Spinal Cord Lesion: Effects of and Perspectives for Treatment

V. Dietz[†††]

ParaCare, Paraplegic Centre, University Hospital Balgrist, Forchstr. 340, CH-8008 Zurich, Switzerland

SUMMARY

Following central motor lesions, two forms of adaptation can be observed which lead to improved mobility: (1) the development of spastic muscle tone, and (2) the activation of spinal locomotor centers induced by specific treadmill training. Tension development during spastic gait is different from that during normal gait and appears to be independent of exaggerated monosynaptic stretch reflexes. Exaggerated stretch reflexes are associated with an absence or reduction of functionally essential polysynaptic reflexes. When supraspinal control of spinal reflexes is impaired, the inhibition of monosynaptic reflexes is missing in addition to a reduced facilitation of polysynaptic reflexes. Therefore, overall leg muscle activity becomes reduced and less well modulated in patients with spasticity. Electrophysiological and histological studies have shown that a transformation of motor units takes place following central motor lesions with the consequence that regulation of muscle tone is achieved at a lower level of neuronal organization which in turn enables the patient to walk. Based on observations of the locomotor capacity of the spinal cat, recent studies have indicated that spinal locomotor centers can be activated and trained in patients with complete or incomplete paraplegia when the body is partially unloaded. However, the level of electromyographic activity in the gastrocnemius (the main antigravity muscle during gait) is considerably lower in the patients compared to healthy subjects. During the course of a daily locomotor training program, the amplitude of gastrocnemius, electromyographic activity increases significantly during the stance phase, while inappropriate tibialis anterior activation decreases. Patients with incomplete paraplegia benefit from such training programs such that their walking ability on a stationary surface improves. The pathophysiology and functional significance of spastic muscle tone and the effects of treadmill training on the locomotor pattern underlying new attempts to improve the mobility of patients with paraplegia are reviewed.

KEYWORDS

spinal cord injury, spasticity, reflexes, locomotion, load receptor

SPASTICITY

Clinical aspects

This paper will focus on the pathophysiology of patients with lesions of the spinal cord. Although there are some differences between

[†]tel: 0041 1 386 39 01; fax: 0041 1 386 39 09
e-mail: dietz@balgrist.unizh.ch

cerebrally and spinally mediated spasticity, the main features such as paresis, leg muscle activation during gait, reflex behaviour and the pathophysiology of spastic muscle tone, are quite similar (Dietz, 1992).

Spasticity is associated with numerous physical signs, such as muscle hypertonia and exaggerated tendon reflexes, including clonus. Lance (1980) defined spasticity as a velocity-dependent resistance of muscle to stretch due to the activation of tonic stretch reflexes, while rigidity is defined as an even resistance throughout the range of passive movement. In addition, in spasticity antigravity the muscles (arm flexors/leg extensors) are predominantly affected. Spastic signs are accompanied by a variable degree of paresis which, together, constitute a syndrome known as spastic paresis.

On the basis of the clinical signs, a widely accepted conclusion was drawn concerning the pathophysiology of spasticity (that is, exaggerated reflexes are responsible for muscle hypertonia) which has influenced treatment. Drug therapy, therefore, is usually directed to produce a reduction in the activity of stretch reflexes. The function of these reflexes during natural movements and the connection between exaggerated reflexes and the disorder of movement known as spastic paresis, however, is frequently not considered. In reality, the physical signs of spastic hyperreflexia have little relationship to a patient's disability, which is due to impairment of functional movement.

Clinical observations have already given rise to doubts about such a direct relationship between reflex excitability, spasticity, and disability:

1. Following an acute stroke, tendon reflexes can be exaggerated early, while spastic muscle tone develops over weeks.
2. In healthy subjects, a connection between the excitability of reflexes and motor performance has not been demonstrated.

Neuronal regulation of functional movements, such as locomotion, is achieved by a complex interaction of spinal and supraspinal mechanisms. Rhythmic activation of leg muscles by spinal interneuronal circuits is modulated and adapted to the body's actual needs by a multisensory afferent input. Electrical activity of leg muscles, which results from a close interaction between these different mechanisms, is translated into functionally modulated muscle tension by the mechanical properties of muscle fibers (Gollhofer et al., 1984). Spinal programming, as well as reflex activity, are under supraspinal control. Disturbances of this supraspinal control lead to characteristic gait impairments seen in cerebellar and extrapyramidal disorders, as well as in spastic paresis (for review see Dietz, 1992).

The evolution of spastic signs and symptoms

Following an acute lesion of pyramidal and extrapyramidal tract fibres (cf Nathan 1994; Benecke, 1993), changes in physical signs occur over months. They are only partially understood pathophysiologically (Hiersemenzel et al., 2000) Initially, flaccid paresis is present and tendon reflexes are absent (a rather rigid muscle tone can suddenly develop in acute brainstem lesions). Flaccid paresis may last for weeks after a traumatic spinal cord lesion but following an acute stroke, tendon reflexes may be exaggerated after a few days, while spastic muscle tone develops over weeks and increases over several months. These changes in muscle tone are not reversible and are usually more pronounced in spinal than in cerebral lesions.

Pathophysiologically, it was suggested that neuronal reorganization occurs after a central lesion (see Mendell, 1984 in cat and see Carr et al., 1993 in children); this may involve

1. novel connections (e.g. sprouting, functional strengthening of available connections),
2. changes in strength of inhibition, and
3. denervation supersensitivity.

Recent observations indicate, however, that following a spinal cord lesion, sprouting of primary afferents is not seen in cat (Nacimiento et al., 1993) and is unlikely in man (Ashby 1989) as a cause of spasticity. Reduction of pre-synaptic inhibition of group Ia fibers occurs (Burke & Ashby, 1972; Delwaide, 1973; Faist et al., 1994) and seems to correlate with the excitability of tendon reflexes. In addition, after a few weeks, changes in mechanical properties occur in the leg extensor (Dietz et al., 1981) and arm flexor (Ibrahim et al., 1993) muscles, which may contribute to spastic muscle tone. Structural changes of the spastic muscle and of connective tissue become most prominent one year and more after an acute lesion (Hufschmidt & Mauritz, 1985; Sinkjaer et al., 1993). Little is known about the time course of spastic symptoms after one year.

Pathophysiological basis of therapy

At present, no direct therapy is available for improvement of central paresis. That is to say, disconnection of lower from higher motor centers can not yet be remedied. Functional electrical stimulation (FES) of paralyzed muscles may compensate for certain aspects of the paresis but is, however, still in an experimental stage (Yarkony et al., 1992; Quintern et al., 1989).

Treatment of spasticity is usually directed to reduction of stretch reflex activity as it is assumed that exaggerated reflexes are responsible for increased muscle tone and this somehow accounts for the spastic movement disorder. Studies of muscle tone and reflex activity are usually done under passive motor conditions with the patient resting (cf. Thilmann et al., 1990; 1991). On the other hand, extensive investigations of functional movements of leg (Dietz and Berger, 1983; Berger et al. 1984) and arm (Powers et al., 1989; Dietz et al., 1991; Ibrahim et al., 1993) muscles, however, did not reveal any causal relationship between exaggerated reflexes and a disorder of movement. The reciprocal mode of leg muscle activation during gait is preserved in spasticity, but exaggerated stretch reflexes and spasticity are associated with an absence or reduction of the functionally essential polysynaptic (or long latency) reflexes. Tension development during functional movements (Berger et al., 1984) does not depend on exaggerated monosynaptic stretch reflexes. The overall leg muscle activity is reduced during functional movements in patients with spasticity of spinal and cerebral origin. According to electrophysiological (Dietz et al., 1981; Sinkjaer et al., 1993) and histological (Edström, 1970; Dietz et al., 1986) findings, a transformation of motor units takes place following a supraspinal lesion so that regulation of muscle tone is achieved by a lower level of neuronal organization.

The default to a simpler regulation of muscle tension following paresis due to a spinal or a supraspinal lesion is basically advantageous for a patient; it enables him to support the body during gait and, consequently, to achieve mobility in almost every case with a unilateral lesion. Rapid movements are, however, no longer possible because modulation of muscle activity is absent. Following a severe spinal or supraspinal lesion, these transformed processes can become excessive with unwelcome sequelae such as painful spasms and involuntarily induced movements.

Therapeutic outcomes in spasticity of both spinal and cerebral origin should be considered in terms of physiotherapeutic approaches (Dietz, 1996). These should be directed to train and activate residual motor functions and to prevent secondary complications, such as muscle contractures and spasms. Antispastic drug therapy is the second tool. It reduces muscle tone and spasms by the induction of paresis (Hoogstraten et al., 1988) which may interfere with the performance of functional movements. Antispastic drug therapy is, therefore, predominantly of benefit for immobilized

patients in whom it reduces muscle tone and relieves muscle spasms, both of which may also improve nursing care for these patients.

Physiotherapeutic approaches

Depending upon the neurophysiological situation, physiotherapy may represent the most definitive mode of treatment for mobile as well as immobilized spastic patients. Again this statement is not based on hard data. Active and passive manipulative forms of physiotherapeutic treatment are of great importance for both groups of patients. On the one hand, residual motor functions should be trained. On the other hand, contractures of muscle and joints which are difficult to treat when established must be prevented at an early stage by frequent muscle stretch. Physiotherapy within a water-filled pool, i.e. under-water therapy, seems to be promising as recent experiments revealed profound effects on postural reflexes (Dietz et al., 1989).

On the basis of divergent empirical evidence, different physiotherapeutic procedures are applied. Proprioceptive neuromuscular facilitation (PNF) and myofeedback techniques are meant to activate spinal motoneurons reflexly. The techniques of Bobath and Vojta are primarily concerned with the treatment of children with cerebral palsy. Stereotyped movements become activated by such stimulation techniques when they are applied to specific dermatomes and joints. The Vojta method tries to activate complex movements which are believed to be programmed in the central nervous system. In contrast to this, the Bobath method tries to inhibit spastic symptoms in flexor muscles of the upper extremity and in the extensors of the lower extremity.

All these techniques hope to achieve the following benefits and goals:

- avoidance of secondary complications, i.e. pneumonia, skin ulcerations and thrombosis;
- prevention and treatment of muscle contractures;
- reduction of muscle hypertonia with the additional application of warm/cold packs;
- training of posture and automatically performed movements with the induction of voluntarily initiated and controlled complex movements;
- learning and training of coordinated movements by the involvement of tactile, auditory, vestibular and visual cues;
- appropriate application of supportive aids, such as rollator, wheelchair, crutches, orthoses and technical equipment (e.g. special shoes).

All these techniques are based on old theories, and for none of them exist controlled studies documenting a positive effect of the treat-ment. Therefore, it is not yet possible to perform an appropriate evaluation and recommendation indicating the superiority of one of these techniques compared to the other one in the treatment of a spastic patient. Nevertheless, physiotherapy must be part of a multidisciplinary integrated approach to patients. It also includes ergotherapeutic and nursing assistance. These all are meant to achieve greater mobility and, as far as possible, independence of the patient.

TRAINING OF LOCOMOTOR ACTIVITY

Over the past decade it has been shown that, after a complete spinal cord lesion, a cat can be trained to perform stepping movements on a treadmill. The pattern of leg muscle activation during such locomotion resembles in many aspects the pattern observed in an intact cat (Barbeau & Rossignol, 1987; for review see Barbeau & Fung, 1992).

Although there is strong evidence for a spinal locomotor generator in many mammals (for review see Grillner, 1981; Barbeau & Rossignol, 1994), its existence has, until recently, been questioned in man (Kuhn, 1950; Illis, 1995). Evidence for the

human spinal pattern generator was suggested by spontaneously occurring step-like movements (Calancie et al., 1994) and myoclonus (Bussel et al., 1988), as well as from late flexion reflexes (Bussel et al., 1989) and from locomotor movements induced on a treadmill with body support in paraplegic patients (Dietz et al., 1994; 1995; for review see Barbeau & Rossignol, 1994). Recent studies showed that a locomotor pattern can be induced in complete paraplegic patients when leg movements were assisted externally (Dietz et al., 1994, 1995; Dobkin et al., 1995). Nevertheless, the amplitude of leg muscle EMG activity in these patients was small compared to healthy subjects, (most probably due to the loss of noradrenergic influences from brainstem centers) such that no leg movements resulted from this leg muscle activation.

The beneficial effect of locomotor training in incomplete paraplegic patients is well established (Fung et al., 1990; Wernig & Müller, 1992; for review see Barbeau & Rossignol, 1994) and recent investigations showed that patients who undergo locomotor training have greater mobility compared to a control group without training (Wernig et al., 1995). Nevertheless, it remained unclear to what extent these training effects are due to a training of spinal locomotor centers. Only by systematic recordings of leg muscles EMG, reflecting the activity of spinal neuronal circuits, the effect on this presumed 'spinal locomotor pattern generator' can be separated from rather non-specific effects on muscles and tendons. Observations on patients with paraplegia due to a lesion of the cauda, i.e. of peripheral nerves, show that a locomotor training indeed results in an improvement of locomotor function which is *not* connected with a corresponding change in leg muscle EMG activity (Dietz et al., 1998a,b). Therefore, the improvements of locomotor function described earlier for cat (Barbeau & Rossignol, 1987) and man (Wernig & Müller, 1992; Barbeau & Rossignol, 1994;) can be partially attributed to non-specific effects on the locomotor apparatus, i.e. muscular tendon-systems.

Body unloading is obviously of crucial importance to induce training effects on the locomotor centers. The range of body unloading that allows stepping movements and optimal activation of leg muscles for body support by the legs during the stance phase is limited in paraplegic patients. Afferent input from receptors signaling contact forces during the stance phase is essential for the activation of spinal locomotor centers (cf. Harkema et al., 1997), and therefore it should also be important for the training effects described here. Although the amplitude of leg extensor EMG in both paraplegic and healthy subjects depends upon the actual body load during the stepping movements, the absolute level of EMG activity is considerably lower in patients than in healthy subjects. This makes the body unloading necessary for the locomotor training. There is, indeed, increasing evidence in cat (Pearson & Collins, 1993) and man (Dietz et al., 1992) for a contribution of load receptors to the activation of leg extensors during stance and locomotion.

Recovery of spinal cord function and locomotion

Recent studies have shown that during locomotor training gastrocnemius (GM), EMG activity increases during the stance phase, even in complete paraplegic patients (Dietz et al., 1995). Nevertheless, this improvement of locomotor activity could have been attributed to spontaneous recovery of spinal cord function, i.e. of spinal locomotor centers. It is well known that recovery of spinal cord function can occur over several months following spinal cord injury (Katho & El Masry, 1994; Curt & Dietz, 1996; 1997; 1998). From the recent observations in both incomplete and complete paraplegic patients, there can be little doubt that the increase of leg extensor EMG

activity, connected with a decrease of body unloading, occurs independently of the recovery of spinal cord function assessed by clinical and electrophysiological means (Dietz et al., 1998a, b). Of course, clinical and electrophysiological tools may be too crude to rule out recovery of any spinal cord function. Nevertheless, locomotor training obviously plays an important role for the effects on extensor muscle EMG.

In complete paraplegic patients, a spontaneous development of a locomotor pattern could be observed (Dietz et al. 1998a). However, this occurred after spinal shock had disappeared and the pattern reached a plateau usually about 4 weeks later. In contrast, under locomotor training which usually started about 2 to 4 weeks after spinal shock disappeared, GM EMG activity further increased during the stance phase after the time when a plateau had been expected to be reached spontaneously. This effect was connected with progressive loading (i.e. reduced unloading) during locomotion.

In addition, one might argue that the increase of GM EMG during the course of training is mainly due to the decrease of body unloading. However, after statistical separation of the (un)loading effect, there remained a significant effect of training. Therefore, one may conclude that there are specific training effects on spinal locomotor centers which can lead to an improvement of locomotor function in paraplegic patients (Dietz et al., 1998 a,b).

Looking ahead it may be important to discover new means to further enhance the amplitude of leg extensor EMG activity in complete or almost complete paraplegic patients in order to achieve an even greater mobility in such patients. This may be achieved by the application of new noradrenergic drugs which have a more selective action on EMG activity compared to the ones already applied (clonidine and epinephrine, see Dietz et al., 1995). The most promising approach may, however, be to induce some regeneration of corticospinal axons within the spinal cord. Recent experiments in rats (Bregman et al., 1995) indicate that this goal may be achieved during the next few years.

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