After spinal cord injury (SCI) of the cat or rat neuronal centres below the level of lesion exhibit plasticity that can be exploited by specific training paradigms. In individuals with complete or incomplete SCI, human spinal locomotor centers can be activated by appropriate afferent input. This includes to facilitate and assist stepping movements of the legs and to provide body weight support (BWS) standing on a moving treadmill. Individuals with incomplete SCI benefit from such a locomotor training such that they improve the ability to walk over ground. Load- and hip-joint-related afferent input seems to be of crucial importance for both the generation of a locomotor pattern and the effectiveness of the training. It appears to be a critical combination of afferent signals that is needed to generate and improve a locomotor pattern after SCI. Mobility of individuals after a SCI can be improved by taking advantage of the plasticity of spinal neuronal circuits and can be maintained with persistent locomotor activity. Since several years driven gait orthoses can provide a standardized locomotor training. In the future, if regeneration approaches can successfully be applied in human SCI, even individuals with complete SCI may recover walking ability with locomotor training. Presently, individuals with complete SCI, spinal neuronal circuits undergo a degradation of their function 1 year after injury.

Contents

1. Introduction ............................................................................................................................... 459
2. Physiological basis of locomotion in humans ...................................................................................................... 460
3. Target for rehabilitation: plasticity of the central nervous system................................................................. 460
4. Locomotor function after spinal cord injury .................................................................................................. 460
   4.1. Neuronal capacity of spinal cord from cat to humans .................................................................................. 461
   4.2. Effect of locomotor training in paraplegic patients ...................................................................................... 461
   4.3. Relevant afferent input .............................................................................................................................. 461
5. Assessment of function during rehabilitation .................................................................................................. 462
6. Outlook .................................................................................................................................................. 462
Acknowledgments ........................................................................................................................................ 462
References ................................................................................................................................................. 462
plasticity could then be exploited for rehabilitative purposes by the
use of task-specific training approaches following a neural injury
[14,19].

2. Physiological basis of locomotion in humans

Leg muscle activation during locomotion is produced by spinal
neuronal circuits within the spinal cord, i.e. the spinal pattern
generator (CPG, for review see [13]). For the control of human loco-
motion, afferent information from a variety of sources within the
visual, vestibular and proprioceptive systems is utilised by the CPG.
The convergence of spinal reflex pathways and descending path-
ways on common spinal interneurons seem to play an integrative
role (for review see [14]), similar as in the cat [43]. The generation
of an appropriate locomotor pattern depends on a combination of
central programming and afferent inputs as well as the instruc-
tion for a respective motor condition. This information determines
the mode of organization of muscle synergies which are designed
to meet multiple conditions of stance and gait ([13,14,20,21]; for
review see [33]).

Central mechanisms and afferent inputs interact in such a way
that the strength of a reflex in a muscle or a synergistic group of
muscles follows a program that is dependent on the actual task. The
actual weighting of proprioceptive, vestibular and visual inputs to
the equilibrium control is context-dependent and can profoundly
modify the central program. Through this weighting, inappropriate
responses are largely eliminated (for review see [33]). Any evalu-
ation of reflex function has to be assessed in connection with the
actual motor program, the biomechanical events, including their
needs and their restraints.

3. Target for rehabilitation: plasticity of the central nervous
system

There is increasing evidence that a defective utilization of affer-
ent input, in combination with secondary compensatory processes
is involved in typical central movement disorders, such as spasticity
and Parkinson’s disease. Furthermore, cat (for review see [39]) and
human (for review see Refs. [14,16]) experiments show that neu-
neral networks underlying the generation of motor patterns are
quite flexible after central or peripheral neural lesions. Therefore,
the aim of rehabilitation should concentrate on the improvement
of function by taking advantage of the plasticity of neuronal cen-
ters, and should less be directed to the correction of isolated clinical
signs, such as the reflex excitability.

There is convincing evidence in spinal animals that a use-
dependent plasticity of the spinal cord exists [27,39]. When
stepping is practiced in spinal cat, this task can be performed more
successfully than when it is not practiced [31,32]. The training of any
motor task provides sufficient stimulation to initiate a reorganiza-
tion of neural networks within the spinal cord and, for example,
to generate locomotion. Consequently, the loss of motor capacity
following neural injury can become enhanced when locomotor net-
works are no longer used, for example, following a stroke [27]. In
contrast, a much greater level of functional recovery might be possi-
ble if the concept of use-dependence is applied in both the clinical
and rehabilitative settings [27].

A considerable degree of locomotor recovery in mammals with
a spinal cord injury can be attributed to a reorganization of spared
neural pathways ([8,10]; for review see [9]). It has been esti-
1
mated that if as little as 10–15% of the descending spinal tracts
are spared, some locomotor function can recover [3,36]. If the loss
of supraspinal input to the spinal cord is complete, these neuronal
networks that exist below the level of the lesion adapt to gener-
ate locomotor activity even in the absence of supraspinal input
[11,12,49].

4. Locomotor function after spinal cord injury

4.1. Neuronal capacity of spinal cord from cat to humans

In the cat, recovery of locomotor function following spinal cord
trasection can be improved using regular training even in adult
animals [1]. When stepping was not stimulated, the cat lost the
ability to step spontaneously. During such a locomotor training
the animal was supported and thus only beared a part of its body
weight. Locomotor movements of the hindlimbs were induced by
a treadmill while the forelimbs stood on a platform. With ongoing
training the body support was decreased associated with improv-
ing locomotor abilities. Later on the cat was able to completely take
over body weight and perform well-coordinated stepping move-
ments [2]. The locomotor pattern at this stage closely resembled the
pattern of the normal adult cat. Furthermore, hindlimb exercise in
adult rats after spinal cord transection can normalise the excitabil-
ity of spinal reflexes [46]. Thus, it can be concluded that the training represents an important factor for the recovery of locomotor function. Recently, stepping movements could also be demonstrated in a monkey after transection of the spinal cord, suggesting that also the isolated primate spinal cord is capable of generating hindlimb stepping movements [47].

Human locomotion is not basically different from that described for the cat but is based on a quadrupedal neuronal co-ordination (for review see [15]). Step-like movements are present at birth and can be initiated spontaneously or by peripheral stimuli. The EMG activity underlying this newborn stepping is centrally programmed and, as it has also been observed in anencephalic children, it is likely that spinal mechanisms generate the EMG activity [28]. The apparent loss of locomotor movements in accidentally spinalized humans has been suggested to be due to a greater predominance of supraspinal over spinal neuronal mechanisms [30]. Nevertheless, there are indications that in humans spinal interneuronal circuits exist which are involved in the generation of locomotor EMG activity [5] similar to those described for the cat [2]. Furthermore, involuntary step-like leg movements described in a patient with an incomplete injury to the spinal cord [29,37], as well as the behaviour of a propriospinal clonus released after cervical trauma [4], are indicative for a spinal pattern generator in humans.

4.2. Effect of locomotor training in paraplegic patients

In patients with incomplete or complete paraplegic a bilateral leg muscle activation combined with coordinated stepping movements can be induced in partially unloaded patients standing on a moving treadmill [23,24]. The leg movements have to be assisted during the first phase of the training (dependent upon the severity of paresis) in incomplete and during the whole training period in complete paraplegic patients. Walking in incomplete SCI patients is usually achieved only at a low speed [41]. While the pattern of leg muscle electromyographic (EMG) activity is similar to that seen in healthy subjects, the EMG amplitude is considerably smaller in complete compared to incomplete paraplegics. Both patient groups have smaller EMG levels compared to the healthy subjects. Despite the reduced EMG activity, spastic symptoms (e.g. increased muscle tone, exaggerated reflexes) are present in both patient groups. This supports earlier suggestions claiming that alterations of mechanical muscle fibre properties are mainly responsible for the clinical signs of spasticity.

When the EMG of tibialis anterior and gastrocnemius muscles is analysed over the step cycle, it becomes evident that leg muscle EMG activity is about equally distributed during muscle lengthening and shortening in both healthy subjects and patients during locomotion. Furthermore, imposing locomotor movements in complete paraplegic patients with full body unloading does not lead to a significant leg muscle activation [25]. This indicates that stretch reflexes are unlikely to play a major role in the generation of the leg muscle EMG pattern in these patients, but that it is rather programmed at a spinal level.

During the course of a daily locomotor training program, the amplitude of gastrocnemius EMG activity increases significantly during the stance phase, while an inappropriate tibialis anterior activation decreases [23,24]. This is associated with a greater weight bearing function of the extensors, i.e. body unloading during treadmill locomotion can be reduced. These training effects are seen in both incomplete and complete paraplegic patients. Only patients with incomplete paraplegia benefit from the training program in so far as they learn to perform unsupported stepping movements on solid ground. Patients with complete paraplegia experience positive effects upon, the cardiovascular and musculoskeletal systems, i.e. they suffer less from the spastic symptoms. Successive reloading of the body during the training may serve as a stimulus for extensor load receptors which have been shown to be essential for leg extensor activation during locomotion in both cat [40] and man [17,22]. The generally smaller EMG amplitude in patients with complete paraplegia may be due to a loss of input from descending noradrenergic pathways to spinal locomotor centres [2].

For an improved locomotor training during the last years special devices were developed (Fig. 1). A driven gait orthosis (DGO) was designed primarily for the training of patients with a spinal cord injury [6,7] and an electromechanical gait trainer for the restoration of gait in stroke patients [48].

4.3. Relevant afferent input

For a successful training of patients with a spinal or cerebral lesion, the appropriate afferent input has to be provided to activate spinal neuronal circuits. In healthy subjects during locomotion multi-sensory proprioceptive feedback is continuously weighted and selected. According to recent observations made in healthy subjects [21,22], small children [38] and patients with paraplegia [25,29] afferent input from load receptors and hip joints essentially contribute to the activation pattern of leg muscles during locomotion.

It is suggested that proprioceptive input from extensor muscles, and probably also from mechano-receptors, in the foot sole provide load information [18]. The signals arising from load receptors are likely to be integrated into the polysynaptic spinal reflex pathway, which adapts the programmed locomotor pattern to the actual ground condition. The afferents that signal hip-joint position are suggested to come from muscles around the hip. The role of this afferent activity is to shape the locomotor pattern, to control phase-transitions and to reinforce ongoing activity. Short-latency stretch and cutaneous reflexes may be involved in the compensation of irregularities and in the adaptation to the actual ground conditions.

5. Assessment of function during rehabilitation

Owing to the exquisite task-dependent regulation of nervous system function clinical tests must be functional and specific. At present it is a common, well-accepted approach to score isolated clinical measures, such as reflex excitability, muscle tone, or voluntary force of single muscles. For example, muscle tone and spasm frequency can be assessed by the Ashworth scale and Penn spasm frequency scale, respectively [42]. For patients with spinal cord injury, the American Spinal Injury Association (ASIA) has developed a standardized neurological assessment, i.e. the ASIA classification of motor and sensory deficits [35]. The question is first, whether such scoring systems can serve as a sensitive outcome measure for new interventional therapies and second, whether they can reflect the functional impairment, which is the most important aspect in terms of the patients' quality of life.

Only recently has a score been developed which relates to function. Locomotor ability has been classified into 19 items [26]. A current study indicates that a close relationship between motor scores and locomotor ability exists only in patients with moderately impaired motor function. Patients with a low motor score undergoing a locomotor training can achieve an improved locomotor function without a change in motor score [14,34]. In these cases, relatively little voluntary force in the leg muscles (reflected in the ASIA score) is required to achieve the ability to walk (cf. Fig. 2).

For the future, the effectiveness of any new interventional therapy should be assessed by functional scores in combination with
motor scores of selected limb muscles. Motor and sensory scores are most likely to reflect the spontaneous recovery of function, as they depend on the integrity of cortico-spinal connections. In contrast, improvement of locomotor function after SCI also reflects the plasticity of neuronal circuits below the level of lesion. With the combined assessment of voluntary force and automatic function, the superiority of any new interventional therapy on functional mobility even that of almost completely paraplegic patients. Electrophysiological and biomechanical recordings of locomotion in rats with spinal cord lesions has provided information that this model can be applied in humans with spinal cord injury [36].

6. Outlook

The advantage of gait analysis represents the quantitative assessment of a functional movement with its underlying neuronal mechanisms and biomechanical consequences. In the future, this approach may further be developed to extract the factors responsible for a movement disorder. For future application in the rehabilitation field, gait analysis may help to select the most effective pharmacological and physiotherapeutical approaches. This may not only be of benefit for the patient but also could lead to reduced health care costs as most physiotherapeutical approaches are not based on controlled studies and their effectiveness was never convincingly demonstrated. For future application in the clinical diagnosis, gait analysis may help to achieve an early diagnosis and detection of subtypes of a movement disorder with the consequence of an early onset of an appropriate training (for review see [14]).

With the gait analysis of patients with a central motor lesion, the best therapeutical approach and the effect of any treatment on the locomotor function can be determined. Such an analysis has revealed, for example, that the development of spastic muscle tone can be advantageous, in that it provides body support during stepping movements. This knowledge has, of course, consequences for physiotherapy and drug application.

In severely affected parietic patients the strength of leg muscle activation is not sufficient to build up enough muscle tone or to control limb movements for locomotion. One approach to enhance spinal locomotor activity in the patients with incomplete and complete paraplegia represents the search for substances which influence the gain of leg extensor EMG activity. The most promising approach for the future may be to induce partial regeneration of the lesioned spinal cord tract fibres. Recent experiments in the rat have indicated that after inhibition of neurite growth inhibitors, a partial regeneration can occur (for review see Refs. [44,45]). Connected with appropriate locomotor training this approach may improve functional mobility even that of almost completely paraplegic patients. Electrophysiological and biomechanical recordings of locomotion in rats with spinal cord lesions has provided information that this model can be applied in humans with spinal cord injury [36].

Acknowledgments

Work included in this article was supported by the “Swiss National Science Foundation” (Grant No. 31-64792.01) and the NCCR Neural Plasticity and Regeneration.

References
