Teaching the Spinal Cord to Walk

A flurry of recent work suggests that, with proper training, some patients with spinal cord injuries can regain at least a limited ability to walk.

Two years ago, 27-year-old Thorsten Sauer grabbed a therapist's hand and took his first steps in 6 years. At the time, he had been confined to a wheelchair since the 1989 motorcycle accident that had partially torn his spinal cord, leaving him almost totally paralyzed from the ribs down. But in 1995, prompted by a television news program, Sauer traveled from his hometown of Erlangen, Germany, to participate in an experimental program run by neurophysiologist Anton Wernig of the University of Bonn. At Wernig's clinic, located near Karlsruhe, a therapist hoisted Sauer and helped him walk slowly on a treadmill for 3 meters while grasping parallel bars. "It was amazing," Sauer recalls.

Today, after completing Wernig's 10-week program, in which patients step on treadmills assisted by specially trained therapists and a harness that can support part of their weight, Sauer pushes a wheeled walker around his apartment, stopping to grab books off shelves formerly out of reach. With help, he can even climb a few stairs. And Sauer is not alone. Dozens of other spinal cord-injury patients once confined to wheelchairs can now walk, although in a limited way, thanks to Wernig's program.

The idea that training can restore some walking ability is buttressed by a growing body of evidence in cats and now in humans. It shows that, contrary to dogma, the adult mammalian spinal cord can perform on its own, largely independent of the brain, many of the functions necessary for walking. What's more, recent data show that neural circuits governing locomotion in the spinal cord can "learn," by altering their connections, in a way that may help explain some of the improvements Wernig is seeing (see sidebar). "There is a flurry of activity and a pretty upbeat mood. People think that training procedures can enhance the abilities of [those with] spinal cord injuries," says Kerri Pearson, an expert on the neurophysiology of walking at the University of Alberta in Edmonton, Canada.

More work will be needed to confirm these encouraging, but early, results. Indeed, even supporters caution that no one knows how much improvement individual patients can expect from the treatment. Furthermore, many patients with spinal cord injuries—who number 200,000 in the United States alone—will not benefit from the approach. In particular, notes Stein Grillo, a neurophysiologist at the Karolinska Institute in Stockholm, Sweden, training is unlikely to produce useful walking in patients whose cords are so badly damaged that no connections survive between their brains and the region below their injury.

Those people would have a lot of trouble voluntarily keeping control of their legs started or stopped walking. In addition, he says, locomotor training does not restore balance. As a result, quadriplegics like actor Christopher Reeve, who can't use their arms to hold onto walkers and other devices for stability, could not learn to walk without being held upright.

But if the approach does someday prove successful in larger clinical tests, it might ultimately change the way many individuals with spinal cord injuries are treated. Today, doctors often leave such patients alone, except for therapy to strengthen healthy muscles or maintain flexibility. Current rehabilitative techniques such as helping patients stand or having them cycle their legs in the air have not proved consistently helpful.

The new work, however, "is saying to a person in a wheelchair, 'This may not be your lot,'" says J. Thomas Mortimer, a biomedical engineer at Case Western Reserve University in Cleveland. And even though he concedes that training will not restore normal walking, Mortimer notes that merely being able to walk a few paces and climb a few stairs could vastly improve such a person's life, enabling him to enter a friend's home, a movie theater, or a narrow bathroom that would otherwise be off limits to him.

Moving to the beat

The first inklings that the mammalian spinal cord houses the sophisticated neural machinery needed for walking emerged in 1910, when Charles Sherrington, a neurophysiologist at Oxford University in the United Kingdom, found that cats whose spinal cords had been completely cut could perform limited stepping motions. But it was decades before anyone could conclusively pin the engine of locomotion to the spinal cord.

In 1967, Anders Lundborg and his colleagues at the University of Göteborg in Sweden isolated the spinal cord in adult cats by cutting its link to the brain and also paralyzing all the muscles to deprive the cord of movement-related sensory cues. The researchers then activated the animals' spinal neurons with an injection of L-dopa, a precursor for one of the cord's main neurotransmitters, noradrenaline. They found that the neurons that flex the legs and those that extend them fired in an alternating pattern.

The researchers concluded that the spinal cord holds a "rhythm generator" for locomotion that beats like the heart and is independent of both sensory cues and the brain. In the 1970s, Grillo and Peter Zanger, then also...
Watching “Walking” Nerves Learn

Researchers have long known that in the brain, learning goes with subtle changes that strengthen or weaken the connections between neurons. As a result, they’ve assumed that similar neuronal “plasticity” also underlies the ability of the spinal cord to learn how to control walking after an injury destroys connections to the brain (see main text). But while plasticity had been seen in other motor systems, no one had directly seen it in the spinal cord’s walking circuits—until now, that is.

Working with cats, neurobiologist Keir Pearson of the University of Alberta in Canada and his colleague, Patrick Whalan and Gordon Huber have shown that the influence of sensory nerves in the spinal locomotor system can adapt to compensate for an injury. “If you want any motor system that involves reflexes to work precisely, those reflexes must be modifiable. Our work provides the first glimpse of this type of thing in the locomotor system,” says Pearson, whose team’s results were published in 1995 and 1997 in the Journal of Neurophysiology.

The Pearson team members made the discovery serendipitously while studying the way sensations from the leg muscles influence walking in the cat. In 1994, while conducting those experiments, they cut a sensory nerve in a calf muscle called the lateral gastrocnemius (LG). When this nerve is stimulated, the signals it sends to the spinal cord elicit in the leg’s motor neurons responses that prolong stance—keeping a walking animal’s leg extended and on the ground. This helps coordinate the timing of each step.

They then cut the nerve, they noticed that stimulating it didn’t keep the leg on the ground as long. At the same time, the cats began walking more normally again. So Whalan and Pearson began to wonder whether some change in the spinal cord might be compensating for the damage to the LG sensory neuron.

To find out, Pearson’s team cut the LG nerves in one hind leg on each of 10 adult cats. Then, after 3 to 28 days, team members stimulated both the LG nerve and a sensory nerve in another calf muscle—the medial gastrocnemius (MG)—while the cats walked on a treadmill. Within 5 days, the researchers found, the ability of the severed LG nerves to prolong stance was much lower than that of the controls, while the stance-prolonging ability of the MG nerves in the injured legs had increased. Thus, the neuronal circuitry had changed to compensate for an injury-induced deficit.

To prove that the changes had taken place in the cord and not the brain, Pearson and Whalan repeated the experiment in another group of cats, this time cutting the spinal cord in nine of them. With the cord now isolated from the brain, those animals, the researchers found the same decreased influence of the LG nerve in all of the cats that could be evaluated; in some of them, they also saw an increased effectiveness of the MG nerve. This showed that at least part of the plasticity occurred in the cord.

The mechanism underlying this plasticity is so far unknown. But Pearson speculates that walking may produce “activity-dependent competition,” in which two sensory nerves with similar functions compete for influence in the spinal cord. If one neuron is then cut, its connections to spinal neurons will weaken, allowing the competing nerve to exert greater influence.

If sensory feedback from walking does influence the strength of spinal connections, this type of plasticity could underlie the improved walking that can be induced in some paraplegics by locomotor training. Pearson suggests that the sensory or motor weakness—in this case, from a spinal cord rather than peripheral lesion—it could help a patient improve the rhythm of his or her walk as the cord learns to send an extended leg to start the next step.

—L.W.

at the University of Goteborg, confirmed Lundberg’s results and extended them. They showed that the cord can produce not only a basic locomotor rhythm but also a more detailed electrical pattern in which different neural signals are sent to different leg muscles.

While researchers were picking up electrical activity in several spinal cords, various labs were seeing signs that it might have functional consequences. Grillner’s team found, for example, that kittens whose spinal cords had been cut walked well, as could adult cats temporarily, if they were given certain drugs immediately after their cords had been cut. But adult cats with older injuries walked poorly. They needed help placing their paws, balancing, and supporting their weight. And few experts believed such animals could improve. The mature cord was seen as too inflexible to make the subtle adjustments in its wiring required for independent locomotion after an injury.

But two neurophysiologists, Reggie Edgerton and Serge Rossignol, leading separate teams at the University of California, Los Angeles (UCLA) and the University of Montreal in Canada, weren’t so pessimistic. Indeed, both teams showed, in a series of studies in the 1980s, that chronic “spinal cats,” as the animals with severed spinal cords are called, can relearn the locomotor pattern of a normal cat.

In one study published in 1987, for instance, Rossignol and his former postdoctoral student Hughes Barbeau, now at McGill University in Montreal, demonstrated dramatic improvements in the walking abilities of three spinal cats after two to three sessions a week, during which they were trained to walk with their hindlimbs on a treadmill. The animals at first had to be held up by their tails, but they eventually became able to support their hindquarters while they stepped. They also learned to place their paws sole-first on the treadmill and to take longer, more natural-looking steps. At the same time, mathematical measurements constructed from video images of the cats walking showed that their joint angles and leg movements began to mirror those of intact walking felines. In addition, the cats’ leg muscles also began to exhibit more normal patterns of electrical activity.

Then, in the early 1990s, Edgerton’s team members discovered that what an injured spinal cord learns can be surprisingly specific. They compared the walking abilities of three groups of spinal cats: untrained animals, those trained to step, and others trained only to stand. The team showed that the step-trained cats could, after 5 months, walk more naturally and rapidly than the untrained cats. By contrast, the cats that had practiced standing could hardly step at all. This shows, Edgerton says, not only that the cord can learn but that what it learns depends on the exact sensory input it receives.

“If you teach a cat to step, it learns to step. If you teach it to stand, it learns to stand, but it can’t step,” Edgerton concludes.

Despite these encouraging results, most experts dismissed the idea that humans with
spinal cord injuries might also learn to walk if trained properly. They had never seen it happen before to people who after all are not cats.

One exception was Barbeau at McGill. In a study conducted in 1999, his group trained 10 patients on a treadmill, using the harness that could support up to 40% of their body weight. After 6 weeks of training, the researchers saw significant improvements—in both the treadmill and on the ground—"in either the amount of weight a patient could support while walking or in walking speed, depending on whether a patient could walk without support when the study began. By 1999, Wernig's group had also developed a machine that would help patients learn to walk.

Small steps for man

Few researchers paid attention to these studies because they were too small, lacked controls, and were at least unsupported by other evidence that the human spinal cord contains the neural machinery needed for locomotion. By 1998, though, many such evidence had emerged when Blair Calancie at the Miami Project to Cure Paralysis published a case study of a man who had partially severed his spinal cord 17 years before. A week after the man began an intense physical therapist regimen that included some walking, he reported that his left leg suddenly began "walking" one night when he was lying on his back. Because the walking was involuntary, it suggested, Calancie says, that the man's movements were not controlled by his brain but had arisen largely in the spinal cord. Indeed, when Calancie and his colleagues measured the electrical activity of the leg muscles, which reflects that of the nerves controlling them, they found that, in cats, the extensor and flexor nerves were firing alternately with clocklike regularity.

Since then, several groups have added to evidence that the human spinal cord can generate spindly-like electrical patterns when exposed to sensations associated with walking. For example, Volker Dietz and his colleague at the University Hospital Balgrist in Zurich, Switzerland, induced elements of stepping in 10 paraplegics whose spinal cords were completely disconnected from their brains by placing them on moving treadmills with each one's weight supported in a harness. They found that the patterns of leg muscle activity in these patients were similar to those in healthy subjects during treadmill walking.

In that same year, Wernig and his team in Germany published the first strong documentation that the spinal cord's walking program can be trained after an injury. In their study, published in the European Journal of Neuroscience, the researchers compared results with partially paralyzed patients whom they trained on the treadmill for 3 to 20 weeks with those of matched controls treated conventionally with other forms of exercise. Of 36 patients with recent cord injuries who were wheelchair-bound at the start of the study, 33 learned to walk independently, at least with less weight, after treadmill training. By comparison, only 12 of 24 wheelchair-bound controls became independent walkers with conventional therapy. And 25 of another 33 patients with older injuries who had been wheelchair-bound learned to walk independently with Wernig's program, compared to just one of 14 controls.

Just last year, in the Journal of Neurophysiology, Susan Barkenas, Bruce Dobkin, and their UCLA colleagues reported detailed evidence from the human spinal cord that helps explain how a program of exercise walking might help paraplegics.

Speeding recovery. As the lines indicate, before clonidine treatments, a cat with a severed spinal cord can barely move its hind legs (B), but afterward (C), the movements approach those of a normal cat (A).

While four patients with complete cord injuries walked with assistance on a treadmill, the researchers recorded the electrical activity in three leg muscles and the instantaneous load on each leg. They did the same in two abled-bodied people, who walked unassisted.

In both sets of subjects, the researchers found that the spinal cord's output, as measured by muscle activity, depended greatly on the load on the legs. The greater the load, the higher the activity. What's more, the activity was timed to the phase of the step cycle so that it rose just when appropriate to facilitate stepping. The results provide "exciting evidence," Edgerton says, that the human spinal cord relies on complex sensory information, including load, to orchestrate walking.

Some day such data will help optimize training regimens by giving researchers a better idea of exactly what kinds of sensory cues the spinal cord needs to govern walking most effectively. But it may take years before more clinicians adopt locomotor training as part of their rehabilitation programs. For one thing, experts schooled in other approaches are not convinced that treadmill walking is better—in part because they may be unfamiliar with the evidence, and in part because no large-scale comparison study has yet been done. "I don't think there are any of these novel techniques have been proven superior to conventional treatment," says John Ditunno, a rehabilitation specialist at Thomas Jefferson University Hospital in Philadelphia.

Even proponents of the new approach urge caution. "A lot more studies need to be done to show that training is significant," notes Edgerton. "We're confident that it does, but we need to be careful because that's an important conclusion."

Some of these studies may not be long in coming. Calancie's team at the Miami Project to Cure Paralysis has already begun testing locomotor training with both a treadmill and a ceiling-mounted circular track to which patients are harnessed, allowing them to step forward something like a shirt sliding on a neck at a dry cleaning shop. The track enables somewhat more realistic walking than a treadmill because patients move over the ground instead of having the ground move under them, Calancie says.

And there may be other, very different improvements on the way. In a paper to appear this month in the Journal of Neurophysiology, Rossignol, Barbeau, and their graduate student Connie Chau showed that the drug clonidine, which they knew helped turn on the cord's locomotor pattern, can speed the recovery of cats from spinal cord transaction when combined with locomotor training. "Within a week," Rossignol says, "the cats are walking with their hindlimbs" without needing more of the drug. Without clonidine, similar recovery in cats takes 3 to 4 weeks. Thus, in the future, patients might be treated with a combination of medication and walking workouts.

For now, pioneering the young, good natured Thorsten Sauer, who once relished the freedom of a motorcycle, basks daily in the small freedom afforded by walking a few paces on their own. "The human body is not built for sitting," Sauer declares. "Sometimes it should walk."

Ingrid Wickelgren

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PROPRIOCEPTION AND LOCOMOTOR DISORDERS

Volker Dietz

Advances in our understanding of movement control allow us to define more precisely the requirements for the rehabilitation of patients with movement disorders. Most purposeful, complex movements are programmed in the central nervous system (CNS) and adapted by proprioceptive feedback. The selection of and interaction between different sources of afferent input is task dependent. Simple stretch reflexes are thought to be involved primarily in the control of focal movement. For more complex motor behaviours such as locomotion, afferent input related to load and hip-joint position probably has an important role in the proprioceptive contribution to the activation pattern of the leg muscles. There is increasing evidence that movement disorders such as spasticity and Parkinson's disease involve the defective use of afferent input in combination with secondary compensatory processes. This has implications for therapy, which should be directed to take advantage of the plasticity of the CNS.

The study of movement control has relevance to our general understanding of brain function. But it also has implications for specific fields, such as neurology, cognitive neuroscience, rehabilitation medicine and robotics. Our understanding of movement disorders and their appropriate treatment depends on knowledge of the neuronal mechanisms that underlie functional movements. Movement disorders are the focus of one of the most rapidly expanding fields in medicine, leading to increasing costs of treatment and rehabilitation. This review focuses on the role of proprioception during human locomotion, which can serve as a paradigm for functional movements.

In a more general sense, locomotion is representative of movement control. It is a subconsciously performed, everyday movement that is highly reproducible. It is adapted automatically to existing conditions, such as ground irregularities, within a large safety margin. Knowledge about the neuronal control of human locomotion is also of broad interest for clinical reasons. Characteristic disorders of locomotion are often the first sign of a central or peripheral lesion of the motor system. However, impaired movement is not only the direct consequence of a central lesion, reflected in defective programming or reflex functioning. Rather, a movement disorder also reflects secondary compensatory processes that are induced by the primary lesion. In many cases, the altered motor behaviour can be considered as the optimal outcome for a given lesion of the motor system. The complexity of primary and secondary effects of a lesion means that detailed analysis of a movement disorder is required to define the target of any treatment.

Basic aspects of locomotion

It is generally accepted that locomotion in mammals depends on neuronal circuits (networks of interneurons) in the spinal cord (the central pattern generator, or CPG) that can act in the absence of any afferent input. Afferent information influences the central (spinal) pattern and, conversely, the CPG selects appropriate afferent information according to external requirements. In addition, proprioceptive information provides the basis for a conscious representation of our body in space, which becomes severely disturbed in deafferented individuals. Both the spinal locomotor centre (CPC) and the reflexes that mediate afferent input to the spinal cord are under the control of the...
Table 1 | Proprioceptive reflexes suggested to be involved in locomotion

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CPG, central pattern generator.

Control of body equilibrium. A basic aspect of the neuronal control of locomotion is the relationship between the quadrupedal cat and the bipedal human concerning the anti-gravity function of the leg extensors. It has been suggested that the spinal stretch reflex adapts the pre-programmed motor patterns of leg muscles to the terrain, and compensates for unexpected changes in ground level (6). Whereas this neuronal mechanism explains quick, unilateral patterns of reflex activity in leg extensor muscles, more complex bilateral coordination of leg muscle activation is needed to maintain body equilibrium when gait is disturbed by an obstacle. Irrespective of the conditions under which stance and gait are investigated, the neuronal pattern that is evoked during a particular task is always directed to hold the body’s centre of mass over the base of support. All control mechanisms must therefore be considered and discussed in this respect. One consequence is that the selection of afferent input by central mechanisms must correspond to the requirements for body stabilization. Neuronal signals of muscle stretch or length are insufficient for the control of bipedal posture. Only a combination of afferent inputs can provide the information that is needed to control the body’s equilibrium during locomotion.

Interactions between afferent inputs. The control of locomotion involves the use of afferent information from a variety of sources in the visual, vestibular and proprioceptive systems. As a rule, spinal reflex pathways and descending pathways converge on common spinal interneurons to integrate these inputs (5). For example, visual feedback information reduces the activity that arises from the length sensors of muscles (the muscle spindles) (29). Furthermore, the amount of proprioceptive feedback from the legs during various locomotor activities determines the influence of vestibulospinal input on the stabilization of body movement (2,12). Conversely, somatosensory loss increases vestibulospinal sensitivity (25).

Brainstem. In addition, there is phase-linked cortico-spinal control of locomotion in humans (27) and in other mammals (8,9). Voluntary commands have to interact with the spinal locomotor generator to change, for example, the direction of gait or to avoid an obstacle (8,9). For most other rhythmic elementary motor behaviours, such as hopping or swimming, CPGs are also assumed to exist (2). Any disturbance of this finely coordinated interaction between afferent inputs and pattern generation after a central lesion, such as stroke or spinal cord injury, leads to a movement disorder.

Adequacy of animal models. The nature of motor-control mechanisms in humans can usually be deduced only by indirect methods; such mechanisms are inferred from knowledge obtained from animal experiments. Consequently, it is not surprising that new treatments in neurorehabilitation are frequently founded on basic research in quadrupeds (13). For example, research on walking in cats has led to new therapies, such as locomotor training for patients with spinal cord injuries (13).

For most of the basic mechanisms that underlie locomotion, there seems to be no fundamental difference between bipeds and quadrupeds (13,14). Essential spinal neuronal mechanisms, such as the afferent inputs that determine the locomotor pattern (including hip-joint-related and load-receptor-related inputs) are probably similar for quadrupedal and bipedal locomotion.

Nevertheless, there are also differences in the quantitative relationships between central neuronal mechanisms and peripheral input. For example, the regulation of bipedal gait requires specific neuronal mechanisms to maintain the body in an upright position. Furthermore, the ability of the isolated spinal cord to generate locomotor movements is considerably greater in the spinalized cat or rat than in the monkey or in humans (14). These differences might be due to a greater dominance of supraspinal control over spinal neuronal circuits in humans.

**Spiralization**
Surgical separation of the spinal cord from the brain.

**Spinal Stretch Reflex**
Also known as the short-latency reflex, this is the simplest reflex known. Muscle stretch is detected by muscle spindles, the afferent (Ia) fibres of which monosynaptically (and polysynaptically) excite the motor neurons that innervate the same muscle, leading to muscle contraction.
Reflex mechanisms

The adaptation of the locomotor pattern to external demands is achieved by proprioreceptive input that continuously modulates the programmed pattern during locomotion according to information from peripheral sensors. Proprioreceptors include receptors of the locomotor system that are located in the muscles and tendons, as well as other mechanoreceptors in the joints and the skin. The impulses of these receptors—which signal, for example, muscle stretch or tension—are conveyed to the spinal cord by afferent nerve fibres of different diameters, and hence of different excitability and conduction velocity. On the basis of these differences, the input from various types of receptor can be separated into fibre types of group I and group IV (Table 1). For example, impulses from static muscle length (spindles) are mediated by group Ia afferents, whereas those representing static muscle length are carried by group II fibres, and information about tension developed at the tendons (measured by Golgi organs) is transmitted by group Ib fibres to the spinal cord. Only the group Ia fibres have direct excitatory connections to the motor neurons of the same muscle—they are part of the monosynaptic stretch reflex, which has a characteristic short latency (~40 ms). The other afferent fibres converge on spinal interneurons that project in a more complex way to the motor neurons of leg muscles; consequently, their afferent input usually leads to responses in synergistic muscle groups with a longer latency (starting at ~70–80 ms). This pathway represents the polysynaptic, or long-latency, reflex mechanism (Table 1).

For methodological reasons, there has been a bias towards the simplest reflex system, the monosynaptic stretch reflex, in experimental studies of the afferent sources that contribute to the regulation of human gait. Most studies have focused on the contribution of type Ia afferents using the H-reflex technique (which measures the monosynaptic reflex response of the muscle to low-intensity electrical stimulation of group Ia afferents). However, as I discuss below, the contribution of this reflex system to the regulation of locomotion is limited. The significance of, for example, type Ib, II or III afferents to locomotor movements has been underestimated.

In fact, there is multisensory afferent input during locomotion both in the cat and in humans. This proprioreceptive input arises from muscles, skin, joints and tendons. One of the primary functions of proprioceptors is to detect unexpected events and to initiate rapid compensatory electromyographic (EMG) responses (Table 1). Recently, it has become clear that proprioceptors have further roles—for example, in the regulation of motor output during unperturbed movements.

Three reflex systems that are involved in locomotion are described in the following sections. For two reflex systems, the source of afferent input is clearly defined: the monosynaptic reflexes, which are mediated by group Ia afferents; and the cutaneous reflexes, which are mediated by skin afferents. The third reflex system, the polysynaptic reflexes, integrates afferent inputs from different sources.

Monosynaptic reflexes. The monosynaptic reflex was described in detail as early as 1922 (Ref. 20) and represents the most extensively investigated proprioreceptive reflex system. Monosynaptic reflex responses can be recognized clearly by the characteristic short-latency latency of the EMG responses after muscle stretch in different motor conditions.

The potential significance to locomotion of group Ia afferent input lies in the fact that its gain can be modulated by presynaptic inhibition (Ref. 21) (that is, type Ia excitatory input to the motor neurons can be attenuated, for example, by supraspinal influences) and by changes in muscle-spindle sensitivity (Ref. 22, 23). This sensitivity is controlled by the fusimotor system, which can vary the strength of activation of intrafusal muscle fibres in muscle spindles by gamma motor neurons. Muscle-spindle activity probably also contributes to an internally modeled reafference that combines with
motor commands to ensure the accuracy of body movements. These internal models also have implications for the normal and impaired control of human locomotion.

During locomotion, the threshold and amplitude of the soleus H-reflex is modulated over the entire step cycle. The functional implications of this modulation of group Ia afferent input during locomotion are suggested to be threefold. First, facilitation of the gastrocnemius/soleus stretch reflex at the end of the stance phase contributes to compensation for ground irregularities and assists during the push-off phase. Second, the depression of type Ia inputs to leg extensor motor neurons during the swing phase prevents the occurrence of the extensor stretch reflex during ankle dorsiflexion. And third, type Ia afferents are proposed to have an important role in the continuous online control of joint movements.

Nevertheless, the functional significance of monosynaptic stretch reflexes during gait remains unclear, largely for reasons related to the properties of the monosynaptic stretch reflex itself. The monosynaptic reflex system is highly sensitive to small inputs, and its function during gait should, therefore, be restricted to compensation for small ground irregularities. This is consistent with the observation that leg muscle vibration, which excites type Ia afferent input, affects human locomotion only a little.

**Cutaneous reflexes.** Muscle responses induced by electrical stimulation of a sensory nerve of a limb are mediated by cutaneous reflexes. These reflex responses appear in different muscles of the limb with a latency that is compatible with a spinal pathway. In human leg muscles, the task dependency of cutaneous reflexes has been shown in standing versus running or walking, and in cycling versus static contraction. Cutaneous reflexes in leg muscles are sensitive to the specific motor task that is performed, and undergo profound modulation depending on the context in which they are evoked. Furthermore, cutaneous reflex modulation is nerve specific: that is, it depends on the nerve that is stimulated, and this seems to be important functionally. Certain features of cutaneous-reflex modulation, such as task dependency, have been suggested to include central pattern-generating elements. Such influences of the CPG on rhythmical and cyclical leg movements would be in parallel with observations made in the cat.

**Polysynaptic reflexes.** It has been proposed that polysynaptic reflexes are mediated mainly by muscle proprioceptive input from group II afferent fibres (for example, from static muscle spindles or skin) and possibly from group III fibres (carrying information mainly from joint capsules and ligaments) (FIG. 2a). Polysynaptic spinal reflexes produce functionally useful compensatory responses during locomotion, which are more complex than simple stretch-reflex responses.

As this pathway is polysynaptic, it allows the integration of inputs from muscle, joint and cutaneous afferents, and convergence with commands from supraspinal centres to common spinal interneurones. In addition, this reflex system has excitatory and inhibitory connections to both extensors and flexors. The sensory input determines the direction, velocity and amplitude of the adjustment that is needed to restore the subject's centre of gravity over the feet and to generate the required pattern of leg muscle activation. Consequently, this reflex system leads to functional activation of synergistic muscle groups of both legs, and it can clearly be separated from segmental stretch-reflex responses, which affect only individual muscles.

A polysynaptic pathway also mediates the effects of flexor-reflex afferent (FRA) fibres. Although the modulation of flexion reflexes has several similarities to the polysynaptic spinal reflexes discussed above, there are also distinct differences.

The sensory input determines the direction, velocity and amplitude of the adjustment that is needed to restore the subject's centre of gravity over the feet and to generate the required pattern of leg muscle activation. Consequently, this reflex system leads to functional activation of synergistic muscle groups of both legs, and it can clearly be separated from segmental stretch-reflex responses, which affect only individual muscles. A polysynaptic pathway also mediates the effects of flexor-reflex afferent (FRA) fibres. Although the modulation of flexion reflexes has several similarities to the polysynaptic spinal reflexes discussed above, there are also distinct differences. First, in people with spinal cord lesions, there is a loss of polysynaptic spinal reflexes, but the flexor reflex can still be elicited. Second, the characteristic feature of the flexor reflex is to serve as a withdrawal reflex to noxious stimuli, which is released as a direct response by the CPG, rather than in modulating the locomotor pattern.
adapt to irregularities of the ground. And third, the activity of spinal polysynaptic reflexes depends on the presence of contact forces, whereas flexor reflex responses can be elicited by tibial nerve stimulation independently of loading.52

Two main sources of afferent input are probably integrated in the polysynaptic reflex system: load-related and joint-position-related information. Load receptors, or graviceptors, are thought to signal the influence of gravity on the body to the spinal cord. There is only indirect evidence for such receptors in humans. For many years, the question of how the position of the body’s centre of mass relative to the feet is signalled to the CNS has been neglected in most studies of human locomotion. To achieve appropriate gain control of posture, reflexes, information is needed that signals the influence of gravity on the body. This information is insufficiently provided by muscle stretch receptors and the vestibular system.

**Essential sources of proprioception**

During locomotion, multisensory proprioceptive feedback is continuously weighted and selected. This process depends on the requirements of a particular locomotor task and the availability of afferent input. According to observations made in healthy subjects, small children (Box 1) and patients with paraplegia,53 afferent inputs from load receptors and hip joints make essential contributions to the activation pattern of leg muscles during human locomotion.

It has been proposed that proprioceptive input from extensor muscles, and probably also from mechanoreceptors in the sole of the foot, provides load information.54 The afferents that signal hip-joint position come mainly from muscles around the hip. The role of this afferent activity in rhythmic locomotion is to shape the pattern, to control phase transitions and to reinforce ongoing activity. Simple stretch and cutaneous reflexes might be involved in compensating for irregularities and in adapting to ground conditions.

**Load-related afferent input.** A potentially excitatory function of load receptors during locomotion was first described for the extensor muscles of the cat55-57. Extrinsic load receptors are also suggested to provide essential information about the body’s centre of gravity during locomotion in humans58,59. Experiments in the cat indicated that these receptor signals might arise from Golgi tendon organs and be carried by type Ib afferents to the spinal locomotor generator.

In humans, the influence of load receptors on the regulation of stance and gait became evident from studies of infant stepping60 and of weightlessness induced in adult humans either during space flight61 or by water immersion45. Furthermore, it became clear that body load has an effect on the magnitude of the polysynaptic response, but not on the short-latency stretch reflex in the gastrocnemius46,47,48,49,50,51. An influence of load-receptor input on vestibular-evoked postural responses was also described recently for asymmetrical standing62 (unequal distribution of body load on the two legs). It was suggested that there is a central interaction between load-related afferent input from the periphery and descending signals.

The effect of load-receptor input on leg extensor activation during the stance phase of gait might be reinforced by heteronymous reflexes from ankle dorsiflexors.63 One can assume that, during the stance phase of locomotion, type Ib afferents from extensors inhibit the flexors.64 This is functionally meaningful because the load on the stance limb must decrease before swing can be initiated. In addition, extensor reflexes are reinforced during the stance phase by positive feedback, which contributes to load compensation without leading to instability.

**Joint-position-related afferent input.** In the cat, there are two main sources of afferent input that lead to rhythm entrainment and/or resetting of locomotor activity. Such input can either block or induce a switch between the alternating flexor and extensor locomotor bursts. The first of the different sources that satisfy these criteria is related to load, whereas the second is related to hip position.65,66 For example, a locomotor rhythm can be entrained by using rhythmic hip movements in spinalized67 and decerebrate68 cats. The afferents that signal hip-joint position come mainly from muscles that act around the hip. It has been suggested that receptors of the hairy skin can also provide high-fidelity information about knee-joint movements in humans69.

In humans, observations made in infant stepping and in the isolated spinal cord of people with paraplegia...
(see below) highlight the significance to locomotor activity of receptor input from the hip joint. By contrast, the contribution of ankle-joint input to human locomotion seems to be restricted to the stretched muscles around the ankle joint [21].

**Differential control of flexors and extensors**

In recent years, several studies have indicated that there is differential control of leg flexor and extensor muscles under functional conditions (Fig. 2a). Furthermore, some observations (see below) indicate that there is centrally determined dominance in the control of leg flexor activity, but that proprioceptive input determines extensor activation.

In humans, there are powerful presynaptic inhibitory effects of flexor group I afferents on extensor group I afferents, but these effects are weak from extensors to flexors [20]. Corticospinal projections to lower-limb motor neurons in humans are stronger to the flexor tibialis anterior muscle than to the extensor soleus muscle [31]. In line with this, the effect of transcranial magnetic stimulation of the leg area of the brain is restricted mainly to the flexor muscles at distinct phases of swing during locomotion [22]. During human locomotion, gastrocnemius EMG activity is modulated continuously by peripheral afferent input, whereas the EMG of the tibialis anterior is predominantly centrally determined [22]. In cat locomotion, weak static fusimotor effects are present in extensors, but there are strong effects in flexor muscles [32]. Finally, in recent models of locomotor control [33], the neuronal circuits that control leg flexor activity on both sides reciprocally inhibit each other during walking, whereas the extensor half-centres (spinal neuronal circuits that are responsible for the activation of leg extensor muscles) are not directly coupled to each other. Accordingly, flexor activity is an important source of modulatory signals from spinal interneurons to the motor cortex in humans [34] and in cat [35].

**Locomotor capacity of the isolated spinal cord**

Evidence for a spinal pattern generator for locomotion in humans has come from studies of spontaneously occurring step-like movements [36] and from locomotor movements induced on a treadmill with body-weight support in people with incomplete and complete paraplegia [37,38]. Load-related input has an important role in inducing and training the locomotor pattern in these patients [38]. However, the strength of leg muscle activation remains low compared with that of healthy subjects, and the effects of training are lost over time in people with complete paraplegia [38]. These results indicate that there is training-induced plasticity of neuronal centres in the isolated spinal cord that is dependent on specific afferent input. This might be of relevance for future interventional therapies (by combining training with regeneration-inducing agents).

In a recent study, locomotor movements were assisted by a DRIVEN CANT ORTHOSIS (DCO) that allowed stepping movements to be induced even with 100% body unloading [39]. Under these conditions, physiological locomotor-like movements alone did not lead to leg muscle activation, this occurred only in combination with loading of the legs. This was the case for both healthy subjects and people with complete paraplegia or tetraplegia. In addition, the DCO allowed the effects of 'locomotor movements' restricted to hip joints to be studied in people with complete paraplegia [32]. An important observation was that the pattern of leg muscle activation was almost unchanged after knee-joint movements were blocked in these patients. Furthermore, isolated joint movements of the foot evoked only local responses. This indicates that afferent input related to hip-joint position has an important influence on leg muscle activation by the isolated spinal cord.

**Movement disorders**

Any damage to the central or peripheral nervous system can be followed by an impairment of proprioception that leads to a movement disorder. Here, only the frequently occurring movement disorders associated with spasticity and Parkinson's disease are dealt with.

**Spasticity.** After a central motor (cerebral or spinal) lesion, a profound alteration of proprioception occurs in the form of a disinhibition of short-latency stretch reflexes and the loss of functionally important long-latency reflexes (Fig. 3). These changes are associated with two forms of adaptation that can lead to an improvement in mobility: the development of spastic muscle tone, which compensates for part of the loss of supraspinal drive; and plasticity of spinal locomotor centres, which can be specifically trained.
The impaired supraspinal control of spinal reflexes results in a loss of inhibition of short-latency reflexes, which leads to hyperexcitability of the simple stretch reflexes. This is combined with reduced facilitation of the functionally more important polysynaptic, or long-latency, reflexes, which leads to a reduced proprioceptive contribution to leg muscle activation during gait. Therefore, spastic gait is associated with reduced and less well-modulated leg muscle activity. Consequently, the development of tension in leg extensor muscles during gait differs from that in healthy subjects and seems to be independent of exaggerated stretch reflexes (Fig. 3). Furthermore, after a central motor lesion, the modulation of both cutaneous and short-latency stretch reflexes during the step cycle is impaired. As a consequence, the fast regulation of motor neuron discharge, which characterizes normal muscle activation, is absent. This contributes to the impairment of walking ability in people with spasticity.

Although muscle spasticity is neural in origin, there is good evidence that spastic muscles are abnormal (Fig. 3). For example, reflex stiffness of ankle extensors in people with spastic hemiparesis seems to be normal, but the intrinsic muscle stiffness is significantly higher than in control muscles. Even the clinically assessed muscle hypertonia in hemiparetic patients is found to be associated primarily with muscle contracture and less with exaggerated reflexes. In line with these observations, recent studies indicate that spasticity results in a major alteration of the normal muscle–joint anatomical relationship.

Changes in the mechanical properties of muscle fibres can be attributed, at least in part, to muscle shortening. This might be the result of a decrease in the number of sarcomeres along the myofibrils, accompanied by increased resistance to stretch. These observations highlight the need to develop new rational treatment procedures to replace the anti-spastic drugs that are frequently prescribed for mobile people with spasticity. For example, by appropriate training programmes, compensatory processes could be guided in a preferable way.

In conclusion, after a central motor lesion, motor units are transformed in such a way that regulation of muscle tone is achieved at a lower level of neuronal organization, which in turn enables the patient to walk. Therefore, the altered regulation of spastic gait can be considered as compensating for the loss of central motor–system function.

**Parkinson’s disease.** Several reports have indicated that force control in Parkinson’s disease is impaired during both voluntary movements and locomotion. Impaired load sensitivity develops with age and becomes exaggerated in Parkinson’s disease. The consequence of such an impaired load–receptor mechanism is a reduction in leg extensor activation that is proposed to contribute to the gait disorder (Fig. 2b). A similar, although opposite, change in threshold or bias has been described in cerebellar patients, who show hypermetric postural responses during stance.

It is unclear how dysfunction of the basal ganglia could affect load perception and loading responses during gait. In this context, it is interesting to note that the administration of levodopa (3,4-dihydroxyphenylalanine, or l-DOPA) or dopamine agonists is associated with a depression of proprioception in Parkinson’s disease. The enhanced activation of the tibialis anterior during the swing phase of gait in people with Parkinson’s disease might reflect defective extensor suppression of the flexor burst-generating circuitry. The control of gait in these patients relies more on visual information and is exerted through modulation of leg flexor EMG activity. This is in keeping with the more general observation that visual information can substitute to some extent for the reduced proprioception. A strong dependency of people with Parkinson’s disease on visual cues during walking becomes evident when an optical flow pattern is imposed during stepping on a treadmill. Whereas the walking velocity of healthy subjects is affected for only a short time by the pattern, people with Parkinson’s disease continuously change their speed with the movements of the optical flow.

**Reliability of clinical tests**

Neurorehabilitation is one of the most rapidly expanding fields in medicine, and this is leading to increasing costs of various forms of treatment. Only recently have studies been conducted to address the effects of rehabilitation treatments on locomotion and functional-level outcomes, especially in people with hemiparesis after stroke and with Parkinson’s disease. Nevertheless, the assessment of isolated physical signs still prevails. Therefore, an important aim for the future is to establish standardized functional tests.

**Physical signs and function.** Movement disorders are usually the first and most pronounced symptoms of an impairment in motor–centre function. The physical signs obtained during clinical examination, including reflex excitability and muscle tone, can lead to a diagnosis, but give little information about the pathophysiology, course and appropriate treatment of a movement disorder. For example, stretch–reflex excitability and muscle tone differ fundamentally between the passive (clinical examination) and active (movement) conditions. An appropriate treatment should not be cosmetic (that is, correcting an isolated clinical parameter that does not affect function). For adequate therapy of a movement disorder, it is essential to understand and analyse the function of the reflexes and motor centres that are involved, and their interaction with the biomechanical effector system in the motor task that is impaired. Adapted behaviour emerges as an integration of the biomechanical effector system and control properties of the nervous system.

This requires evaluation of the behaviour and function of neuronal (EMG) and biomechanical (joint movement) measurements, as any changes in these systems might lead to a movement disorder. Nevertheless,
it is important to be aware that any change in a measurement might be secondary to or compensate for the primary dysfunction of the motor system that is involved in the impaired movement. The effect of any treatment, either drugs or physical therapy, has to be assessed on the basis of function.

There are three requirements for appropriate evaluation of a therapeutic effect on function: that the spontaneous recovery of function be separated from the effect of any therapy; that the intensity and duration of a particular physical therapy, which strongly influences its effect, be determined; and that patients' functional impairments be made comparable by the use of internationally standardized scores for classification.

**Appropriate assessment of function.** Owing to the exquisite task-dependent regulation of nervous system function (discussed earlier), clinical tests must be functional and specific. At present, it is a common and 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 the Perin spasm-frequency scale, respectively. For people with spinal cord injury, the American Spinal Injury Association (ASIA) has developed a standardized neurological assessment—the ASIA classification of motor and sensory deficits. 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 that relates to function. Locomotor ability has been classified into 19 items. An ongoing 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 who undergo intensive locomotor training can achieve improved locomotor function without a change in motor score (Fig. 4 and V.D. et al., unpublished observations). In these cases, relatively little voluntary force in the leg muscles (reflected in the ASIA score) is required to acquire the ability to walk when functional training is given.

For the future, the effectiveness of any new interventional therapy should be assessed by internationally accepted functional scores for upper- and lower-limb movements in combination with motor scores of selected limb muscles. Motor and sensory scores are most likely to reflect a spontaneous recovery of function, as they depend on the integrity of corticospinal connections. By contrast, improvement of locomotor function after spinal cord injury also reflects the plasticity of neuronal spinal centres below the level of the lesion. With the combined assessment of voluntary force and automatic function, the superiority of any new interventional therapy on functional movements might reliably be assessed.

**Conclusions**

Effective rehabilitation after a central motor lesion depends on the following points. First, knowledge about the neuronal mechanisms that are involved in the normal movement, and about the interactions between the central programme and afferent inputs. It is also necessary to take into account the possibility that a movement disorder is the consequence not only of the primary motor lesion, but also of secondary processes that can be compensatory and should be supported during rehabilitation. The aim of rehabilitation should focus on an improvement of function by taking advantage of the plasticity of neuronal centres, rather than being directed towards the correction of isolated clinical signs, such as reflex excitability. Finally, to monitor the outcome and assess the effectiveness of any interventional therapy, standardized functional tests should be established.
82. This paper a physiological basis for the differential neural control of lower limb muscles.
95. This paper provided clear evidence that increased muscle tone in spastic hemiparesis is due, in large part, to muscle contracture.
101. Acknowledgements

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Contribution of stretch reflexes to locomotor control: a modeling study

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Abstract. It is known that the springlike properties of muscles provide automatic load compensation during weight bearing. How crucial is sensory control of the motor output given these basic properties of the locomotor system? To address this question, a neuromuscular model was used to test two hypotheses. (1) Stretch reflexes are too weak and too delayed to contribute significantly to weight-bearing. (2) The important contributions of sensory input involve state-dependent processing. We constructed a two-legged planar locomotor model with 9 segments, driven by 12 musculotendon actuators with Hill-type force-velocity and monotonic force-length properties. Electromyographic (EMG) profiles of the simulated muscle groups during slow level walking served as actuator activation functions. Spindle Ia and tendon organ Ib sensory inputs were represented by transfer functions with a latency of 35 ms, contributing 30% to the net EMG profile and gated to be active only when the receptor-bearing muscles were contracting. Locomotor stability was assessed by parametric variations of actuator maximum forces during locomotion in open-loop (“deafferented”) trials and in trials with feedback control based on either sensory-evoked stretch reflexes or finite-state rules. We arrived at the following conclusions. (1) In the absence of sensory control, the intrinsic stiffness of limb muscles driven by a stereotyped rhythmical pattern can produce surprisingly stable gait. (2) When the level of central activity is low, the contribution of stretch reflexes to load compensation can be crucial. However, when central activity provides adequate load compensation, the contribution of stretch reflexes is less significant. (3) Finite-state control can greatly extend the adaptive capability of the locomotor system.

1 Introduction

At an international symposium on movement and sensation held in Cairns, Australia in 2001 we made the provocative suggestion that stretch reflexes do not contribute substantially to load compensation in mammalian locomotion (Prochazka et al. 2002). We made this suggestion on the basis of the relatively small size and long latency of electromyogram (EMG) responses that occur after ground contact in the stance phase of the locomotor step cycle. Some initial biomechanical modeling we had done indicated that these responses may only have a modest effect on the kinematics of quadrupedal gait.

Classical studies demonstrated many years ago the ability of the spinal cord to produce the basic locomotor rhythm in the absence of sensory feedback (Brown 1911). Brown coined the term “intrinsic factor” to describe the underlying neural mechanism, and more recently Grillner renamed this the “central pattern generator” (CPG) (Grillner and Zangger 1974). The fact that under some circumstances rudimentary weight-bearing locomotion can occur in the absence of sensory input indicates that the biomechanical properties of the limbs provide some flexibility in load compensation (Pearson et al. 2003). However, studies on animal and human subjects have also shown that after sensory loss gait is far less coordinated and less able to adapt to changes in terrain and body posture (Bickel 1897; Lajoie et al. 1996; Bloem et al. 2002). Thus two main roles are usually attributed to sensory feedback: it provides control of the stiffness of individual muscles and it allows higher-level control of balance, stability, and coordination.

Stretch reflexes associated with locomotion, on which we will concentrate in the following discussion, have been extensively studied with a variety of physiological techniques for over a century. Most of the studies have dwelt on the electrical responses of muscles to electrically evoked sensory inputs or to imposed muscle stretching and shortening. The amplitude of sensory-evoked EMG responses is modulated throughout the
step cycle (Akazawa et al. 1982; Capaday and Stein 1986; Dietz et al. 1990; Stein et al. 2000), so that the contribution of stretch reflexes has been posited to be highest when the receptor-bearing muscle is active. Estimates of the relative contribution of stretch reflexes to overall muscle EMG during locomotion are in the range 25%–35% (Yang et al. 1991; Bennett et al. 1996; Stein et al. 2000). But if the sensory input due to ground contact is removed at the onset of the stance phase of cat locomotion (“foot-in-hole” experiments), changes in EMG appear surprisingly late (30–40ms) (Gorassini et al. 1994). In another set of experiments, stretch of the ankle extensors after ground contact was artificially exaggerated (Gritsenko et al. 2001). This confirmed the timing of the stretch reflexes and further emphasized the modest size of the reflex components in unperturbed steps.

So what is the functional role of the stretch reflexes during locomotion? After recovery, deafferented animals show little change in yield of the limb during the stance phase of level overground locomotion, though in more demanding tasks abnormally large yielding can occur (Abelew et al. 2000). However, in experiments of this type it could be that compensatory changes in central drive learned over a period of time may replace the missing stretch reflex components and thereby mask the role of these reflexes under normal conditions. The ideal experiment would be to study locomotor performance when sensory input is suddenly abolished. It is hard to see how this manipulation could be done in real animals, but it is certainly possible in biomechanical simulations. We have used these in this study to test the following two hypotheses: (1) Stretch reflexes are too weak and too delayed to contribute significantly to weight-bearing and (2) the important contributions of sensory input involve state-dependent processing.

2 Methods

2.1 Structure of the locomotor model

We developed a planar locomotor model of two hind limbs attached to a horizontal torso supported at the front by a frictionless wheel (Fig. 1). Each hindlimb comprised four rigid-body segments (thigh, shank, foot, and toes) that were driven by six musculotendon actuators. All joints were modeled as frictionless revolutes. The model was developed using Matlab version 6.1 software (The MathWorks, USA) coupled to Working Model 2D version 5 software (Knowledge Revolution, USA). The foot interactions with the ground were modeled with the use of Working Model software. The following parameters were chosen to minimize slipping: the coefficient of restitution was set to 0.1 and the coefficient of Coulomb friction to 10. The results were computed using the Kutta-Merson numerical integration method with 0.1-ms fixed steps and 1/100 mm error tolerance.

In the model to be presented, the dimensions, masses of the segments, and moment arms of the actuators were chosen approximately to mimic those of a cat. All simulations were started just prior to foot contact, with initial velocity of the trunk and leading leg segments set to 0.7 m/s. We intentionally did not strive for a rigorously accurate model as we were seeking conclusions that would generalize across a large range of parametric variation (see Discussion). Internal properties of the individual actuators were modeled by Hill-type force-velocity (Hill 1938) and linear force-length (Gillard et al. 2000) relationships. Muscle force was calculated as

\[ F = F_{\text{max}} \cdot f_r \cdot f_l \cdot a_t + F_{\text{passive}} \cdot f_{l, \text{passive}}, \]

where \( F \) is muscle force, \( F_{\text{max}} \) is the maximum isometric force, \( f_r \) and \( f_l \) are the force-velocity and the force-length relations respectively, \( F_{\text{passive}} \) is the maximum passive force, \( f_{l, \text{passive}} \) is the normalized passive force-length relation (Fig. 2a), and \( a_t \) is muscle activation, whose dynamics were described by the He-Zajac-Levine excitation-contraction coupling equation (He et al. 1991):

\[ a_t + \frac{1}{\tau_{\text{act}}} \cdot \left( \frac{\tau_{\text{act}}}{\tau_{\text{deact}}} + \left[ 1 - \frac{\tau_{\text{act}}}{\tau_{\text{deact}}} \right] \cdot u_t \right) \cdot a_t = \frac{1}{\tau_{\text{act}}} \cdot u_t, \]

where \( \tau_{\text{act}} \) and \( \tau_{\text{deact}} \) are activation and deactivation time constants (20 ms and 40 ms, respectively) and \( u_t \) is motoneuron excitation described by Eq. 6.

Electromyographic (EMG) profiles of the simulated muscle groups during slow level walking (Fig. 2b) served as CPG outputs to the musculotendon actuators. Swing and stance durations were set to 30% and 70% of the step cycle period, respectively, which is an appropriate phase relationship for slow gait with a cycle period of 600 ms (Goslow et al. 1973; Halbertsma 1983). The activation profiles were based on a large number of locomotor studies and have been described elsewhere (Yakovenko et al. 2002).
sets of force parameters in Fig. 4 using the following formula:

\[ I = \frac{1}{n} \sum_{i=1}^{n} r_i^2, \]

(3)

where \( r_i \) is the vector magnitude defining distance from the center of the “stable” volume to each individual parameter set and \( n \) is the total number of parameter sets (100 “stable” simulations). Locomotor performance was analyzed in the plane formed by the two principal component vectors that accounted for most of the variability in the data.

The analysis was repeated in the model where the length of the ankle was increased to match the relative segment lengths of a horse. The reason for repeating the analysis in the “horse” model was to test whether our basic conclusions held in the face of large changes in limb geometry (Fig. 1). The length of the ankle relative to the femur and tibia in the horse is double that in most other mammals.

2.3 Stretch reflex model

The stretch reflex model comprised simulated feedback from spindle Ia and tendon organ Ib afferents onto homonymous motor pools. Heterogeneous excitation and reciprocal inhibition components of afferent feedback, described by Lundberg (Engberg and Lundberg 1969), were neglected for the sake of simplicity. The contributions of Ia and Ib afferents to the output of homonymous motoneuron pools were represented by the following formulæ derived from the literature (Prochazka 1999):

Ia model:

\[ f_{\text{IA}}(l, v) = K_{\text{IA}} \cdot (21 \cdot v^{0.5} + 200 \cdot l + 60), \]

(4)

Ib model:

\[ f_{\text{IB}}(s, F) = K_{\text{IB}} \cdot \frac{(s + 0.15) \cdot (s + 1.5) \cdot (s + 16)}{(s + 0.2) \cdot (s + 2) \cdot (s + 37)} \cdot F, \]

(5)

where \( f_{\text{IA}} \) is a time function of the Ia afferent firing rate response to changes of muscle length and velocity, \( l \) is the muscle length in rest length units, \( v \) is the muscle velocity expressed in rest length per second, \( f_{\text{IB}} \) is the tendon organ response in the frequency domain, \( s \) is a frequency domain operator, and \( K_{\text{IA}} \) and \( K_{\text{IB}} \) are gain coefficients. The middle of the range of motion of each musculotendon actuator was chosen as its rest length. Note that the above equations are in the time and frequency domains, respectively. Though Eq. 3 can be written as a differential equation in the time domain, its filtering properties are then very difficult to infer. Inspection of Eq. 3 indicates that tendon organs act as high-pass filters, with 20 dB/decade increases in transmission occurring between the following pairs of frequencies: 0.15–0.2, 1.5–2, 16–37 rad/s (i.e., ~0.02–0.03, 0.2–0.3, and 2.6–5.9 Hz). Matlab Simulink allows a mixture of time and frequency domain transfer functions within the same model.
The Ia and Ib reflex feedback contributed to the muscle contractile force with a latency of 35 ms (Gorassini et al. 1994; Gritsenko et al. 2001). This feedback was active only when the CPG EMG profile for the receptor-bearing muscle was nonzero to satisfy the known modulation of the stretch reflex within the step cycle (Capaday and Stein 1986). The gain coefficients \( K_i \) and \( K_b \) were adjusted so that the Ia and Ib signals each added a mean of 15% to the CPG EMG component throughout a full locomotor cycle. Thus, together both signals contributed 30% to the CPG EMG profiles, which is in accordance with the suggested reflex contribution to the EMG during walking (Bennett et al. 1996; Stein et al. 2000). When the stretch reflex component was present, the excitation function in Eq. 2 was of the form

\[
 u_t = CPG_t + f_{Ia} + f_{Ib}.
\]

### 2.4 Finite-state rules

The following IF-THEN rules were used to model higher-level control of phase switching in the step cycle (Granat et al. 1993; Prochazka 1993):

1. Stance to swing transition: IF stance AND ipsilateral hip is extended AND ipsilateral leg is unloaded, THEN swing.
2. Swing to stance transition: IF swing AND ipsilateral hip is flexed AND ipsilateral knee is extended, THEN stance.

The thresholds for the firing of these rules were determined on a trial-and-error basis. The schematic of all control systems implemented in the model are shown in Fig. 2c.

### 3 Results

#### 3.1 Simulation of "deafferentation" experiment

Figure 3 illustrates two examples of the type of experiment mentioned in the introduction, where a sudden change in sensory feedback occurs during locomotion. In the left panels (Fig. 3a–c) sensory feedback was suddenly withdrawn, whereas in the right panels (Fig. 3d–f) sensory feedback was suddenly added. In both cases the sensory inputs contributed about 30% to the overall muscle activation profiles as described above. In the example on the left the amplitudes of the centrally generated components were deliberately chosen to produce forces that alone would be insufficient for weight bearing, whereas in the example on the right the CPG activation levels were chosen to be sufficient to produce stable locomotion. In the first case, withdrawal of the stretch reflex contribution led to a collapse of the model, from which one would conclude that stretch reflexes are crucial to maintaining stable locomotion. This would refute the suggestion we made in Cairns (hypothesis 1 above) that stretch reflexes are too weak and too delayed to contribute significantly to weight...
Again there will be a restricted range of peak ankle extensor force compatible with stable locomotion. When combined with the stable combinations of the other two variables, the stable region may now be represented by the shaded volume in the three-dimensional plot. By calculating eigenvectors and eigenvalues for the data autocorrelation matrix it is possible to define orthogonal axes along which the parameter combinations making up the volume are the most spread out. These axes thus “account for” the largest amount of variation in the data and are called the “principal components” (PC). Principal component analysis (PCA) can be extended to all six parameters.

3.2 Locomotor performance in the absence of sensory feedback

Locomotor performance was explored in six-dimensional parameter space of musculotendon actuator forces using a gradient-descent method with random initial position. Figure 5 shows sets of parameters associated with stable locomotor performance of the model driven by the CPG alone (gray circles) and the CPG with the addition of stretch reflexes (black upward triangles). Figure 5a–c show the projections of six-dimensional data on the planes formed by the three extensor actuators, whereas Fig. 5d–f show the projections of the same data on the planes formed by the remaining predominantly flexor actuators. The origin of the plots corresponds to zero force in all actuators. It is clear from Fig. 5 that stable locomotion can emerge over a fairly large range of force parameter variation, even in the absence of sensory feedback. Similar results were previously obtained using inverse dynamics or neural networks to optimize activation patterns (Taga et al. 1991; Taga 1998; Neptune et al. 2001; Ogihara and Yamazaki 2001).

3.3 Effect of stretch reflexes on locomotor performance

Figure 5 shows a stability plot for the cat model where stretch reflexes contributed about 30% of the overall activity (see Eq. 6). In Fig. 5a–c the volume of stability associated with the model with sensory feedback (upward triangles) extends much closer to the origin than in the “deafferented” model (gray circles). This was also the case for the “horse” model (not illustrated). This indicates that stretch reflexes are capable of increasing extensor muscle stiffness when central drive is low and thus provide the necessary load compensation. Despite the long latency of the reflexes and their dynamic nature, their 30% mean contribution essentially takes the place of the missing 30% of central activation. This explains the destabilizing effect of a sudden removal of the stretch reflex contribution in Fig. 3a–c where the central activation levels were low. A contribution of stretch reflexes to flexor activity does not seem essential judging by the
Fig. 5a-f. Locomotor performance plots of stable trials of models without sensory feedback (gray circles) and with stretch reflex (black upward triangles) are plotted as projections on the planes of three extensor (a–c) and three mainly flexor (d–f) musculotendon actuators. Horizontal and vertical axes represent maximum isometric force at muscle rest length ($F_{max}$ in Eq. 1) of the corresponding musculotendon actuator. The large region of stability of the model without sensory feedback indicates that the intrinsic stiffness of the muscles suffices to compensate for kinetic and kinematic variations over a fairly large parametric range. Since the origins of the coordinate systems largely overlapping stable parameter spaces of both models in Fig. 3d–f.

In the example in Fig. 3d–f the addition of stretch reflexes when central activation was adequate to provide stable locomotion has a destabilizing effect. However, if we consider all the stable simulations obtained, the calculated moment of inertia (see Eq. 3) of the model with stretch reflexes was 1.9 times larger than that without ($I_{CPG+SR} = 5.6 \times 10^4 N^2$, $I_{CPG} = 3.0 \times 10^4 N^2$). This indicates that stretch reflexes can contribute significantly to load compensation and, taken over the entire parameter space, may even stabilize locomotion in many cases.

3.4 Contribution of state-dependent control to locomotor stability

In the stretch reflex modeling above, the cycle frequency of the CPG pattern was invariant. This placed constraints on the range of gait velocities consistent with stability. Adaptive control of cadence based on sensory information about actual biomechanical states might therefore be expected to increase stability. To test this hypothesis we implemented simple sensory rules to trigger the transitions between flexion and extension phases of the centrally generated pattern of muscle activation profiles. Figure 6 shows the extent to which IF-THEN sensory rules controlling step transitions (see Methods) stabilized the simulations in the cat model with CPG and stretch reflexes active. Figure 6a and c shows locomotor performance plots in the plane of two first principal components of the stable sets of parameters associated with the model with stretch reflexes in Fig. 5. The stability region is further defined by a contour plot, which shows the amount of time that elapsed in simulations before the model collapsed. In Fig. 6c the stable region was enlarged by about 30% compared with that in Fig. 6a. Note that the main increase of stability coincides with the direction of the increasing force of hip extensor actuator, which regularly leads to an increase of forward velocity.

An analysis of the velocities of gait corresponding to the stable and unstable regions showed that stability was associated with a fairly narrow band of gait velocities. Figure 6b shows that gait velocity was closely related to stride length for all of the stable simulations. This is not surprising given that the frequency of the CPG rhythm in all of these simulations was constant. If stride length increases at a constant step cycle frequency, velocity...
must increase, or stability is lost. Consider the case where hip flexor forces are large but body velocity is low. The leg swings far forward and at ground contact the ground reaction force points back, decelerating the body. If velocity drops to zero before the center of mass moves over the point of support, further forward motion becomes impossible and the model collapses backward. As we shall see, stretch reflexes do not fundamentally change this effect because in essence they just augment the inherent load compensation mechanism provided by muscle stiffness and viscosity (Partridge 1966). On the other hand, conditional control can increase the range of stable velocities by adapting the cadence (cycle frequency) to the actual kinematics of the limb. The range of velocities of the stable simulations shown in the plot of Fig. 6d was greatly increased, showing that adaptive control of cadence granted by IF-THEN rules was associated with the increased range of stability.

### 3.5 Closed-loop gain of stretch reflex during locomotion

Figure 7 shows the dependence of the response of the system on the amplitude of the feedforward commands in our model. It is clear that increases in the central command are associated with decreases of the contribution of the stretch reflex loops. This cannot be attributed to changes in the generalized forces because these changes are quite small (Fig. 7b). Rather, Fig. 7c demonstrates that higher activation levels drive the extensor muscles to operate at substantially shorter

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**Fig. 6a–d.** PCA locomotor performance plots and plots of mean gait velocity vs. stride length of stable trials of models with CPG and stretch reflexes (a, b) and with CPG, stretch reflexes, and IF-THEN rules (c, d). The contour lines connect points of equal stability measured in seconds of stable gait. The region of stability in the model with IF-THEN rules is about 30% bigger, particularly in the direction of increase of hip extensor force. Labeled straight lines in a and c represent projections of the six-dimensional force axes (axis vector magnitude is 250 N) on the plane of the first two principal components. b Velocity was proportional to stride length in stable locomotion because the cycle frequency of the centrally generated pattern was constant in these trials. Stability was confined to a fairly narrow band of velocities. d Addition of IF-THEN rules to the control system shown in a and b increased the range of stable gait velocities.

**Fig. 7a–c.** Strength of stretch reflexes is modulated by muscle length. a Relationship between CPG amplitudes and relative reflex contribution for four sets of reflex gains. Both parameters are normalized to the minimal activity level required to produce stable locomotion in the “deafferented” model. Notice the decrease in the reflex component with the increasing CPG amplitude. b Mean extensor force did not change significantly with CPG amplitude except at the highest reflex gains. c Mean muscle length decreases with increasing CPG amplitudes. This effectively decreases stretch reflex loop gains (see text).
4 Discussion

The purpose of this study was to gain insight into the contribution of sensory input to the control of locomotion. Though many experiments have been done on locomotor stretch reflexes, most of these have been limited to EMG measurements (Capaday and Stein 1986; Gorassini et al. 1994; Gritsenko et al. 2001) rather than kinetic or kinematic changes of the whole limb (Sinkjaer et al. 1988; Pearson et al. 1999). The amount of EMG activation attributable to reflexes elicited by muscle length and force changes during the step cycle is generally less than 35% of the total (Stein et al. 2000). Furthermore, the reflex components have rather long latencies (Gorassini et al. 1994; Gritsenko et al. 2001). Finally, bursts of sensory input from stretch receptors elicited by electrical stimulation (Whelan and Pearson 1997) or by muscle vibration (Ivanenko et al. 2000) have surprisingly little impact on the kinematics of locomotion. All of these findings led us to propose that the biomechanical consequences of stretch reflexes elicited in the course of unperturbed gait did not contribute significantly to load compensation during weight-bearing locomotion.

The biomechanical modeling described in this paper was done to test the following hypotheses: (1) Stretch reflexes are too weak and too delayed to contribute significantly to weight bearing and (2) the important contributions of sensory input involve state-dependent processing. The results did not support hypothesis 1, but they did support hypothesis 2.

Hypothesis 1 was not supported because stretch reflexes could rescue stable locomotion in cases where the amplitudes of the CPG activation profiles were insufficient to support locomotion. On the other hand, adding stretch reflex components to CPG activation profiles that were adequate to support stable locomotion tended to increase body height, propulsion, and speed. When these increases were inappropriately scaled between muscles, locomotion became unstable. Thus, although hypothesis 1 was not supported, stretch reflexes nonetheless only seem to contribute significantly when central activation levels are low.

Regarding hypothesis 2, the incorporation of IF-THEN rules increased stability and in particular greatly increased the range of cadences and velocities of stable locomotion, even though the time course of the actual muscle activation profiles did not change. How could gait velocity vary without the activation profiles changing? The answer is that the triggering of, say, the stance-swing transition terminates the reading out of the extensor muscle activation profiles, even if they are only half completed, and initiates the reading out of the flexor activation profiles. Similarly, flexor profiles are terminated earlier in the next half cycle. The interesting point here is that cadence and gait velocity can be varied over a wide range without changing the time course or amplitude of the activation profiles but merely by skipping parts of these profiles and resetting to a new part of the step cycle. To our knowledge, this possibility has not been recognized until now.
It is important to mention some of the restrictions and limitations of the modeling performed. A general criticism of modeling of this type is that when the model contains many parameters, there is scope for choosing sets of parameters that fit one’s favored hypothesis. To safeguard against this, we deliberately avoided making the models represent faithfully the anatomy of a particular “animal”. Furthermore, our approach to the exploration of parameter space using an observer-independent stability search algorithm and PCA allowed for an unbiased representation of stability over several hundred sets of parameters in two models that represented extremes of limb geometry. The conclusions we drew regarding the two hypotheses were therefore broad based and not model specific, i.e. they remained valid in the face of a large range of parameter variations.

This is not to say that we were able to explore all types of parameter variations that could influence the conclusions. For example, the muscle models did not take into account the hysteretic property of short-range stiffness (Rack and Westbury 1973). We intend to add this characteristic in future modeling work. We did not explore all possible muscle spindle and tendon organ models (Prochazka and Gorassini 1998), nor did we vary the latency of the stretch reflex or try to represent separate short-, medium-, and long-latency reflex components or heterogeneous reflex connections. There is in any case considerable uncertainty in the literature regarding the relative sizes of such components. In previous modeling, we found that varying reflex latencies within reasonable limits did not substantially change muscle kinetic responses (Prochazka et al. 1997). By varying the level of the stretch reflex contribution during locomotion we found that closed-loop gain of the sensory evoked responses depended strongly on muscle length and velocity. This dependence was previously implicated in stabilizing positive force feedback (Prochazka et al. 1997). Since estimation of the gain of the closed-loop reflex system during various tasks poses a considerable experimental challenge, the relative level of contribution of the stretch reflex to muscle excitation remains a contentious issue. Models such as ours may greatly clarify and assist in evaluation of components of feedforward and feedback systems of motor control.

To conclude, our model provided insight into the interplay between neural commands and biomechanical properties of the musculoskeletal actuators of the locomotor system. The main conclusion was that homonymous stretch reflexes are capable of adjusting muscle forces at several joints to achieve weight bearing during gait, and this is particularly significant when central activation is low. Simple finite state rules provide dramatic improvements in flexibility and stability of level overground locomotion in our model. Cadence is constantly adjusted to kinematic state. This also raises the possibility that gait velocity could be controlled by changing the firing thresholds of sensory rules in a state-dependent controller. Our method of testing stability by exploring parametric space using PCA is novel and provides a systematic measure of the generality of the conclusions.

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Research Article

Single joint perturbation during gait: neuronal control of movement trajectory

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Abstract  The aim of this study was to investigate the effect of single joint displacement on the pattern of leg muscle electromyographic (EMG) activity during locomotion. For the first time, unilateral rotational hip or knee joint displacements were applied by a driven orthotic device at three phases of swing during locomotion on a treadmill. The response pattern of bilateral leg muscle activation with respect to the timing and selection of muscles was almost identical for displacements of upper (hip joint) or lower (knee joint) leg. The leg muscle EMG responses were much stronger when the displacement was directed against the physiological movement trajectory, compared with when the displacement was reinforcing, especially during mid swing. It is suggested that these response patterns are designed to restore physiological movement trajectory rather than to correct a single joint position. Displacements released at initial or terminal swing, assisting or resisting the physiological movement trajectory, were followed by similar and rather unspecific response patterns. This was interpreted as being directed to stabilise body equilibrium.

Keywords  Compensatory EMG responses - Interlimb co-ordination - Locomotion - Movement synergies - Movement trajectory - Neuronal control - Single joint displacement

Introduction

Many similarities exist in the way humans and other mammals co-ordinate their limb movements in response to disturbance during walking (for review see Dietz 2002). Unilateral leg
displacements of support during stance and gait evoke a bilateral response pattern with a spinal onset latency on both sides (Dietz et al. 1986a, 1989). Therefore, it was assumed that a purposeful activation pattern of synergistic leg muscles becomes released by the so-called spinal central pattern generator (for review see Dietz 1992). According to this concept, focal muscle responses to a local displacement play a minor role for the compensatory reaction. From a functional point of view, this interlimb co-ordination is necessary to maintain body equilibrium (Dietz et al. 1989; for review see Dietz 1992).

In most studies on the bilateral co-ordination of leg movements in cat and man one or both legs become perturbed. By such an approach several joints of a limb become displaced. Therefore, the source of the relevant afferent input for the bilateral co-ordination of leg muscle activation is not known. It is an unanswered question whether this input is provided by the displacement of a single joint or by the combination of the afferent input from many sensors within joints and muscles activated by the leg displacement. Nevertheless, there are observations which point out the importance of hip position for initiating the stance to swing transition with an appropriate leg muscle activation for human infant stepping (Pang and Yang 2000). The significance of hip joint afferents for locomotion was also emphasised for the chronic spinal cat (Grillner and Rossignol 1978). Furthermore, entrainment of a locomotor rhythm was obtained by using rhythmic hip movements in immobilised spinal (Andersson and Grillner 1983) and decerebrate (Kriellaars et al. 1994) cats.

The aim of this study was to evaluate the relevance of input related to different leg joints for the generation of the locomotor pattern. Therefore, the effect of single joint displacements on the leg muscle activity during locomotion was studied using a novel approach. For the first time, a driven gait orthosis (DGO) was applied, which allowed induction of a displacement at the hip or knee joint during the step cycle. It was hypothesised that hip and knee joint-related afferent input differentially contributes to the bilateral co-ordination of leg muscle activation.

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### Materials and methods

With the permission from the local Ethical Committee and the informed consent of the volunteers, the leg muscle electromyographic (EMG) responses to unilateral hip or knee perturbations during locomotion were analysed in nine healthy subjects (age 29±5 years). Surface EMG recordings were made from the activity of representative right and left as well as proximal and distal leg muscles (rectus femoris (RF), biceps femoris (BF), tibialis anterior (TA) and medial gastrocnemius (GM)). Subjects walked with the DGO Lokomat (Hocoma AG, Zurich, Switzerland) on a treadmill.

### Driven gait orthosis

A detailed description of the device can be found elsewhere (Colombo et al. 2000). Briefly, the DGO provides drives for the hip and knee joint movements of both legs, whereas the feet can move freely (Fig. 1). Four separate position controllers implemented in a computer based real-time system control the angles of the hip and knee joints. The leg joint trajectories are taken from a database of healthy subjects walking within the DGO (Fig. 2A) and are identical for all...
subjects. Feedback of the actual angle is provided by potentiometers attached to the lateral aspect of the hip and knee joints of the orthosis on both sides.

Fig. 1 Experimental set up. Walking within a DGO
A  Left Hip and Knee Movements

a

b

Desired Hip Movement

left hip angle [deg]

Desired Knee Movement

left knee angle [deg]

gait cycle [%]

Extension

B  Left Leg Muscle EMG Activity

[μV] within Lokomat

without Lokomat

RF

BF

TA

GM
Fig. 2A, B Stepping within the DGO. Joint angle and EMG recordings during one normal gait cycle during stepping within the DGO. A Normal hip and knee joint movements are provided by the DGO; the direction and time frame of the perturbations are superposed on the normal joint angle diagram (b, arrows) and the leg positions at the beginning of the perturbations are indicated by a schematic stick diagram (a, left pertubated leg in black). B EMG activity of upper and lower leg muscles stepping within and without the DGO. The extension/flexion displacements applied to the left hip or knee at various phases of the step cycle are indicated by thin vertical lines.

The DGO is fixed to the treadmill by a flexible parallelogram. A compensation mechanism for the weight of the orthosis is provided. The subjects are fixed to the DGO by straps around the waist, the thighs and the shanks. The orthosis can be adjusted in size at the different segments and, therefore, can be adapted to the different subjects.

**Walking within the DGO**

During treadmill walking, speed was kept constant at 0.53 m/s (1.9 km/h) for all trials. Cadence had to be slightly adjusted according to the leg length of the different subjects. Mean cycle time for the subjects was 2.2 s. After 5 min of habituation within the orthosis, subjects reported few restrictions compared with their normal walking movements. Although there were differences between the locomotor pattern obtained during walking within the DGO and normal walking on the treadmill (Fig. 2B), the timing of EMG activity of the respective leg muscles was largely unaffected. The low walking speed was chosen to enable comparisons with similar measurements in paraplegic patients where this is the normal therapeutic treadmill speed. In addition there are technical restrictions within the DGO for speeds higher than 0.7 m/s.

**Unilateral joint perturbations**

Custom made software was used for the generation of the unilateral joint perturbations released at different phases of the gait cycle. While normal walking movements were always provided for the right leg, perturbations were released in a random order to the left leg. Extension or flexion displacements, assisting or resisting the physiological movement, applied at the left hip or knee joint, were released at three different phases during swing phase of the gait cycle. The 12 modes of perturbations were released only during the swing phase. This is because during the stance phase, interaction with the moving treadmill belt occurs, making it difficult to control. Each perturbation was followed by three to five normal gait cycles, and every condition was applied five times. The duration of one experiment amounted to around 10 min; subjects did not experience fatigue within this time.

Joint displacements were induced by switching from a closed loop position control, using the desired angle values, to an open loop control for 100 ms. After 100 ms the DGO was set back to the closed loop position control. The normal movement trajectory was reached about 200 ms after the onset of displacement; i.e. the displacement did not change the overall duration of the swing phase. The software generated an analog trigger with different amplitudes encoding all conditions and indicating the beginning of the stance phase of the left leg.

The open loop control was the same for all perturbations. The application of the maximal current
of 15 A for the motor at the corresponding joint resulted, on average, in a change in angular momentum of about 6 Nms at the hip and 3 Nms at the knee joint, respectively (measured by built-in force sensors). Some existing variability in angular momentum was due to the different movement directions and velocities, as well as to different inertia of the perturbed part of the limb. Therefore, the influence of the impulse strength on the EMG responses was tested only in five subjects by the application of two weaker impulses (75 and 50% of the original one). These additional measurements with less impulse strength were made for the knee flexion perturbation during mid swing to get not only data with comparable perturbation input, but also data with comparable perturbation output, i.e. displacement amplitude.

Figure 2A shows the timing and direction of all perturbations superimposed on the normal movement trajectories of hip and knee joints during the gait cycle. The resulting displacements depended on the direction of the impulse with respect to the physiological leg movement trajectory and the phase of the step cycle in which the perturbation was released.

Data analysis

For data recording and signal analysis the Soleasy Software (ALEA Solutions GmbH, Zurich, Switzerland) was used. EMG recordings were amplified, band-pass filtered (30–1,000 Hz), rectified and low-pass filtered (10 Hz). All data (EMG, actual hip and knee joint angle trajectories of both legs of the orthosis, and the trigger signal) were sampled at 2,000 Hz.

The data for each perturbation was normalised in time to one gait cycle, and an average over the five repetitions was calculated. In order to get the net effect of the different perturbations on the leg muscle EMG activity, the averaged data of normal walking within the DGO was subtracted from the averaged data of each perturbation condition for every subject. These differences were then normalised in amplitude to the mean EMG activity over one gait cycle of normal walking. The population mean values were calculated over the averages obtained from five subjects for each of the perturbation conditions; with an additional four subjects being included for the mid swing conditions, due to this being the focus of interest. The maximal EMG amplitude within a time frame of 200 ms after perturbation onset was calculated for every muscle in every condition. Differences between perturbation conditions were tested using the Wilcoxon signed-ranks test with level of significance set to \( p < 0.05 \).

The latency between onset of joint displacement and EMG response was determined by the time interval between the deflection of the joint trajectory and the occurrence of an increase in EMG amplitude of twice background level. Visual inspection was used to judge when a signal-to-background EMG ratio of more than two was reached.

Results

The displacements at the hip and knee joints were released at three phases of the swing phase of the left leg (Fig. 2A). During swing, the hip and knee joints both exert first a flexion and then an extension movement whereby this transition occurs at different time points. During mid swing, the hip is still flexing, whereas the knee is already extending. Displacements directed with and
against physiological movement direction were called "assisted" and "resisted", respectively. The displacements at the left hip or knee were perceived by the subjects as weak or moderate perturbations of gait. Most displacements were followed by bilateral EMG responses in upper and lower muscles of both legs. The response pattern also involved muscles which were not affected by the displacements. For a better comparison, the corresponding conditions for hip or knee displacements (i.e. assisting and resisting hip and knee displacement at one phase of swing) were taken together. In Figs. 3, 4 and 5, the impulse strength applied to the left hip or knee was the same in all conditions. Therefore, the resulting joint displacement could differ, i.e. it was smaller in some conditions during assisting displacements.
Fig. 3A, B Population means (with SD) of the rectified and averaged (n=9) net EMG responses in RF, BF, TA, GM of both legs to assisting and resisting displacements, of A the left hip and B the left knee movement, released during mid swing (cycle duration 2.2 s). The individual EMG amplitudes were normalised to the mean EMG activity of the respective muscle during unperturbed locomotion. Below the EMG traces, the net hip or knee deflection movement induced by the displacement is displayed. The release of the displacement at the left leg is indicated by the dotted vertical lines on the left and right leg, respectively. In the schematic diagram the leg position (left perturbated leg in black) is shown for the condition mid swing.

A assisted  resisted

Left Hip Movement
(initial swing)

B assisted

Left Knee
(initial)

RF
BF
TA
GM

50% gait cycle

stimulus
Fig. 4A, B Response pattern to displacements released during initial swing (n=5). See legend to Fig. 3

Fig. 5A, B Response pattern to displacements released during terminal swing (n=5). See legend to Fig. 3

Figure 3 shows the population mean (with SD) of the bilateral net EMG and joint responses to
assisting and resisting hip (Fig. 3A) and knee (Fig. 3B) displacements released during mid swing. Figure 3 shows that when the movement was "resisted" during mid swing, i.e. when the displacement applied was directed against the physiological movement, the amplitude of the responses was stronger compared with the condition when the displacement was assisted, i.e. had the same direction as the physiological movement. A bilateral response pattern was obtained following displacements that resisted the movements with an early activation ipsilaterally of m. rectus femoris (RF) and m. tibialis anterior (TA) and contralaterally of m. biceps femoris (BF) and m. gastrocnemius medialis (GM). The variability of the response pattern among the subjects was rather small. Such a pattern makes sense as the intended movement of the ipsilateral leg becomes restored by such a muscle activation. At the contralateral standing leg, a BF and GM activation took place. This provides enhanced support for balance correction and represents the appropriate compensation of a forward disturbance of body equilibrium evoked by the hip or knee displacement of the swing leg.

When the movement was assisted by the displacement, released during mid swing, the response amplitudes in the muscles of both legs were small or almost absent. Although both impulse energy and displacement amplitude were about the same during the hip displacements, the distinct response pattern during resisting displacements switched to an almost negligible one with small EMG responses (e.g. ipsilateral BF following hip and ipsilateral TA following knee perturbations) during assisting displacements. This difference was statistically significant ($p<0.01$) for the EMG amplitudes of ipsilateral RF and TA as well as the contralateral BF for both hip and knee displacements during mid swing.

Figures 4 and 5 show the population mean (with SD) of the EMG responses to assisting and resisting hip and knee displacements induced during initial (Fig. 4) and terminal (Fig. 5) swing. The responses were smaller and rather independent of the direction of the displacement (i.e. were rather unspecific). They mainly consisted of an ipsilateral RF or RF/TA (initial swing) and BF/GM-activation (terminal swing), respectively. Small but significant ($p<0.05$) differences in EMG amplitude were found only following hip perturbations for ipsilateral TA (initial and terminal swing), contralateral BF (initial swing) and contralateral RF (terminal swing), respectively. They all showed larger amplitudes in the resisting condition. No difference in EMG amplitudes was found following assisted and resisted knee displacements.

There was a striking similarity between the response pattern following corresponding hip and knee displacements during all three phases of swing. This similarity is primarily based on visual inspection and concerned the muscles involved as well as the whole pattern of muscle activation in both legs, while the amplitudes of the EMG responses showed some difference. The latencies of the responses were in the range of 50 to 90 ms (e.g. left RF and TA mid swing) or in the range of 150 to 200 ms (e.g. left RF initial swing, GM terminal swing).

The constant impulse strength (change in angular momentum) resulted in different displacement amplitudes that depended on several factors such as the limb inertia and the direction of the displacement (see Methods). Figure 6 shows the influence of three impulse strengths (100, 75 and 50%) leading to different displacement amplitudes during assisted (Fig. 6A) and resisted (Fig. 6B) hip flexion movements on the response pattern (population mean of five subjects). In general there was a moderate influence of displacement amplitude on the strength of leg muscle response. However, the bilateral organisation of the response pattern remained unchanged. If the displacement amplitudes were less than about 5 deg, even in the resisting displacements no
distinct EMG responses occurred.

**Fig. 6A, B** Effect of displacement amplitude on the response pattern. Bilateral net EMG and joint responses to three different amplitudes of **A** assisting and **B** resisting displacements of left hip movements (100%, i.e. same impulse as applied in Fig. 3; 75% and 50%) released during mid swing. Mean values of five subjects

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**Discussion**

The aim of this study was to evaluate the effect of single joint displacement on the activation of leg muscles during locomotion. To our knowledge, the present work represents the first study on the response pattern to isolated hip or knee displacements during human locomotion. However, one has to take into account some technical restrictions of the present approach such as the low locomotion speed and the limitations in displacement amplitude for a few perturbation conditions. Furthermore, the application of a disturbance to a single joint, as in the present
approach, means it is also likely that sensors around the displaced joint (i.e. skin receptors, force receptors in muscles that cross the joints) become activated. Therefore, the interpretation of some measures has to be made with caution.

The main results obtained were the following: 1) Unilateral hip and knee displacements were followed by a similarly organised pattern of leg muscle activation; 2) During mid-swing the pattern depended on the direction of the displacement with respect to the physiological movement trajectory; 3) Displacements released at initial or terminal swing were followed by a rather “unspecific” response pattern; i.e. the pattern depended little on the displacement direction. The results will be discussed with respect to the relevant afferent input and their possible functional significance.

Specific reactions

The response patterns obtained for displacements during mid swing were basically different dependent on whether the movements were assisted or resisted. They were called ‘specific reactions’. In contrast, the hip and knee displacements released at initial and end of swing evoked similar responses. These were called ‘unspecific reactions’. There was a striking similarity in the response pattern following hip or knee joint displacements for corresponding physiological movement conditions. Mid swing represents the phase just prior to the transition of hip joint movement from flexing to extending and just after this transition of the knee joint (see Fig. 2A). Therefore, different functions of the muscles around the two joints were affected. When displacements resisted these movements, i.e. when a hip extension or a knee flexion displacement was applied, the same pattern of bilateral leg muscle activation occurred. This pattern can be regarded as being compensatory for the respective displacement, i.e. by the RF and TA activation of the displaced leg, the intended movement trajectory becomes restored. On the contralateral, non-displaced leg the BF and GM activation can lead to an extension movement and might provide compensation for perturbation and enhanced body support. Although any conclusion has to be drawn with caution because of the biarticular function of RF, BF and GM muscles, the response pattern seems to reflect the need to maintain body equilibrium simultaneously with the requirement to maintain the locomotor rhythm. This observation stands in contrast to isolated ankle joint displacements, which were followed only by local responses (Sinkjaer et al. 1996, and personal communication).

The difference from the work of Sinkjaer et al. is understandable given that perturbations to more proximal joints have greater intersegmental effects. The question of why some EMG responses in proximal or distal muscles of both sides appeared with a short (spinal) or longer latency, respectively, cannot be answered by this study. The pathways possibly mediating these responses were not an aim of this study. However, according to the latencies, the early responses might be mediated on a polysynaptic spinal level. Such a pathway has also been suggested for corresponding compensatory leg muscle responses following whole leg perturbation during gait (Dietz et al. 1986b; 1987; Gollhofer et al. 1986).

In contrast, almost no distinct EMG responses appeared when assisted displacements were released during mid swing. For the knee joint this observation might partly be due to the smaller displacement amplitude in this condition. Nevertheless, in general, displacement amplitude had only a moderate influence on the response amplitude (cf. Fig. 6).
On the basis of the observations made here one might suggest that if a displacement goes in the same direction as the motor program, it does not need to be modified. On the contrary, if the displacement disrupts the global motor output, a complex feedback reaction on both legs is induced. In addition, in such a condition, the input from activated receptors can be assumed to be fundamentally different, e.g. some muscle afferents are probably only activated during stretch of the contracting muscle. In addition, spindle afferents may act in a task-specific manner during such a functional motor condition. The pattern of leg muscle activation observed here (e.g. following hip/knee movement resisting displacement) is quite similar to that observed during forward displacement of the support (see Fig. 5, Gollhofer et al. 1986), or following obstruction of the swing phase of the whole leg (see Fig. 1, Dietz et al. 1986b) during gait. Also, these response patterns were interpreted as being compensatory for the displacement. Nevertheless, the two conditions of perturbation, i.e. single joint during swing versus—the more natural—whole leg perturbation during stance or swing, can only be compared with caution.

Alternative explanations would be, firstly, that the response pattern represents an attempt to stiffen the leg in order to resist the displacement—this would require both hip and knee movements because of the interaction torques—or secondly, that the reaction reflects a more generalised startle response to the displacement. Due to the fact that the response pattern was purposeful in restoring the normal movement trajectory and concerns the activation of selected proximal and distal leg muscles of both sides, these alternative explanations seem to be rather unlikely. Furthermore, a startle response would be expected to appear not only in two of the 12 randomly released displacement conditions.

One has to be aware that several muscles such as rectus femoris cross hip and knee joints. This fact alone can, however, not explain the specific response pattern, as EMG responses appeared also in muscles neither directly affected by hip or by knee joint displacements (e.g. ipsilateral TA or contralateral EMG responses). Nevertheless, the double joint issue makes it difficult to determine exactly the mechanical effect of the EMG responses in these muscles. This restricts the interpretation of the data to some extent.

On the basis of the observations made here it is supposed that the movement trajectory of the whole leg is controlled by the nervous system rather than the position of a single joint. This is surprising in view of earlier studies indicating the significance of hip joint afferent for initiating the stance to swing transition in infancy stepping (Pang and Yang 2000) and cat locomotion (Grillner and Rossignol 1978; Andersson and Grillner 1983; Kriellaars et al. 1994). The discrepancy to the present results might be due to the differences in geometry and function of the legs during adult bipedal and quadrupedal locomotion, respectively (for review see Dietz 2002).

Non-specific reactions

A rather non-specific response pattern was obtained when displacements were applied to the hip or the knee at initial or end of the swing phase. This means that the pattern of muscle activation in both legs was similar in the conditions of knee or hip movement assisting or resisting displacements in contrast to the displacements released during mid swing. Initial and mid swing are critical phases of the step cycle in so far that body equilibrium becomes transferred from one leg to the other. Displacements released during this phase were associated with a RF and TA activation (initial swing) and a more or less pronounced co-activation pattern of the muscles (terminal swing) of the perturbed leg as well as a small BF and GM activation or negligible
EMG responses in the contralateral leg. This pattern might represent a more unspecific reaction with a stiffening of both legs. A similar co-activation of antagonistic muscles, reported for infants (Okamoto and Goto 1985), was suggested to represent an effective way to minimise the threat to equilibrium (Misiaszek et al. 2000).

**Bilateral co-ordination**

The observation of a bilateral pattern of compensatory EMG responses made here for unilateral hip or knee displacements is in line with earlier observations on the co-ordination of stepping in cat (Grillner and Rossignol 1978; Gorassini et al. 1994; Hiebert et al. 1994, 1996; Schomburg et al. 1998) and infants (Yang et al. 1998; Pang and Yang 2000, 2001). This pattern is based on the organisation of the central pattern generator. The responses to the single joint displacements applied here were similar in their organisation to those seen during unilateral whole limb perturbations during gait in adults (Dietz et al. 1987; Ghori and Luckwill 1989; Prokop et al. 1995; for review see Dietz 1992) and infants (Pang and Yang 2000, 2001). However, in the present study, the strength of bilateral leg muscle activation depended on the direction of the displacement. In contrast, the EMG responses to whole leg perturbations were of similar size independent of the direction of perturbation (Dietz et al. 1987). This discrepancy might be due to the fact that 1) a displacement of the whole leg is more threatening to body equilibrium compared with the displacement of a single joint and 2) displacements here were applied during the swing phase, while those in the earlier studies were applied at mid-stance phase.

According to the observations made here, one might assume that the bilateral response pattern described for whole limb displacements during locomotion can at least partially be attributed to a task-dependent response pattern based on hip and knee joint-related afferent input.

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References


