Management of spasticity in stroke

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Spasticity treatment must be considered in relation to other impairments with functional goals defined prior to intervention. The effects of muscle co-contraction and involuntary limb movement associated with exaggerated cutaneous reflexes or effort as well as stretch reflex hyperexcitability need to be considered. Exacerbating factors such as pain must be identified. Physical therapy and conventional orthoses are the mainstays of spasticity management during acute rehabilitation. Botulinum toxin shows promise but needs further evaluation in the context of acute rehabilitation. Phenol chemodenervation can produce good results in spasticity refractory to standard treatments. Muscle strengthening exercises may be appropriate in chronic hemiparesis without adversely affecting tone. Electrical stimulation may be a useful adjunct to other spasticity treatments. Difficulty demonstrating functional benefit from antispasticity treatment may imply that interventions directed at single motor impairments whether weakness or spasticity are not likely to result in functional benefit, but it is their combination that is important.

Spasticity is abnormal muscle tone recognised clinically as resistance to passive muscle stretch which increases with velocity of stretch. It is more formally defined as: 'a motor disorder characterised by velocity dependent increase in tonic stretch reflexes with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex'[1]. While these definitions are useful for diagnostic purposes, they are too restrictive in terms of understanding and managing the consequences of inappropriate muscle activity found after stroke. While paresis and loss of dexterity are the main causes of motor dysfunction, the impact of spasticity as defined by Lance remains controversial[2]. This controversy partly reflects lack of functional benefit found in some earlier studies of antispasticity treatments. For the purposes of understanding the role of antispasticity treatments on motor recovery following stroke, this article includes the effects of muscle co-contraction and involuntary limb movement associated with exaggerated cutaneous reflexes or effort (associated reactions), in addition to stretch reflex hyperexcitability.

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Pathophysiology

Central to the generation of spasticity is overactivity of the alpha motor neuron (α-MN) pool, which also causes some of the other 'positive' manifestations described above. Lesions restricted to corticospinal tracts cause muscle weakness, loss of dexterity and a Babinski response, but not spasticity. Loss of descending input from cerebral cortex and basal ganglia, through medial and dorsal reticulospinal and vestibulospinal fibres, is thought to be important in causing impaired modulation of monosynaptic input from primary afferent (Ia) fibres (segmental myotatic reflex), and polysynaptic afferent input from cutaneous receptors and Golgi tendon organs contributing to α-MN hyperexcitability[1]. Spinal interneurons play a crucial part in this modulation, in particular through presynaptic and reciprocal Ia inhibition. Inappropriate muscle co-contraction may arise through reduced reciprocal Ia inhibition impeding voluntary limb movement[3]. In addition, nocioceptive and motor pathways have considerable influence on each other, emphasising the clinical importance of pain management in treating spasticity.

Consequences of spasticity

Stroke affecting the motor cortex or internal capsule commonly produces initial hypotonia and absent tendon jerks, followed several days or weeks later by spastic hypertonia in the antigravity muscles. The upper limb adopts an adducted posture at the shoulder and a flexed posture at the elbow and wrist, with the fingers flexed into the palm. In the lower limb there is hip and knee extension, with plantarflexion at the ankle.

In patients with no functionally useful voluntary limb movement, spasticity can maintain an abnormal resting limb posture leading to contracture formation. In the arm, severe flexion deformity of the fingers and elbow may interfere with hand hygiene and dressing, as well as affecting self image. In the leg, abnormal resting posture of the hips and knees may cause difficulty with wheelchair seating and transferring, as well as popliteal fossa and groin hygiene. In severe cases, the heel may be in contact with the buttock, with risk of pressure sores. Severe equinus deformity interferes with donning footwear and use of wheelchair foot plates. Spasticity, therefore, indirectly affects many aspects of self-care through the maintenance of abnormal limb posture. Articular and peri-articular pain caused by the abnormal resting position and immobility of the joints can exacerbate spasticity. Exaggerated reflex responses to cutaneous stimuli may cause painful flexor or extensor spasms, which can interfere with seating, transferring and cause sleep disturbance. In some patients, heterotopic calcification may cause pain and further

encourage abnormal limb posture. The importance of pain relief in the management of spasticity should not be underestimated.

In patients with functionally useful voluntary limb movement, inappropriate co-activation of agonist and antagonist muscles can impede normal limb movement. In the arm, co-activation of the biceps and triceps may affect the placement function. Co-contraction of the forearm flexor and extensor muscles may prevent voluntary extension of the fingers and thus impede relaxation of grip. In the leg, involuntary knee flexion caused by inappropriate hamstring muscle activity with the effort of standing may interfere with weight bearing and walking. Dynamic equinus deformity of the ankle from calf muscle spasticity can impede toe clearance during the swing phase of gait causing the patient to fall as a result their toe 'catching' on the ground. The presence of clonus may have a direct effect on walking by affecting foot placement during standing. Inappropriate activity in the intrinsic muscles of the foot and long toe flexors may cause painful toe flexion and difficulty walking and running. Involuntary big toe hyperextension from extensor hallucis longus overactivity may interfere with donning footwear. Effortful activities (*e.g.* self-propelling a wheelchair, standing and walking) may generate inappropriate muscle activity causing involuntary movements in the paretic limbs (associated reactions). Although the role of associated reactions (AR) during motor recovery is debated, a direct impact is often implied when patients report involuntary limb movement (*e.g.* elbow flexion) interfering with standing or walking balance. In individuals where recovery is arrested during the synergistic stages, AR can become a long-term problem. Not all the consequences of spasticity are negative, for example hip and knee extensor spasticity may allow weight bearing, with the affected limb acting like a splint.

Management

Effective management of spasticity requires a multidisciplinary approach both for assessment and treatment and should not be viewed in isolation from the patient's other problems. Treatment should be directed at preventing abnormal limb or trunk posture and facilitate normal movement in the context of functional activities described above. Although the different approaches are described separately, for the management of an individual patient they should be integrated with one another as well as into the overall rehabilitation programme.

The management of spasticity can be broadly divided into: (i) identifying (usually painful) exacerbating factors (*e.g.* constipation, soft tissue rheumatism, pressure sores and deep venous thrombosis, post stroke pain syndrome) and their treatment; (ii) positioning the patient

during sitting and lying to discourage the development of abnormal posture (therapeutic positioning of the patient aims to manipulate primitive reflexes, *e.g.* tonic neck reflexes and labyrinthine reflexes, released from higher motor control)[4]; and (iii) having access to treatments directed at established spasticity. Physical, pharmacological, electrical stimulation and surgical methods are used in spasticity treatment following stroke.

Physical treatment

Physiotherapy techniques aim to improve motor performance partly through manipulation of muscle tone. Several approaches are used during rehabilitation, although there is lack of evidence to show which is most effective[5]. The Bobath approach[6] advocates reduction of spasticity and primitive postural reflexes prior to facilitating voluntary activity in paretic muscles through attention to trunk posture and controlled muscle stretch of the limbs. Reduction in segmental reflex hyperexcitability through inhibition of distal segmental reflexes via Ib inhibitory interneurons is reported using this approach. The Brunnstrom approach[7] advocates techniques to promote activity in weak agonists by facilitating contraction of either corresponding muscles in the unaffected limb or proximal muscles on the paretic side. This technique focuses on individual muscle groups with the underlying concept that stimulation of the weak agonist muscle will result in Ia mediated reciprocal inhibition in the spastic antagonist muscle. Unfortunately, reduction in Ia reciprocal inhibition often accompanies spasticity and, therefore, this avenue of reflex suppression may not be available. In some patients where weakness predominates, resistive muscle strength training may improve motor performance without necessarily increasing limb spasticity[8]. Concurrent sensory stimulation using heat and cold can cause short-term reduction in spasticity[9] which can be useful adjunct to physical therapy treatment.

An important aspect of preventing and treating abnormal limb posture is maintaining full range of joint movement through regular mobilisation (at least 2 h during a 24 h period is suggested) and the appropriate use of orthoses and serial plaster casting to maintain muscle stretch. Orthotic prescription depends on the type of deformity that needs to be accommodated, the degree of voluntary limb movement and patient usability. Improvements in walking pattern have been demonstrated with ankle foot orthosis in patients with equinovarus deformity[10]. Thermoplastic splints are advocated for the arm while rigid or hinged polypropylene splints are needed to withstand forces in the leg produced during walking. Inflatable pressure splintage is used when rigid splints are not tolerated, particularly for severe finger flexion.

Lycra orthoses offers an alternative to thermoplastic and polypropylene splints for postural management of the upper limb[11].

Drug treatment

The rationale for the type of drug treatment used should reflect the functional problem and the pattern of muscle involvement. With the development of targeted antispasticity treatments, the role of systemic antispasticity agents (*e.g.* baclofen, dantrolene) in a disease which causes 'focal spasticity problems' is likely to diminish, particularly in the context of acute rehabilitation.

Oral baclofen, an effective antispasticity agent which is well tolerated if gradually increased to the maintenance dose (up to 100 mg/day), has an adverse effect on muscle strength (particularly in unaffected muscles), which may increase disability and, therefore, should be used cautiously in stroke patients and certainly should not be a first line antispasticity agent. It still has a role in patients with refractory generalised bilateral limb spasticity, particularly if pain is present. Attention to concurrent medication is important because non-tricyclic antidepressants (*e.g.* fluoxetine) may antagonise the effect of baclofen. If the role for oral baclofen is limited, is there a role for intrathecal administration of baclofen in stroke? Intrathecal baclofen infusion *via* pump is effective in refractory lower limb spasticity where several muscles groups in both legs are affected (*e.g.* spinal cord injury, multiple sclerosis). In stroke patients with unilateral spasticity, there is risk of weakening muscles on the 'normal' side and, therefore, intrathecal baclofen should not be used. Nevertheless, a small study including 3 stroke patients with severe chronic lower limb spasticity, reported tone reduction on the affected side with preservation of muscle strength on the 'normal' side following continuous intrathecal baclofen infusion[12].

A newer systemic drug, **tizanidine** (an α_2-adrenergic receptor agonist) is effective in reducing spasticity in patients with multiple sclerosis and spinal cord injury. Its effects are thought to be mediated via neurons in the locus ceruleous and inhibitory spinal interneurons. Like baclofen, tizanidine also appears to have an anti-nocioceptive effect. Use in multiple sclerosis and spinal cord injury suggests muscle weakness occurs less frequently than with baclofen. Evidence of effectiveness in stroke is limited because comparisons have only been made with diazepam[13] and, therefore, it is not recommended for routine use in stroke.

Dantrolene, while an effective antispasticity agent, causes muscle weakness as well as hepatotoxicity and has not been shown to be useful in stroke[14]. **Diazepam** adversely affects walking and increases the risk of cognitive dysfunction. These drugs should not be used for the routine

management of spasticity in stroke. Although there has been recent interest in the antispasticity effects of **gabapentin**, there is no evidence to support its routine use for spasticity in stroke.

Disability attributable to inappropriate activity in a muscle or group of muscles would suggest an important role for targeted 'local' antispasticity treatment, given that oral treatments may cause generalised weakness. Percutaneous nerve and/or motor point blocks using phenol or alcohol, and intramuscular botulinum toxin type A are currently available targeted treatments.

Phenol nerve blocks have been used to successfully manage abnormal arm and leg posture in chronic hemiparesis (> 6 months post-stroke). In the leg, chemodenervation of the posterior tibial nerve can reduce equinovarus deformity[15], and in the sciatic nerve reduces inappropriate knee flexion. The effect may last from a few months to several years. Following phenol, painful dysaesthesia may occur through damage to the sensory fibres of mixed nerves (*e.g.* median), and vascular occlusion through damage to adjacent blood vessels. Phenol nerve blocks are no longer recommended for treatment of upper limb spasticity[16], although phenol motor point blocks reduce the risk of sensory disturbance. Alcohol (50%) has been used as an alternative to phenol, but it is less effective.

Botulinum toxin type A (BT-A) offers the possibility of local treatment of spasticity without affecting sensation. It is an established treatment for blepharospasm, hemifacial spasm and torticollis and has been used successfully (on an unlicensed basis) for spasticity treatment. BT-A, injected into the spastic muscle, produces chemodenervation by preventing release of acetylcholine at the neuromuscular junction[17]. BT-A acts peripherally to reduce muscle contraction caused by the hyperexcitable α-MN pool. The duration of muscle relaxation is usually 3 months, with loss of effect occurring through axonal sprouting proximal to the affected nerve terminal and the formation of new neuromuscular junctions. The preparations of BT-A currently available are Dysport® and BOTOX®. The potency, measured using a mouse bioassay, of these two preparations is different with 1 mouse unit of BOTOX® being equivalent to 3–5 mouse units of Dysport®[18].

The antispasticity effects of BT-A in stroke have been reported in short-term open studies, which often included patients with other diagnoses[19]. Impact on function has been more difficult to demonstrate, although improvement of limb posture following BT-A can translate into reduced disability and carer burden[20]. The largest reported placebo controlled study in 39 patients demonstrated a dose-dependent reduction in upper limb spasticity[21]. Investigation of BT-A treatment in the leg has been confined mainly to spastic equinus deformity. The largest placebo controlled study in 23 patients with hemiparesis, some of whom had traumatic brain injury, demonstrated reduction in calf spasticity and increased range of voluntary

movement at the ankle after BT-A[22]. Walking speed was not significantly increased compared with placebo. To enhance the effect of BT-A, electrical stimulation of the treated muscles has been used[23] following animal experiments demonstrating increased uptake BT-A and reduced latency of muscle paresis following electrical stimulation. Current opinion advocates use of BT-A in conjunction with conventional physical therapy treatments and orthoses. BT-A may help to predict outcome from more permanent interventions such as phenol nerve blocks and surgery.

The advantages of BT-A over other antispasticity drug treatments is the ability to target specific muscle groups, lack of sensory disturbance, patient tolerability and ease of administration. The disadvantages of BT-A include short duration of action (which might be useful in acute stroke rehabilitation, but in patients with chronic spastic hemiparesis a longer term effect is often required). Distant unwanted muscle weakness may occur at a result of diffusion of toxin across fascial boundaries and systemic spread. Systemic effects such as generalised fatigue, flu-like symptoms, occur infrequently and are self-limiting. It is important to remember that antitoxin is of little value in iatrogenic botulism from overdosage or inappropriate placement of BT-A. Although the evidence to date relates to BT-A use in chronic hemiparesis, it may have a greater role in spasticity treatment during acute stroke rehabilitation. There is also the possibility of reducing contracture by early use of targeted antispasticity treatments[24]. Although animal experiments suggest that contracture may be prevented by BT-A, controlled studies investigating possible benefits of early intervention with BT-A are lacking.

Electrical treatment

Evidence for direct antispasticity effects of electrical stimulation is limited. Transcutaneous nerve stimulation applied over the dermatome corresponding to the nerve supply of the spastic muscle can produce short-lived reduction in spasticity. However, electrical stimulation directed at improving strength of paretic muscles[25] may augment the functional effects of BT-A treatment in the antagonist muscles. Electrical stimulation has also been used to compensate for muscle paresis causing equinus deformity. Electrical stimulation of the common peroneal nerve improved walking speed in patients with chronic hemiparesis whose walking was impaired because of equinus deformity with paresis and spasticity[26].

Surgical treatment

Surgical intervention can be broadly divided into procedures that interfere with the neuronal pathways and procedures that correct musculoskeletal

deformity. Surgical ablation of peripheral nerves is usually reserved for patients in whom conservative antispasticity treatments have failed. Although this approach is inappropriate for mixed nerves, because of the risk of painful dysaesthesia, selective tibial neurotomy in patients with calf spasticity can improve the range of active ankle dorsiflexion[27]. Surgical sectioning of tendon and muscle combined with postoperative serial splintage can be used in patients with persistent deformity (*e.g.* Achilles tendon lengthening for equinus deformity at the ankle). In patients with potential for functional voluntary movement, fractional lengthening of forearm finger flexors, release of elbow flexors and tenodesis may facilitate arm placement and grip.

Key points for clinical practice

- While there is controversy regarding the role of spasticity on motor performance and the rationale for treating it, some of the later studies using targeted antispasticity treatment suggest aspects of motor performance may be improved[28]
- It remains difficult to demonstrate functional benefits from treatments directed at spasticity alone despite evidence of tone reduction. This may relate to the outcomes used, but perhaps reflects the fact that interventions directed at single motor impairments – whether weakness or spasticity – are not likely to result in significant functional benefit, but it is their combination that leads to benefit
- Not only must spasticity treatment be considered in relation to other impairments, but also functional goals defined prior to intervention
- Causes of pain must be identified and treated
- Physical therapy, attention to posture and seating, and conventional orthoses are the mainstays of spasticity management during acute rehabilitation
- Newer treatments – such as botulinum toxin-A and the use of Lycra splintage – show promise, but need further evaluation in the context of acute rehabilitation
- The role of muscle strengthening exercises in post acute rehabilitation may be appropriate for some patients without adversely affecting tone
- Electrical stimulation techniques, although used for movement loss related to muscle paresis may prove to be useful adjunct to other treatments (*e.g.* botulinum toxin-A) particularly for treating spastic equinus deformity

- Phenol nerve blocks can produce good results in leg spasticity refractory to standard treatments and can be useful in patients with chronic hemiparesis where botulinum toxin-A produces beneficial but short term effects
- Existing treatments in combination with the timely use of newer antispasticity drugs makes it likely that the number of patients with refractory spasticity requiring surgical intervention will diminish. Nevertheless, refractory spasticity will occur and, therefore, there is continued need for expertise in surgical interventions.

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