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The Role of Spasticity in Functional Neurorehabilitation- Part I: The Pathophysiology of Spasticity, the Relationship with the Neuroplasticity, Spinal Shock and Clinical Signs

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Abstract

The symptom/clinical sign of spasticity is extremely important in functional neurorehabilitation, since it reduces the functional independence both in the quadruped animal as in the human biped.

This clinical sign/symptom manifests itself alonside with pain, muscle weakness, impaired coordination and poor motor planning, leading to a spastic movement disorder.

To perform a correct FNR protocol an understanding of its pathophysiology is required. In addition FNR often stimulates the property of the central nervous system, which is neuroplasticity, which may potentiate the spastic movement disorder.

In this regard, especially in the human biped, we must take into account the appearance of spinal shock and its development into spastic movement disorder, and therefore, a tight and constant monitoring of clinical signs is essential in order to choose the adequate methods and modalities of FNR.

Keywords: Neurorehabilitation; Neuroplasticity; Multiple sclerosis

Introduction

Spasticity is defined as an increased resistance to a passive movement due to a lowered threshold of tonic and phasic stretch reflexes [1]. Resulting in involuntary and sustained muscle contractions, and it may be present in patients with stroke, cerebral palsy, multiple sclerosis, brain injury and spinal cord injury (SCI) [2,3].

Spasticity appears in the upper motor neuron syndrome (UMN syndrome), being the leading cause of disability in the bipedal human [4] with a central nervous system lesion due to a lesion in the pyramidal and extrapyramidal tracts [5] and it may also appear in lesions of the UMN in the quadruped. Since the quadrupeds spinal cord injuries are predominantly thoraco-lumbar [6] due to the discontinuity of the intercapital ligament [6], the clinical sign of spasticity is frequently addressed in functional neurorehabilitation (FNR) [7-9]. Spasticity both on the biped and quadruped usually develops in the antigravity muscles.

In the human biped, spasticity appears in the upper-extremity flexor muscles as result of a stroke, whereas an excessive muscle spasm is in the lower extremity extensor muscles is secondary to SCI.

In both the biped and quadruped, spasticity limits the motor activity, reducing independence and leading to contractures, pain and muscle weakness [10-13].

The symptom / clinical sign of spasticity, does not manifest itself in an isolation way, but rather as a complex medical condition known as spastic movement disorder (SMD) [14].

This review aims to provide an explanation of the sympton of spasticity that appears in the UMN syndrome, both in the biped and quadrupedal. Through the neuroanatomy and spasticity pathophysiology, it is possible for us to gain scientific knowledge and transpose the clinical evolution of FNR for the UMN syndrome, both from the biped to quadruped, and vice versa.

The spastic movement disorder (SMD), presents spasticity as a symptom in the biped and quadruped, but it´s also accompanied by muscle weakness, impaired coordination, poor motor planning and presence of fatigability quickly [15]. There is an interrelationship between spasticity, immobilization, muscle shortening, muscle contracture, decreased range of motion (ROM) and eventually muscle stiffness. This interrelationship is difficult to diagnose whenever we want to determine wheter a muscle is spastic or whether it presents a contracture. However, when performing the FNR examination in the daily practice, it is already easy to identify a stiff muscle, since it no longer presents range of motion.

Spasticity pathophysiology

The pathophysiology of spacticity is multifactorial. There are several hypothesis at the moment and it's mechanism will quite possibly be discovered once they're all put together. While it is necessary to explain the muscle spasm as much as possible, spasticity pathophysiology can be explained by two mechanisms, which are interconnected:

1 – The spinal mechanism (which consists in the work of motor neurons and their inter-neurons sub-systems)

2 – The supraspinal mechanism of the descending pathways [1,15]

And also two secondary actions considered in the pathophysiology of spasticity which are: the non-neural secondary contributions of the muscular system; and the secondary contribution of neuroplasticity.

Spinal mechanism or abnormal intraspinal processing

Evidence from several experiments on the human biped and the quadruped animal has shown several changes in the excitability of numerous excitatory or inhibitory spinal pathways following a SCI (spinal cord injury). The changes in excitability of the spinal pathways following a spinal cord injury, are described by four processes:

Reduction in post-activation depression

Reduction in pre-synaptic inhibition

Reduction in 1a-reciprocal inibition

Enhancement in the excitability of motoneurons

Reduction in post-activation depression (PAD)

Resulting from the quantity of neurotransmitter released at 1a-motoneuron synapse, wich is decreased due to repeated activations [16]. The PAD has been confirmed in the human biped and in the quadruped animal. However, the PAD, only appears to be reduced when functional functional tests are performed and, therefore, its value is not conclusive [2].

Reduction in pre-synaptic inhibition (PSI)

The PSI adjusts the strength of synaptic inputs to neurons, affecting the levels of neurotransmitter release. The PSI is decreased in the spasticit human biped when performing both at rest and functional tests, but on the quadruped animal the reduction in PSI is not present [2,17,18].

Reduction in 1a-reciprocal inibition

The reciprocal activation of antagonistic muscles during movement is mediated by a disynaptic inibitiory pathway called 1a-reciprocal inhibition [2]. The 1a-reciprocal inhibition is reduced in individuals that have a spinal cord injury [18,19].

A co-contraction is simultaneously the contraction of both agonist and antagonist muscles. In healthy individuals, the voluntary output of the motor córtex, activates the motoneuron of agonist muscles, and through the 1a-interneurons inhibits the innervation of the antagonists muscles, which we refer to as reciprocal inhibition. In the UMN syndrome, the reciprocal inhibition is lost during a central command [20]. It is important to note that the inhibitory interneuron that produces inhibition of the antagonist muscle activity is facilitated by descending tracts, particularly the cortico-spinal tract. The efficacy of this reciprocal inhibition circuit increases with maintenance of the nervous system and can be altered as a result of cortical injury [20]. A healthy biped will need to have varying degrees of reciprocal innervation (meaning the interaction between the agonist and antagonista muscles when both are actively contracted) so as to have a well-coordinated muscle activity function [20].

Enhancement in the excitability of motoneurons

It is the greatest cause involved in the pathophysiology of spasticity after SCI and it has been confirmed in the bipedal human and quadruped animal, having been observed during at rest and functional tests [2].

Several experiments have shown that the muscle spasms indicate an increase in motoneural firing rate, causing a strong muscle contraction [21].

The enhancement in motoneuronal excitability is attributed to changes in motoneural intrinsic properties, such as the activation of persistent inward currents (PICS) and depolarizations of the membrane potential [2,22,23].

PICS are depolarizing currents that do not inactivate with prolonged membrane depolarization, and are regulated by monoaminergic centers in the brainstem [19,24-26]. After a SCI, PICS lose control over the descending pathways [15,25,26], therefore, allowing an uncontrolled action with high motoneuronal firing rate, which explains the muscle spasms observed during spasticity [2-4,11], since the activation of PICS transforms the response of motoneurons in prolonged firing activity responses, thus is permitted an increase in the motoneuronal excitability [2,13,19,22,23].

When the SCI is chronic, the motoneurons are highly sensitive to residual monoamines, allowing the reactivation of PICS and restoration of motoneuronal excitability.

Spasticity arises with the hyperexcitability of motoneurons, but also with increased interneural excitability, which provides a solid explanation, for the enhancement [22] of motoneuronal excitability [2,19,22]. Lastly, it is possible to arrive to the conclusion that the spinal interneurons play a key role in the development of spasticity and that the interneurons system is involved in the stretch arc reflex and in the pathophysiology of spasticity, as it can be showed in **Figure 1,** where the spinal interneurons are essential, not only in the stretch arc reflex, but also in the normal muscular tone. This interneurons system (excitatory and inhibitory), mediate the motor signals [21], and if the excitatory interneurons dominate, the clinical sign of spasticity appears.

The axons of lower motor neurons (LMN) emit collateral branches, which will then synapse with the Renshaw neurons, which in turn form synapses with the LMI. It is believed that the Renshaw neurons provide feedback to the LMN α, inhibiting its activity [27], namely, the recurrent inhibition, however, this process probably plays the major role in the pathophysiology of spasticity [15,28].

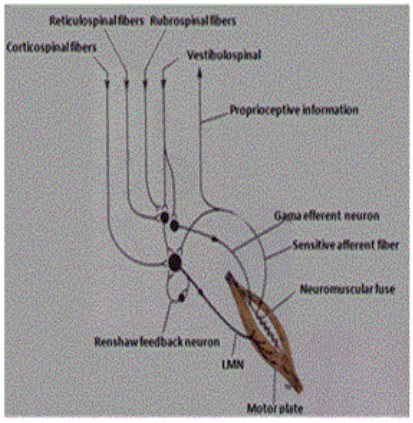

Figure 1 Neurologic dependence of the normal muscular tone [27].

Supraspinal mechanism of descending pathways

There are five major descending motor pathways in the motor system of the human biped and the quadruped animal, the corticospinal tract (CST), the rubrospinal tract, the reticulospinal tract (RST), the vestibulospinal tract (VST) and the tectospinal tract [15].

The CST is the only tract that originates at the level of the motor cortex, all others arises from the brainstem [29]. In the human biped the CST is the main tract involved in voluntary movement, whereas in dogs, the rubrospinal tract is responsible for that function, thus allowing us to classify the human biped as pyramidal, and the quadruped animal as extra-pyramidal (ex.: dog and cat). The main downward tract for the quadruped, the rubrospinal tract, is currently vestigial in the bipedal human [7].

The descending tracts RST and VST are anatomically distinct and differ in terms of cortical control. The dorsal RST in the human biped presents an inhibitory effect of the stretch reflex and is controlled by the motor cortex. It usually meets the lateral CST, as a descending pathway, through the dorsolateral funiculus [3]. On the other hand the medial RST and VST exert an excitatory power at the level of the spinal stretch reflex [3]. The medial RST it is not controlled by the motor cortex.

The RST and VST promote the excitatory and inhibitory balance of downward regulation of the spinal stretch reflex, and therefore an imbalance in the influence of these descending pathways is considered to be one of the major causes of spasticity [3,15,19]. Usually the excitatory system that predominates over the inhibitory system, allowing for an exageration of the spinal stretch reflex [3,19]. Spasticity is maintained by the excitatory influence and its facilitation, which is carried out by the medial RST. The VST plays a minor role.

The way, the most significant cause of spasticity is related to abnormalities in the RST and, in addition, studies confirm that the hyperexcitability of the reticulospinal descending pathways while at rest, occurs during the spastic stages [15].

Also in the quadruped two motor areas of the motor cortex and cerebellum are projected into the pontine and medullary reticular formation. Brain projections are projected into the reticular formation, promoting the neurons and forming the pontine and medullary reticulospinal tract, therefore, the motor cortex processesses as influence over the reticular modulation [30].

The reticular formation has an excitatory and inhibitory effect over motor activities through the pontine RST and medullary RST [30]. The pontine RST originates in the pontine reticular formation and facilitates the antigravity muscles of the carpus, producing an excitatory effect over the α and γ LMN of the extensor muscles, while inhibiting the α and γ LMN of the flexor muscles. The medullary RST originates from the medullary reticular formation and facilitates the flexor muscles, having an excitatory effect over α and γ LMN of the flexor muscles, while inhibiting the α and γ of LMN of the extensors muscles. Both the pontine and medullary RST are under the influence of the cerebral cortex, cerebellum and ascending somatosensory systems, howerever the locomotor generation is in the midbrain on the reticular formation. Both tracts exert a constant balance between facilitation or inhibition at the level of the spinal motor neurons. Thus, the reticular action is essential for locomotion, maintenance of posture and muscle tone [30,31]. In the human biped it is involved in the coordination of fine movements, in the autonomic regulation of respiration, heart rate, blood pressure and modulation of pain [1,32].

Secondary contributions of spasticity

Besides the mechanisms described, we have to consider the importance of the non-neural secondary contributions of the muscular system, as well as the secondary contribution of neuroplasticity which will be described below.

Non-neural secondary contributions of the muscular system

Spasticity can be explained by the occurance of alterations in the mechanical properties of the muscle, which become adaptive to immobilization, leading the muscle to gradually produce a contracture [3,13,15,17,18,28].

Studies have shown that one of the alterations in the mechanical properties of the muscle is the increase in the amount of collagen in the extracellular matrix of muscle fiber bundles [17], which constantly appears in the muscles of three year old children with cerebral palsy [3,17,33].

The alterations in the mechanical properties of the muscle such as stiffness, contractures, atrophy and fibrosis are present in both bipedal and quadrupedal patients with spinal cord lesion (SCL). There is a direct correlation between spasticity, contracture and reduced range of movement (ROM) [18,28].

Secondary contribution of neuroplasticity

In the months after a SCI, motoneurons develop large voltage-dependent persistent inward currents (PICs), which cause sustained reflexes and are associated with muscle spasms. The muscle spasm is obtained through the excitatory postsynaptic potential (EPSP) which lasts long enough to activate the PICs [23].

In acute disorders of the CNS, the symptom of spasticity in the bipedal human and clinical sign in the quadruped animal develops throughout the FNR process, which is thought to be a result of the hyperexcitability of the post synaptic membrane, leading to the formation of new receptors. This phenomenon is designated by denervation supersensitivity.

Following acute injury (stroke or trauma) interneuron activities arise, forming new and abnormal synapses between themselves and the α-motoneuron, leading to the formation of an abnormal reflex pathway [3].

Whenever an acute disorder is presented, we are subjected to injuries in the main descending pathways, leading to damage of the corticospinal tract in humans and the rubrospinal tract in dogs. Thus, in the latter, it is necessary to resort to the neuroplasticity of the RST in order to increase the individual's quality of life, since the hyperexcitability of this downward pathway is, along with other causes, the one responsible for spasticity, particularly in the biped following a stroke. The fact that spasticity develops during FNR, indicates that it is an abnormal phenomenon of plasticity.

Spinal shock and spasticity

In daily practice, it is essential to know when the clinical sign of spasticity appears following a central nervous system injury.

The hyperexcitability of α-motoneurons associated with an exagerated stretch and flexion reflexes in spastic patients can be caused by several factors.

An acute spinal cord trauma, with complete rupture of the descending pathways of the supraspinal regions, will lead to the loss of all spinal reflexes. This condition of arreflexia is referred to as spinal shock [2,31]. In dogs the spinal shock, can last from minutes to hours, whereas in people it can last up to several months [21].

When the spinal shock evolves into spasticity, alterations in the predominance of the type of fibers occur [31].

In 1996, Ito et al found a predominance in type I fibers and a deficiency in type II fibers after performing muscle biopsies in children with spastic cerebral palsy. Type I fibers are the first to be lost and, therefore, an excessive amount of these might explain the gradual increase in hypertonicity [22,31].

Spinal shock can be explained by a hypoexcitability of the α-motoneuron, which turns into hyperexcitability with the development of spasticity [34].

It is known that the activity and excitability of interneurons possess an important influence over the spinal neuronal activity, eventhough the alterations in activity that occur during spinal shock and its transition to spasticity are unknown [34].

Following a SCI in the biped, a first phase of spinal shock is observed, with loss of tendon tap reflexes below the level of the lesion. The second phase is one of transition (3-8 weeks after SCI) and is characterized by the reappearence of the tendon tap reflexes. At last, the third phase of the spastic syndrome, is characterized by increased muscle tone, involuntary muscle spams, and exaggerated tendon tap reflexes [34].

In this syndrome exists a prolongation of the time-to-peak of the EPSP, elicited by the sprouting of the primary spindle aferente fibers [35,36].

In cases of stroke, in the biped, spinal shock develops and it can last from 1 to 6 weeks [15,37] due to a balance between the inhibitory pathways of dorsal RST and the facilitatory pathways of the medial RST and VST, in order to obtain an excitability of the spinal stretch arc reflex. When it comes to the muscular co-contraction, certain alterations occur, such as an increase in the 1a afferent input, leading to stimulation of the γLMN and, associated with alternating interneuron circuits allows for motoneuron excitability, reducing the pre-synaptic inhibition of the afferent 1a, and facilitation (instead of inhibition) of the 1b of theαLMN, leading to an greater contraction of extrafusal fibers [3,19]. In addition, due to neuroplasticity, the PICs are activated in the motoneurons, producing self-sustained firing, leading, once again, to hyperexcitability of the αLMN, which is the main cause of spasticity, in the human biped following a stroke. Finally, it is possible to conclude that an abnormal intraspinal process is caused by a hyperexcitability of the αLMN, which is secondary to an imbalance of excitatory and inhibitory inputs from the descending pathways [3,15].

Clinical signs of the spastic movement disorder

The clinical signs of spasticity are specific and characterized by an excessive muscle tone associated with an exacerbated stretch reflex, which lead to the development of the spasm-pain cycle, which in turn produces a weak muscular co-contraction, causing alterations in movement coordination and movement planning, with decreased active assisted range of motion (AAROM) and active range of motion (AROM), causing a state of fatigability in the patient [2,5,14,15,18,28,38].

This reduced state of ROM, along with the changes present in the muscular intrinsic properties, leads to a symbiosis between spasticity and muscle contracture, due to progressive alterations of muscular fibrosis associated with immobilization and muscular atrophy [3,5,18].

At this point, the methods for assessing the degree of spasticity and for monitoring the evolution of the FNR arise, being classified according to the modified Ashworth scale (MAS) [3,18,28,39,40]. The MAS measures the muscular resistance resultant from muscular contractures, with modifications in the muscular composition occuring due to a loss of of sarcomeres and viscoelastic components [28].

Pain is another clinical signal associated with spasticity [14,39], as it can cause a disruption of the muscle fibers due to the release of substances that are excitatory for the muscle nociceptors [41]. Pain possesses a role in the spasm-pain cycle, causing immobilization and leading to greater changes in the intrinsic properties of the muscles which, in turn, cause even more spasm and, successively, more pain and disability [3,14,41,42].

Pain can be divided into nociceptive pain, derived from the skin, the musculoskeletal system or from visceral organs [22], and neuropathic pain, caused by damage to the sensory system of the peripheral nervous system or central nervous system [13,14,42,43].

Pain promotes inadequate postures, leading to the non-use of limbs, which means, no support [14]. As mentioned previously, with the evolution of the process of spasticity, the muscles become abnormally shortened, creating a higher resistance to passive range of motion (PROM) exercises, which can lead to muscular deformities [14], such as those seen in quadrupeds with polineuroradiculoneurophaties secondary to toxoplasma or neospora [44] and in children with cerebral palsy, multiple sclerosis and stroke [14]. There is an association between clinical signs/symptoms of spasticity, muscle weakness and impaired motor coordination [45,46].

Discussion

With this scientific review regarding spasticity, it is possible to obtain information for the management of the clinical signal/symptom of spasticity, which does not manifest by itself but rather through an interconnected triangle between pain and muscle weakness [4,10,11,15,38,46,47].

In a simplified way, we gathered information related to the reduction in Ia reciprocal inhibition, which consists in the activation of motor neurons of the agonist muscles, followed by an inhibition of the innervation of antagonistic muscles (by the Ia interneurons). This physiological process of muscular co-contraction is altered and, therefore, motor coordination is not observed [2,18,20].

The entire system of interneurons system is involved in the pathophysiology of spasticity, but mainly the group of excitatory interneurons, which cause motoneural excitability [2,15,19,22,23]. In addition, the importance of Renshaw neurons in the pathological process of spasticity and, consequently, the recurrent inhibition were discussed [27]. According to what has been described, the imbalances in the descending pathways, especially in the RST and VST, when it comes to excitatory and inhibitory balance, are associated with spasticity [3,15,19]. Everything is potentiated by modifications in the mechanical properties of the muscle. This intrinsic cause is the one responsible for the development of a contractured and, eventually, stiff muscle with a decreased ROM (non functional) [9,18,48].

Conclusion

It is essential to study the transition of a clinical presentation of spinal shock into spasticity, especially for the human biped and in order to follow adequate FNR protocols that stimulate neuroplasticity of the RST without originating the pain-spasm-pain cycle.

To conclude, in FNR, it is very important to differentiate a spastic muscle from a contracture and even from a stiff muscle. An early evaluation of these differences allows for an increase in functional mobility of the patients. This way, with the comparison between the human biped and the quadruped animal, it was possible to arrive to the conclusion that there is an interconnection between both pathophysiologies of spasticity, making it possible to reassess the nomenclature and to introduce the concept of UMN syndrome in veterinary medicine, already used in human medicine, in regard to spasticity.

Finally, it is possible to conclude, through clinical evidence, that the dog and cat are perfect for the evolution of FNR in human medicine.

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