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Review article

Breakthroughs in the spasticity management: Are non-pharmacological treatments the future?

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ABSTRACT

The present paper aims at providing an objective narrative review of the existing non-pharmacological treatments for spasticity. Whereas pharmacologic and conventional physiotherapy approaches result well effective in managing spasticity due to stroke, multiple sclerosis, traumatic brain injury, cerebral palsy and incomplete spinal cord injury, the real usefulness of the non-pharmacological ones is still debated. We performed a narrative literature review of the contribution of non-pharmacological treatments to spasticity management, focusing on the role of non-invasive neurostimulation protocols (NINM). Spasticity therapeutic options available to the physicians include various pharmacological and non-pharmacological approaches (including NINM and vibration therapy), aimed at achieving functional goals for patients and their caregivers. A successful treatment of spasticity depends on a clear comprehension of the underlying pathophysiology, the natural history, and the impact on patient's performances. Even though further studies aimed at validating non-pharmacological treatments for spasticity should be fostered, there is growing evidence supporting the usefulness of non-pharmacologic approaches in significantly helping conventional treatments (physiotherapy and drugs) to reduce spasticity and improving patient's quality of life. Hence, non-pharmacological treatments should be considered as a crucial part of an effective management of spasticity.

1. Introduction

Spasticity is defined as a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes, which results from an abnormal intra-spinal processing of primary afferent inputs. Such motor disorder follows a central nervous system (CNS) damage that dissociates the motor and sensory components of the diastaltic arch, thus inducing a segmental hyper-excitability [1].

Spasticity can be associated with a variety of symptoms and signs belonging to upper motor neuron syndrome, including clonus, dystonia (muscle constriction in the absence of any voluntary movement), extensor or flexor spasms, spastic co-contraction (contraction of both the agonist and antagonist muscles resulting from an abnormal pattern of commands in the descending supra-spinal pathway), abnormal reflex responses (exaggerated deep tendon reflexes and associated reaction), loss of dexterity, muscle fatigue, weakness, stiffness, fibrosis, and atrophy [2–6].

Many CNS diseases, including stroke, multiple sclerosis (MS), cerebral palsy (CP), and spinal cord injury (SCI), can provoke spasticity. Three main lesion sites have been suggested to induce spasticity: the brainstem, the cerebral cortex (in primary, secondary and supplementary motor areas) and the spinal cord (pyramidal tract) [7]. Of note, spasticity in MS is believed to be due to either axonal degeneration or demyelination within specific descending tracts, or both, thus leading to an inhibitory/excitatory imbalance at spinal network level [8].

Initially, CNS damage determines a local anarchic neuronal reorganization and, as a consequence, a dysfunctional and maladaptive connectivity among several brain structures, including supplementary motor, cingulate motor, premotor, posterior and inferior parietal areas, and cerebellum [9]. These pathologic rearrangements contribute to subcortical hyper-excitability, leading to an increased muscle activity and exaggerated spinal reflex responses to peripheral stimulation [7]. Such hyperactivity may depend on: i) disinhibition of the normal reflex activity (deep ten-

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don reflexes and flexor withdrawal reflexes); ii) release of primitive reflexes (e.g., Babinski sign); iii) hyper-active tonic stretch reflex; and iv) muscle fiber metabolic modifications concerning fiber group I (low-oxidative) and II (fast-twitch) [1,10]. In addition, the damage of large networks contributing to cortico-spinal output produces a decreased firing rate at lower motorneurons, and therefore a loss of strength [11]. Consequently, limb immobilization and disuse lead to muscle atrophy, which includes a decline of normal weight-bearing, sarcomeres, skeletal muscle mass, and a reduction in bone mineralization with an accumulation of connective tissue and fat [12,13]. These phenomena further exacerbate the disability and side-effects induced by spasticity.

Moreover, spasticity produces an internal rotation and adduction of shoulder coupled with flexion at the elbow, wrist and fingers, and an adduction and extension of the knee, with equinovarus foot [15,16]. This may also affect the truncal musculature, resulting in poor postural control [16]. Such pathologic postures depend on the imbalance of forces between the agonist and antagonist muscles, affecting the static joint position and dynamic limb movements [16,17].

Even though spasticity has not exclusively negative aspects for the patient, since a paretic limb may allow the patient to continue walking, standing, and transferring, there is a great variety of dramatic short- and long-term negative consequences on daily life activities. In fact, spasticity can *per se* cause a severe disability, owing to: (i) several impairments with body structures or physiological function, such as restricted joint range of movement, loss of dexterity, abnormal limb postures and pain; (ii) activity limitations in limb use, which can interfere with mobility, transfers, and independence with activities of daily; (iii) difficulty with provision of care to an affected limb by the person with MS or their caregivers, such as maintaining palmar hygiene or applying a splint or orthotic; and (iv) restrictions in 'participation' limiting societal roles relating family, work and life situations. Altogether, such issues are very limiting concerning daily life activities and the quality of life (QOL). Therefore, spasticity needs to be carefully assessed and requires an accurate long-term management. A successful treatment of spasticity depends on the clear comprehension of the underlying pathophysiology, the natural history, and the impact on patient's performances.

1.1. When to treat spasticity

Some predictive factors for spasticity development need to be carefully recognized to initiate as soon as possible an adequate treatment. These factors include: (i) a high degree of paresis at stroke onset; (ii) limb hypoesthesia; (iii) more severe paresis at 16 weeks compared to the first week; and (iv) a Modified Ashworth Scale (MAS) of $\geq$2 in at least one joint within 6 weeks after stroke [18,19]. In addition, it has been previously proposed that before treatment is initiated, the following should be considered [13,14]: Does the patient need treatment? What are the aims of treatment? Do the patient and caregivers have the time required for treatment? Will treatment disrupt the life of the patient and caregivers? A striking preliminary consideration consists in the indications and expectations for treatment, as a reduction of leg muscle tone may worsen mobility if tone compensates for leg weakness, allowing the patient to stand. Indeed, careful assessment of the role spasticity plays in substituting for strength (specifically, to facilitate with transfers) is important to avoid decreasing, rather than increasing, function. Manual dexterity and strength also do not improve by reducing muscle tone, which means that treatment of spasticity may not lead to an improvement in function. Hence, the ability of muscles to function after spasticity reduction may vary. Treating spasticity does not always facilitate the acquisition of previously undeveloped skills. As a consequence, clearly identifying the goals of the patient and caregiver is vital. A key factor of spasticity management is the achievement of an individualized, patient-centerd goals, which are set collaboratively with patients, their caregivers, and the rehabilitation team in a functional context [20] and which are a reliable index of a successful outcome, demonstrated in one or more domains of clinical scales [21]. Such goals are derived and prioritized through a multidisciplinary process, where goals are specific, measurable, achievable, realistic and timely [22], and they may be focused on reducing symptoms or impairments, as well as improving the activity level (active and passive function) and the participation and QOL. Patient participation is required to achieve the goals with improvement in the patient's personal potential as a result. To achieve such goals, the following issues should be taken into account: (i) *nursing care*, including preventing or treating contractures and decubitus, body positioning, bladder catheterization, orthotics fitting, facilitating caregiver work, pain management, sleep quality; (ii) *movement improvement*, including unmasking of voluntary movements, accelerating the "spontaneous" recovery process, modifying the "immature" motor pattern, using new recovery techniques to promote guided neuroplasticity, and new functional pattern in moving and walking; (iii) *daily life activities optimization*, including transfers, getting around, putting on clothes, personal hygiene, driving, and so on; (iv) *QOL improvement*, with regard to independent living; and (v) *social and professional reintegration*. In addition, the elimination or avoidance of triggers that can provoke or enhance spasticity (e.g., urogenital infections, constipation, pain) and prevention of complications (including contractures and pressure sores) may also be important [23–25]. Another striking question when treating spastic muscles concerns the impact of their antagonistic muscle groups. While often weak, these muscle groups themselves may be spastic. Treatment of the agonist muscle without treatment of the antagonist muscle may create an additional problem instead of a solution.

In summary, a proper and clear comprehension of the spasticity underlying pathophysiology, its natural history, and the impact of spasticity on patient's performances are of outmost importance to select the most adequate therapeutic option to patient's conditions and goals.

1.2. How to treat spasticity

To treat spasticity, we have currently available a wide repertoire of intervention that can be divided in the following categories: (i) preventative measures; (ii) therapeutic interventions (physical therapy, occupational therapy, hippotherapy, hydrotherapy) and physical modalities (including vibration and electrical currents); (iii) Positioning/orthotics (including taping, dynamic and static splints, wheelchairs, and standers); (iv) oral medications (such as baclofen and dantrolene); (v) injectable neurolytic medications (Botulinum toxins and phenol); and (vi) surgical intervention. For simplicity, we can summarize such approaches into pharmacological and non-pharmacological (Table 1). The former includes oral and injective drugs, while the latter comprehends physical, instrumental, and surgical approaches.

Generally speaking, these categories can be implemented in a neurorehabilitation program [20] by using: (i) uni-disciplinary therapy, e.g. physiotherapy (PhT) or occupational therapy only; (ii) individual pharmacological and non-pharmacological treatment modalities or physical interventions that may form a component of a rehabilitation program; and (iii) multidisciplinary rehabilitation programs involving the provision of a coordinated program by a specialized team of health professionals, delivered by two or more disciplines medical, nursing, physiotherapy, occupational therapy, orthotists, and others.