriate way to define “standardized” rehabilitation protocols that take into consideration the physical condition and walking ability of a particular subject with a SCI.

Although there has been an abundant number of publications suggesting the effectiveness of such interventions on walking performance (e.g. case reports: (Behrman and Harkema, 2000; Gardner et al., 1998; Protas et al., 2001) and cohort studies: (Wirz et al., 2005; Hesse et al., 2004; Wernig et al., 1995; Wernig et al., 1998, 1999; Wirz et al., 2001), there are only a limited number of trials that used a randomized controlled design to evaluate their effectiveness. According to a recent systematic review (Mehrholz et al., 2008b, a), only four studies matched the inclusion criteria (i.e. randomized controlled trial comparing locomotor training to any other exercise provided with the goal of improving walking function after SCI or to a no-treatment control group). One of these four studies investigated the effectiveness of a combination of BWSTT and task-oriented physiotherapy versus physiotherapy alone (Dobkin et al., 2006). Furthermore, a robotic-assisted BWSTT versus manual BWSTT study (Hornby et al.) and a BWSTT with manual assistance in combination with FES versus conventional physiotherapy study were included (Postans et al., 2004). In the fourth included study, subjects with SCI were randomly assigned to 1 of 4 different BWSTT assisted-stepping groups, including: (1) treadmill training with manual assistance, (2) treadmill training with electrical stimulation, (3) over-ground training with stimulation, or (4) treadmill training with robotic assistance (Field-Fote et al., 2005). For all studies using robotic supported BWSTT, the “Lokomat®” was used (Colombo et al., 2000; Colombo et al., 2001). In total, 222 subjects with SCI were included and the overall conclusion of this systematic review was that there was no statistically significant effect of locomotor training on walking function after SCI comparing BWSTT, with or without functional electrical stimulation, or robotic-assisted locomotor training (Mehrholz et al., 2008b, a). The efficacy of conventional physiotherapy should therefore not be underestimated (van Hedel, 2006) and studies on how these interventions could optimally combined to result in the most effective gait rehabilitation program should be evaluated.
6. Assessment of walking function after spinal cord injury

To determine the effectiveness of interventions on walking function, it is important to first establish measures that assess walking function, as there is currently no gold standard for the quantification of ambulatory function (Ditunno et al., 2005; Lam et al., 2008a). According to the International Classification of Function, Disability and Health (ICF), a SCI could result in effects that can be assessed on the level of body-functions and -structures, activities and participation.

In the field of neurorehabilitation, most outcome assessments take place on the level of body-functions and -structures, such as the neurological motor and sensory scoring according to the ASIA protocol, neurophysiological assessments such as somato-sensory evoked potentials (SSEPs) to assess afferent impulse conductivity of spinal tracts, as well as MEPs to assess corticospinal tract function. Clinical measures, such as the Modified Ashworth Scale (Haas et al., 1996) for spasticity, are also applied. However, changes at the level of body-functions do not necessarily reflect changes in an activity. For example, as previously mentioned, although there is a good correlation between leg muscle strength (body-function) and walking speed (activity) (Kim et al., 2004), an increase in leg muscle strength does not necessarily relate to a change in walking capacity, and vice versa (Wirz et al., 2006). Additional factors can influence this relationship, such as the fact that more leg muscle strength is required for walking in subjects with a tetraplegia as compared to subjects with a paraplegia, as they are less able to support their bodyweight due to reduced upper extremity strength (Wirz et al., 2006).

Therefore, increasingly, more assessments at the ICF activity level have been introduced. These measures can be divided into capacity and performance qualifiers. Capacity indicates that the activity is assessed in a strictly standardized way, including a standardized environment. Performance indicates that the activity is assessed in a less standardized manner, for example in the subjects own environment.

The 10 meters walking test (10MWT), which assesses short duration speed and the 6 minutes walking test (6MinWT), which assesses the distance covered during 6 minutes can be considered walking capacity tests. Performed at the subject’s preferred speed, they were shown to be valid tests (van Hedel et al., 2005b), see also Fig. 3A, as they correlated well with each other and the revised Walking Index for Spinal Cord injury (WISCI II), which assesses the need of the subject to depend on walking aids and personal assistance (Ditunno and Ditunno Jr, 2001). The WISCI II has been evaluated extensively over the past years and can also be considered a valid, reliable and responsive measure to assess walking capacity after SCI (Ditunno et al., 2007; Ditunno et al., 2008a; Ditunno et al., 2000), although slight differences between USA and European rehabilitation standards need to be taken into account (van Hedel et al., 2008; Ditunno et al., 2007). Furthermore, the Timed Up and Go Test (TUG) evaluates the ability to stand up from a chair, walk 3 meters, turn around, walk back and sit down again (van Hedel et al., 2005b).

The 10MWT has been shown to be more reliable than the 6MinWT and the TUG (van Hedel et al., 2005b), see Fig. 3B, as the 6MinWT and the TUG show improved performance when they are applied repeatedly. It is therefore recommended that the subjects perform these tests at least once, before performing the actual measurement.

In a group of 22 ASIA D subjects (i.e. with a sensory-motor incomplete lesion and good lower extremity muscle strength), the 10MWT and 6MinWT were shown to be more responsive compared to the WISCI II and the ASIA lower extremity motor score (van Hedel et al., 2006). In fact, in these subjects the WISCI II and ASIA lower extremity motor score reached a ceiling effect only 3 months after SCI. In a more recent study that included a larger number of SCI patients, this result was confirmed (Fig. 3C), but no additional difference in responsiveness was found between the 10MinWT and the WISCI II (van Hedel and Dietz, 2009). At present, the combined application of the 10MWT and the WISCI II is advised (Jackson et al., 2008).

When comparing the 10MWT and 6MinWT, the 6MinWT provided no additional information to the 10MWT, when subjects were able to perform both tests (van Hedel et al., 2007). Apparently, in SCI patients, the distance covered during 6 minutes does not reflect cardiovascular endurance, e.g. (Butland et al., 1982). Indeed, this was already described for subjects with stroke (Dobkin, 2006). Furthermore, although the relationship between the TUG and the 10MWT change with the time after SCI (van Hedel et al., 2008), the correlations between these tests remain quite high. We therefore conclude that the 6MinWT and the TUG provide only little additional information, when the 10MWT has been applied.

While the timed walking tests can be considered “capacity” test, the mobility items of the Spinal Cord Inde-
Fig. 3. Psychometric properties of the 10 meter walk test (adapted from (van Hedel et al., 2005b; van Hedel and Dietz, 2009)). A, Validity is indicated by the correlation coefficients between the 10 meter walk test, the revised Walking Index for Spinal Cord Injury (WISCI II), the Timed Up and Go test (TUG) and the 6 minute walk test. B, Intra-rater and inter-rater reliability is presented using Bland-Altman plots. C, Internal responsiveness is quantified using the Standardized Response Mean (SRM) for ASIA C and D subjects (between brackets: the number of observations). SRM values indicate: 0.20, small; 0.50, medium; > 0.80, large responsiveness.

Furthermore, clinically important levels of ambulation were defined using the SCIM II indoor and outdoor mobility items (van Hedel, 2009). For example, subjects who achieve a preferred walking speed of at least 0.15 m/s are likely to walk indoor using walking aids, but require a wheelchair for outdoor mobility. A walking speed of 0.45 m/s indicates that walking with aids, both indoor as well as outdoor, should be possible. Those who can walk at least 0.70 m/s are likely to walk without any aids, both indoor as well as outdoor. These specific levels of walking speed can be used as clinical endpoints for both rehabilitation and research.

7. Conclusions

While basic stepping movements are generated at the spinal level, the control of human locomotion depends more on supraspinal control as compared to most
mammalian models used to investigate locomotive control. In subjects with a SCI, locomotion depends even more on cortical control, as the attentional demand is higher and visual feedback is required more. After a motor complete SCI, the probability to achieve some ambulatory function is rather low, while in motor incomplete SCI subjects, the chances of regaining some stepping ability are high. Various mechanisms can play a role during the improvement of ambulation in these incomplete SCI subjects. While there are no indications that spontaneous regeneration or repair mechanisms underlie the improvement, both spontaneous and induced neural plasticity, as well as compensation, can contribute. Several therapeutic interventions, such as task-oriented physiotherapy, and manual and robotic supported BWSTT are directed at exploiting neural plasticity. Although it is likely that these interventions contribute significantly to an improvement in ambulation, differences in effectiveness between these interventions have not yet been convincingly demonstrated. To accurately monitor changes in ambulation, several assessments such as the 10MWT, the WISCI II and the SCIM mobility items have been shown to be valid, reliable and responsive measures that can be applied in the field of SCI rehabilitation. Future important issues remaining to be addressed include as how to optimize rehabilitation protocols and how to translate experimental interventions from bench to bedside so as to maximally enhance ambulatory function in severely affected subjects with a SCI.

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