Pattern Generators in Locomotion: Implications for Recovery of Walking After Spinal Cord Injury

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The role of the human spinal cord in complex processing of sensory information during locomotion has traditionally been thought to be minimal compared to other mammals. However, the evidence from experimental models of animals after spinal transection demonstrates that the spinal cord of at least some adult mammals can execute full weight bearing stepping independent of brain input. The interaction of sensory information derived from the moving limbs with central pattern generators in the spinal cord have been identified as important components of the neural control of locomotion. Some of the features of central pattern generation important for successful locomotion in animals include recognition of order of neural events, interpretation of patterns of sensory input in a state-dependent manner, and the availability of multiple neural circuits for successful stepping. If the human has similar potential to generate locomotion based on circuits within the spinal cord, then taking advantage of these mechanisms may enhance locomotor recovery after spinal cord injury (SCI). Recent evidence suggests that the human lumbosacral spinal cord can process complex sensory information during locomotion in the absence of detectable supraspinal influence. Also, activity-dependent plasticity is evident in spinal neural networks involved in the generation of stepping in humans. Locomotor training, a new approach to gait rehabilitation, is based on providing specific sensory information related to locomotion and repetitive practice usually on a treadmill with body weight support and manual assistance if needed. This approach takes advantage of the plasticity and motor learning capacity of the human spinal cord. Functional recovery of walking after SCI may be significantly improved by implementing locomotor training in new rehabilitative strategies that focus on enhancing recovery below the level of lesion. Key words: *central pattern generation, clinical trials, functional neuroimaging, locomotion, motor learning*

The role of the human spinal cord in complex processing of sensory information during locomotion has traditionally been thought to be minimal. The human spinal cord has been viewed primarily as a conduit for information transmitted to and from supraspinal centers, with its most complex functions limited to processing simple spinal reflexes such as the stretch reflex. This perspective was derived from the notion that supraspinal systems are responsible for executing the details of complex tasks including locomotion. However, the evidence from experimental models of cats after spinal transection demonstrates that the adult mammalian spinal cord can execute full weight bearing stepping over a range of speeds independent of supraspinal input.[1–8] The ability of the mammalian spinal cord to generate locomotion raises the issue of the level of independence of spinal control of locomotion from supraspinal control in humans.[9–11] If the human spinal cord has similar potential to generate locomotion as shown in the cat, then maximizing this source of neural

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Top Spinal Cord Inj Rehabil 2000;6(2):82–96

control after spinal cord injury (SCI) may enhance locomotor recovery.

Features of Central Pattern Generation That Facilitate Stepping

Central pattern generation has been identified as an important component of the neural control of locomotion by the mammalian spinal cord.[12–20] The generation of oscillatory flexor and extensor ventral root output from the neural circuits of the spinal cord in the absence of oscillatory input from the brain or from the periphery defines central pattern generation. There are numerous examples of central pattern generation among motor systems of vertebrates and invertebrates. This pattern can approximate the electromyographic (EMG) pattern observed during normal locomotion. Although the mammalian spinal cord alone can generate complex motor signals that mimic stepping, effective weight-supported locomotion over a range of speeds can only occur when there is the interaction of sensory information derived from the moving limbs projected to these oscillatory neural networks. Some of the features of central pattern generation important for successful locomotion are described below.

Recognition of order of neural events

Locomotion is generated by neural activation of specific groups of motor pools and their corresponding muscles in an orderly sequence. The ability to generate continuous motor oscillations without any supraspinal or peripheral oscillatory input demonstrates that spinal networks are "aware" of which neuronal circuits were active immediately preceding a given point within a cycle and which neural groups are most likely to be activated next. This does not mean that there is the hard and fast selection of the same sequence of neurons every cycle, but it does imply that the networks regulate the probability of a given set of neurons becoming active at any specific time within a step cycle. This feature provides a significant level of control of locomotion to these neural circuits within the spinal cord.

Recognition of patterns of afferent input is state-dependent

The spinal cord also seems to recognize ensembles or patterns of afferent input.[21–24] For example, the spinal cord can recognize and respond to isolated segments of sensory input, such as dorsiflexion of the ankle, but during stepping the spinal cord "expects" specific sensory input that represents the dynamics and kinematics of both limbs consistent with the phase of the step being executed at the time. Thus, this ensemble of input throughout all phases of the step cycle seems to be recognized as a pattern that the spinal neurons can associate with locomotion.

Interpretation of the ensemble of sensory information is state-dependent, enabling the spinal cord to make appropriate decisions. Not only are step-associated patterns of sensory information recognized, but a given pattern of input to the spinal cord is unique to a phase of the step cycle. For example, the spinal cord at a given phase of a cycle seems to have "expectations" as to which combination of sensory pathways should be active. When one limb is loaded in mid stance, then the contralateral limb afferents should be signaling information related to an unloaded state, that is, activation of flexor muscles during the swing phase. Throughout the step cycle, state-dependent conditions are signaled by complex sensory input or supraspi-

nal input that can be "interpreted" or matched by the spinal cord circuitry.

The concept of state dependence goes further in that a given pattern of sensory input and the motor response to this input can be modulated over a period of minutes, hours, weeks, and even months. Many different types of cellular and intercellular events must contribute to the changing state dependence over time periods beyond that which occurs within a step cycle. Although we do not know the specific nature of these events, diurnal fluctuations, bladder infections, and neuromuscular activity levels are obvious contributors after SCI.

Multiple neural pathways can be used to accomplish a step

Multiple combinations of neural pathways can be activated at any given phase of a successful step cycle. This is illustrated by the normal step-to-step variations routinely observed during walking. The EMG pattern of groups of muscles and the dynamics and kinematics of limb motion are highly variable even in the most controlled and constant conditions that can be provided for a series of steps. This variability appears to be a normal intrinsic property of the spinal networks that control locomotion. Likewise, there are multiple neural solutions to execute walking. This concept of multiple solutions has particular significance with respect to rehabilitative strategies to improve locomotion after SCI. The implication is that if some supraspinal pathways are damaged, there are alternative mechanisms (solutions) for completing a step. When the extent of the combined adaptive potential of both the supraspinal and spinal pathways is understood, rehabilitative efforts may be improved by taking advantage of these alternative solutions.

The spinal cord can learn to perform a motor task in the absence of input from the brain

The concept that the spinal cord can learn to perform a motor task is in direct conflict in at least two ways with current dogma. First, it is often assumed that all motor learning resides in supraspinal structures such as the cerebellum and motor cortex. Second, it is thought that there is little adaptive potential within the spinal networks that generate locomotion. However, experimental evidence shows that the neural substrates for learning a motor task include physiological and biochemical adaptations that occur in both supraspinal and spinal circuits. In fact, there is an emerging body of research consistent with the concept that the lumbosacral spinal cord can learn to execute complex motor tasks such as standing and stepping.

Cats with complete transection of the thoracic spinal cord could be trained to either stand or step with the hindlimbs.[3,5,6,25] Independent hindlimb stepping or standing was accomplished in the absence of supraspinal input by repeatedly providing appropriate sensory information related to either stepping or standing, respectively. The level of loading and velocity of stepping are important cues for facilitating successful hindlimb stepping. Further, the specificity of training was critical to the success of the motor tasks. For instance, when cats that had been trained to stand attempted to step, their performance was more impaired than both cats that had been trained to step and cats with no training.

The neural mechanisms underlying these changes in motor performance are incompletely understood. In chronic spinal-transected animals, spinal networks that contribute to locomotion significantly increase

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their potential for inhibition.[26] There is some evidence that this elevated level of inhibitory potential returns toward normal levels after chronic spinal-injured animals are trained to perform stepping. These inhibitory influences seem to be manifested in both glycinergic and GABAergic neurotransmitter systems. Currently, there is an insufficient level of understanding of these biochemical changes to develop a pharmacological strategy for retraining locomotion in humans.[27] In the future, however, significant changes in locomotor function may be obtained by modulating levels of inhibition and excitation after SCI using a combination of pharmacological and use-dependent mechanisms.

The Role of Central Pattern Generation in Human Locomotion

Most of the observations suggesting the presence of central pattern generation in humans have been based on the ability of the lower limbs to generate some alternating movement in individuals with severe or clinically complete SCI.[28–34] However, all of the participants who had oscillating motor behavior also had preserved segmental sensory input to the spinal cord. Experimental evidence supporting central pattern generation in the spinal cord requires, by definition, the observation of oscillating neural patterns in the absence of oscillating sensory and supraspinal input. Therefore, definitive evidence of central pattern generation in humans seems unlikely. We suggest, however, that the critical issue for the recovery of locomotion after SCI is not the ability of the spinal cord in isolation to execute oscillations in flexor and extensor motor pools. Rather, it is the ability of the spinal cord to interpret ongoing sensory input in combination with the intrinsic ability of neurons to oscillate that is most critical.

We have investigated whether neural networks intrinsic to the human lumbar spinal cord can interpret complex sensory information in a state-dependent manner and integrate compromised supraspinal signals in a functionally appropriate manner. Our studies included individuals with clinically complete SCI as well as people with profound but incomplete SCI and nondisabled individuals to allow comparisons among individuals with varying levels of supraspinal input available to the spinal cord. The experimental model consists of suspending individuals over a treadmill by a harness attached to an overhead lift. Data collection included EMG activity of 16 lower limb muscles, joint angles, ground reaction forces, and the amount of body weight support provided during stepping on the treadmill (BWST).[35,36] Manual assistance was given by trainers to facilitate stepping patterns as needed. The trainers monitored the limb and joint kinematics during stepping and attained an optimal stepping pattern by adjusting the treadmill speed, body weight support (BWS), and level of manual assistance. This pattern was then practiced repetitively during step-training sessions for locomotor

training. The duration of step-training bouts depended on (1) the prevalence of the fatigue of the participant, (2) the maintenance of appropriate joint kinematics throughout the gait cycle, and (3) the ability to properly shift the weight and maintain the preferred limb-loading patterns in the legs.[37]

Evidence for recognition of patterns of afferent input that is state-dependent

We observed consistent patterns of EMG activity that were linked to the timing of the stance and swing phases of locomotion in the participants with clinically complete SCI during stepping with BWST and manual assistance.[35,36] The amplitudes of EMG activity in most of the lower limb muscles studied increased at faster treadmill speeds.[38] Further, the relative amplitude modulation remained similar for a given phase of the step cycle. The extensor EMG amplitudes of the SCI participants were higher during the stance phase and the flexor EMG amplitudes were higher during the swing phase, which is typical of normal walking. Some participants in both ASIA A and ASIA C SCI classifications can execute the swing phase more independently at the faster than at the slower speeds. The level of loading on the lower limbs also provides cues to the human lumbosacral spinal cord that facilitate stepping.[36] Increasing the load on a limb increased the mean amplitudes of the EMG, the ipsilateral soleus, medial gastrocnemius, medial hamstrings, and to a lesser extent the tibialis anterior in clinically complete SCI, clinically incomplete SCI, and nondisabled participants. Thus, the human spinal cord is sensitive to specific afferent feedback related to limb loading and the velocity of stepping and utilizes this sensory information to produce locomotor movements.

The sensory input associated with the position of the legs during standing also modulates the motor output of the spinal cord (unpublished observations). After several weeks of specific locomotor training, three participants with clinically complete SCI were able to stand in place with partial BWS. When one limb was placed in an extended position bearing weight similar to mid stance of the gait cycle, the contralateral limb consistently flexed. Much less or no flexion was generated when the contralateral leg was unloaded and in flexion. These data show the significance of the afferent input in defining the motor output of the contralateral limb, even in a static state. When individuals with clinically incomplete SCI attempted lower extremity flexion, their ability to execute this movement was dependent on the contralateral limb's kinetics and kinematics. Their ability to flex the leg voluntarily consistently improved when the contralateral limb assumed an extended position while bearing weight. These results support state-dependent, regulatory properties of neural activation by the spinal cord, which can play a critical role after SCI.

Evidence that multiple neural pathways can be used to accomplish a step

One example of capitalizing on the synergistic nature of multiple levels of neural control can be seen in understanding the interactions of arm and leg motion. Weight bearing on the arms, for example, appeared to inhibit rhythmic stepping with the lower extremities, but a reciprocating arm swing, in a natural coordinated fashion, facilitated stepping. Arm swing can be an integral component of afferent input needed to facilitate lower extremity motor output for walking. Visintin and Barbeau demonstrated that

lower limb EMG activity was higher while individuals with incomplete SCI walked in a harness on a treadmill with BWS compared to walking while supporting the same amount of body weight through the arms on parallel bars.[39]

Individuals with clinically incomplete SCI frequently can initiate stepping overground by stretching the hip musculature and simultaneously unloading the leg to facilitate the swing phase of the step cycle.[40,41] Extending the hip at the end of stance and the timing and level of unloading of the limb were critical in the initiation of swing in individuals with clinically incomplete and complete SCI (Fig. 1). Several studies in the cat not only demonstrated the relationship among hip extension, unloading of the limb, and the swing phase, but also demonstrated that this response is spinally mediated.[42–44] Functional recovery of walking after SCI may be improved by taking advantage of alternative neural solutions to execute a successful step that rely on the interaction of spinal neural networks interacting with specific sensory information related to locomotion.

Can the human spinal cord learn to perform a motor task in the absence of input from the brain?

It is reasonably clear that some individuals with incomplete SCI can regain significant levels of locomotor capability from locomotor training using BWST and manual assistance.[41,45–50] Dietz and colleagues also used repetitive step training with BWST for several weeks in clinically complete SCI participants and reported an increase in the EMG amplitude of one medial gastrocnemius muscle.[51–53] However, no leg movements or changes in limb kinematics were found. While these investigators interpreted this singular increase in EMG amplitude as a training effect and evidence for spinal cord learning, it remains unclear as to whether the change could be attributed to a greater level of weight bearing in the legs.[36]

We recently found that neuromuscular adaptations during step training resulted in a marked increase in the level of independence in generating stepping movements in participants with long-standing, clinically complete SCI. The evolution of stepping with minimal or no assistance in the individuals with SCI who were studied was associated with changes in amplitude and burst patterns of EMG activity of the lower limbs, as well as with improved kinetics and kinematics of stepping that were more typical of normal locomotion (Fig. 2). After several months of training, two participants with clinically complete SCI routinely needed very little manual assistance to achieve accurate foot placement or to maintain adequate knee extension at the end of the stance phase. Under optimal conditions of limb loading, treadmill belt speed, and appropriate kinematics, participants with clinically complete SCI could generate 3–10 consecutive steps without assistance on at least one leg. In all individuals with clinically incomplete SCI who were studied, the assistance provided by trainers decreased while the participants' tolerance for greater weight bearing improved. These results suggest that humans have conserved spinal neural networks that show activity-dependent plasticity and can generate locomotion when provided with afferent input that is typical of normal weight bearing walking in much the same way that step training enhances this capability in spinal transected cats.

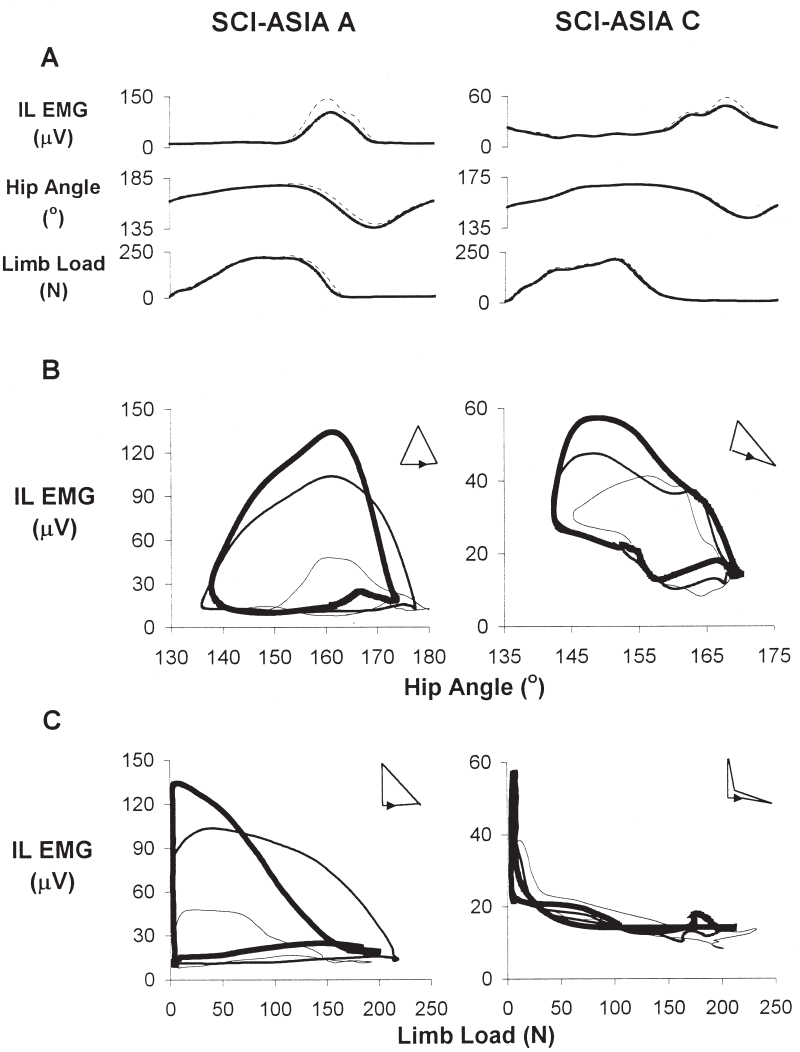

Fig 1. Iliopsoas (IL) EMG activity, hip angle, and limb load from individuals with clinically complete (SCI-ASIA A; left panel) and clinically incomplete (SCI-ASIA C; right panel) spinal cord injury. (A) The IL EMG amplitude (rectified, high-pass filtered at 32 Hz, low-pass filtered at 5 Hz), hip angle (degrees), and limb load (Newtons) from seven consecutive steps at 0.63 m/s from an ASIA A and an ASIA C participant are normalized to a common step cycle duration and represented by the average (thicker lines) and average +*SD* (thinner lines). When the limb load is greater than zero, the foot is in contact with the treadmill belt. (B) The relationship between IL EMG amplitude and hip angle throughout the step cycle is shown at 0.36 m/s (thinnest line), 0.63 m/s (medium line), and 0.81 m/s (thickest line). Each line represents an average of seven consecutive step cycles. (C) The relationship between the IL EMG amplitude and level of limb

Clinical Implications of Locomotor Training

Conventional gait rehabilitation after SCI focuses on two approaches. First, therapists facilitate motor recovery through strengthening and endurance training of the uninvolved muscle groups. Second, there is an emphasis to compensate for nonremediable deficits by using braces and assistive devices for support.[54] Conventional therapies for walking have been successful primarily in patients with the ability to at least flex the hips and flex and extend the knees against gravity.[55,56] In contrast, the locomotor training described earlier is based on the plasticity and motor learning capacity of the spinal cord. This neural circuitry is dependent, first, on receiving the specific sensory input associated with performance of a motor task and, second, on repetitive practice of that task. If the human spinal cord can learn by responding to specific sensory cues related to locomotion, then the understanding of these mechanisms can lead to improved approaches to gait rehabilitation after neurologic injury.

Our demonstration of continuous stepping on a treadmill in participants with a complete SCI, induced by locomotor training, was accomplished only after we recognized and developed a method to optimize some of the sensory cues associated with locomotion. The locomotor training provides a means of repetitively presenting phasically appropriate sensory cues to locomotion. Some of the sensory cues and pattern of cues that can affect locomotor function in SCI participants included: (1) generating stepping velocities approximating normal walking speeds (0.75–1.25 m/s); (2) providing the maximum sustainable load on the stance limb; (3) maintaining an upright and extended trunk and head; (4) approximating normal hip, knee, and ankle kinematics for walking; (5) assuring kinematically correct synchronization of extension of the hip in stance and unloading of limb with simultaneous loading of the contralateral limb; (6) avoiding weight bearing on the arms and facilitating reciprocal arm swing; (7) facilitating symmetrical interlimb coordination; and (8) minimizing sensory stimulation that would conflict with sensory information associated with locomotion, for example, stimulation of extensor afferents during swing and flexor afferents during stance. It appears that, at least in some participants with SCI, the nervous system can relearn the task of walking when the spinal cord can receive those patterns of sensory information that normally occur with weight bearing stepping. Repetitive presentations of these sensory patterns as occurs during locomotor training increases the probability even further that successful locomotion can be recovered.

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load of the same step cycles as panel A are shown. Insets in the top right corner of panels B and C display the temporal direction of each relationship with an arrow placed at the point of initial foot contact. Both ASIA A and ASIA C SCI participants executed the swing phase without physical assistance from the trainer at 0.81 m/s, but not at 0.36 m/s, and shared similar temporal and amplitude modulation of IL EMG patterns in response to changes in speed. Regardless of the speed of stepping, the onset of the IL EMG burst and initiation of swing were tightly coupled and always occurred during the phase of limb unloading in the ASIA A and ASIA C participants.

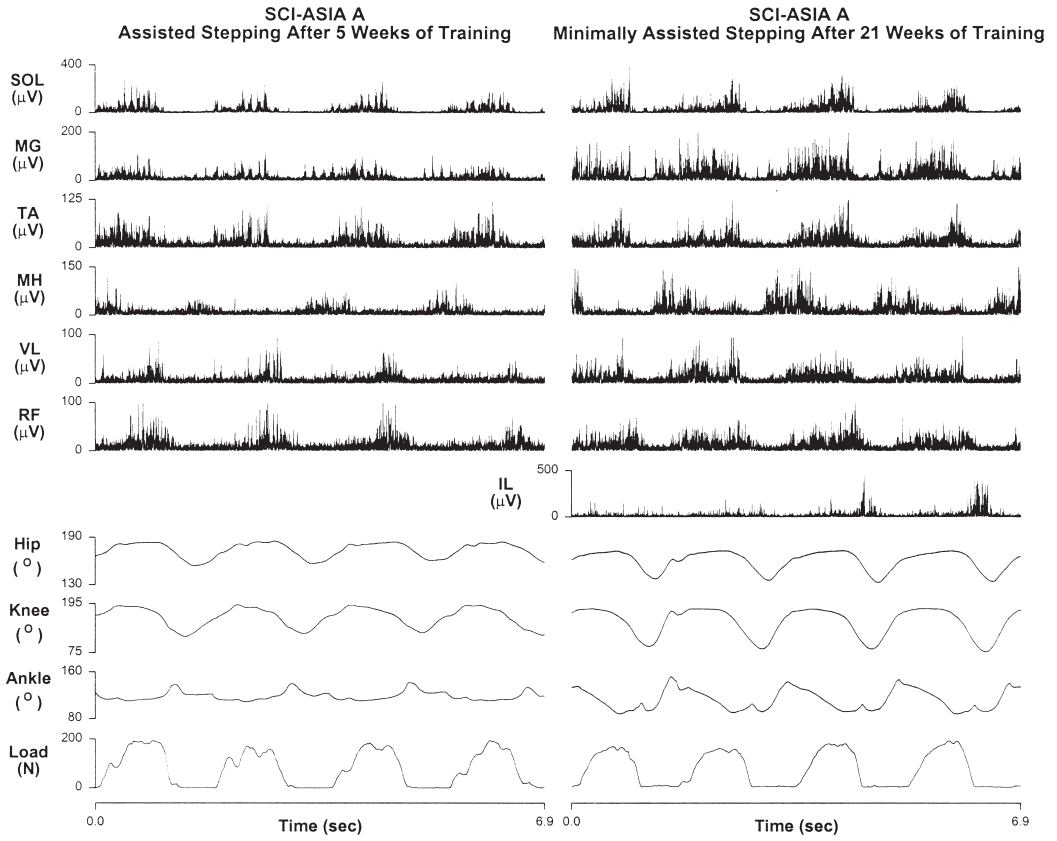

Fig 2. EMG activity (rectified, high-pass filtered at 32 Hz) from SOL, MG, TA, MH, VL, and RF; hip, knee, and ankle angles; and limb load (Newtons) from the left limb during stepping at 0.54 m/s with BWST after 5 weeks and after 21 weeks of training from an individual with clinically complete SCI are shown. This participant generated EMG bursts in the lower limbs synchronized with the kinematics of stepping. Within several weeks of step training, joint excursions increased, EMG burst amplitudes increased, and some muscles developed EMG burst patterns for the first time. These changes were muscle specific and remained linked to the kinematics and kinetics of the step cycle.

Relationship to the mobility of individuals with SCI and sparing of spinal tracts

What descending input to the spinal locomotor pools would enable overground walking with a reciprocal gait after locomotor retraining? In a study of the neuropathology of individuals after complete and incomplete SCI and of controls, the minimum number of corticospinal fibers needed to execute volitional movement with leg strength graded 2 (muscle twitch) to 3 (movement against gravity but not resistance) on the British Medical Council Scale was 3.5% to 10% of the total number of axons at the T4 level.[57] Kakulas[58] related fiber counts in specific

tracts to sensorimotor function. Six chronic, clinically incomplete and four complete SCI participants were examined post-mortem. At the T4 level, controls had about 41,000 nerve fibers in the lateral corticospinal tract. Sparing of about 3,000 fibers on one side was associated with voluntary foot motion. Participants with complete motor loss had about 2,000 residual fibers. When touch and vibration were intact, about 117,000 of 452,000 fibers in the controls were spared. Lesions of the spinal cord that completely spare the lateral or ventral funiculi in nonhuman primates permitted walking, and the presence of as little as about 25% of white matter tracts allowed this.[59] It remains to be determined whether spared descending inputs that cross a spinal lesion can gain greater synaptic control over the thoracolumbar motor pools, if locomotor training is implemented to reproduce the segmental sensory inputs that typically arise during normal ambulation.

Given the plasticity of the spinal locomotor pools, even a slight increase in descending activity via modest restoration of specifically or nonspecifically targeted inputs combined with locomotor training might substantially improve the ability to walk.

In the near future, efforts in the neural repair of SCI using cell implants, bridges, genetic manipulations, and other biologic and pharmacologic interventions may require optimal training paradigms to enhance the synaptic efficacy of new inputs on neuronal targets. Given the plasticity of the spinal locomotor pools, even a slight increase in descending activity via modest restoration of specifically or nonspecifically targeted inputs combined with locomotor training might substantially improve the ability to walk. Following both complete and incomplete SCI, it will be important to determine which specific modes of sensory information are best utilized for training and how these variables might differ depending on the nature and duration of SCI.

Functional Neuroimaging of Reorganizing Locomotor Networks

Passive and voluntary movements of the distal lower extremity during functional magnetic resonance imaging (fMRI) may allow clinicians to monitor the success of physical therapies that engage and, in a sense, reeducate the locomotor networks to function under new circumstances. Such neuroplasticity has been observed in the cortical representations for the hand and trunk in people with complete SCI.[60,61] Positron emission tomography (PET), performed in people with complete SCI, revealed an expansion of the hand's topographic map toward the leg area during hand movements and greater bilateral activation of the thalamus and cerebellum.[61] Changes in representational maps for leg movements were also found by intracortical microstimulation of the leg area after amputation of a hindlimb in monkeys.[62] Cortical representations in the primary motor cortex that represented the hindlimb region evoked hip stump, trunk, and tail movements. These representations had "invaded" those for the leg.

Functional neuroimaging could open a real-time window on the changes in cortical and subcortical activity induced by a biological and retraining regimen for walking. We

injected 2-fluorodeoxyglucose into a participant and had him walk for 30 minutes before placing him in the scanner. Activations were greatest in the paramedian primary sensorimotor cortices for the legs, the cerebellar vermis and hemispheres, the occipital cortex for vision, and the temporo-parieto-occipital junction for integrating sensory input.[63] This finding is consistent with the ascending and descending pathways and nodes of the locomotor network. Functional MRI using the blood oxygenation level-dependent (BOLD) contrast technique measures the small percentage changes in blood flow that are coupled to neuronal activation. Unlike PET scanning, this technique cannot measure actual blood flow or metabolism. An fMRI study of the lower extremity, of course, cannot be accomplished during walking.

Functional magnetic resonance imaging studies using the BOLD technique were performed after the completion of locomotor training in an incomplete SCI participant with a lesion at T6 who had been step trained with BWST to walk over ground. Passive movement engaged a much larger representation than found in the control participants that included the foot, leg, and low trunk movement representations of the primary sensorimotor cortex. Voluntary compared to passive movement activated an expanded, simultaneous representation for the right foot, leg, and trunk's primary sensorimotor map, along with larger than normal activations in the distributed motor system that included the SMA, insula, and premotor cortex. He had better motor control of the left foot. Of interest, the voluntary foot task on the left produced a smaller area of representational activation than that elicited by the right foot, consistent with upper extremity studies that sometimes reveal a shrinking representation as a new or recovering motor skill improves.

The foot and ankle dorsiflexors have a large pyramidal tract representation in the primary sensorimotor cortex, which interacts cortically and within the lumbar motor pools with other locomotor movement representations. Also, segmental sensory inputs from the foot have considerable influence on the spinal rhythm generators, the cerebellum, brain stem locomotor regions, and cortical motor networks. The evolution, distribution, magnitude, and size of activations measured using fMRI over time might reveal information that could be used by the clinician when looking for evidence that a biological intervention was leading to in vivo repair.

Clinical Trial of Locomotor Training

The results of a multicenter, randomized clinical trial of locomotor training using BWST as a task-oriented rehabilitation intervention for recovery of walking after acute incomplete SCI should be reported in 2003. This strategy applies the basic neuroscience research and pilot clinical studies of locomotor training based on use-dependent locomotor learning in the lumbosacral neural circuits, as well as within supraspinal neurons that coordinate leg movements. The intervention partially supports the weight of patients via an overhead lift attached to a harness worn by the participant. Therapists then systematically train patients to walk on a treadmill at increasingly more functional speeds with less weight support. They correct gait deviations and manipulate sensory inputs that enhance control of the stance and swing phases of walking. Therapists at six rehabilitation centers were trained in the ex-

perimental locomotor training approach. The University of California Los Angeles coordinating and data management center randomly assigns eligible participants to a conventional therapy program for mobility versus the same intensity and duration of the experimental locomotor training. One hundred participants with incomplete SCI from below C4 to T10/11 and 100 participants with lesions at T12 to L3 will be entered within 8 weeks of injury and treated for 12 weeks. The two primary outcome measures are the level of independence for ambulation and the maximal speed for walking 50 feet, tested after 12 weeks of therapy and at 6 and 12 months after randomization.

Summary

The mammalian spinal cord maintains a significant level of control of locomotion by the interaction of specific sensory information with central pattern generation. Many features of the neural control of locomotion identified in the mammalian spinal cord, such as recognition of order of neural events, interpretation of patterns of afferent input in a state-dependent manner, and multiplicity of neural circuits available for successful stepping, may have been conserved in humans. Recent evidence suggests that the human lumbosacral spinal cord can process complex sensory information during locomotion in the absence of detectable supraspinal influence. Also, activity-dependent plasticity is evident in spinal neural networks involved in the generation of stepping in humans. Functional recovery of walking after SCI may be significantly improved by implementing locomotor training in new rehabilitative strategies that focus on enhancing recovery below the level of lesion. Locomotor training may also be used in combination with regenerative approaches to enhance functional recovery after SCI. Clinical trials and functional neuroimaging will play an important role in assessing the efficacy of this intervention on the recovery of locomotion after neurologic injury.

Acknowledgements

We thank the members of our research team for their contributions to the work: Janell Beres, Seanna Hurley-Kringen, Uday Patel, and Dorian Rose. We acknowledge the collaboration of Anton Wernig and Sabina Müeller on data obtained from two SCI participants included in the studies described. Also we are indebted to Sabina Müeller and the supporting personnel of Rehabilitation Clinics, Langensteinbach, Karlsbad, Germany, for locomotor training and providing all general daily care and housing for the two SCI participants. This research was supported by research grants NS 36854, NS 16333, T32 HD07416, and M01 RR00865-19 from the National Institutes of Health.

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