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Review

The neurophysiology of deforming spastic paresis: A revised taxonomy

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ABSTRACT

This paper revisits the taxonomy of the neurophysiological consequences of a persistent impairment of motor command execution in the classic environment of sensorimotor restriction and muscle hypo-mobilization in short position. Around each joint, the syndrome involves 2 disorders, muscular and neurologic. The muscular disorder is promoted by muscle hypo-mobilization in short position in the context of paresis, in the hours and days after paresis onset: this genetically mediated, evolving myopathy, is called spastic myopathy. The clinician may suspect it by feeling extensibility loss in a resting muscle, although long after the actual onset of the disease. The neurologic disorder, promoted by sensorimotor restriction in the context of paresis and by the muscle disorder itself, comprises 4 main components, mostly affecting antagonists to desired movements: the first is spastic dystonia, an unwanted, involuntary muscle activation at rest, in the absence of stretch or voluntary effort; spastic dystonia superimposes on spastic myopathy to cause visible, gradually increasing body deformities; the second is spastic cocontraction, an unwanted, involuntary antagonist muscle activation during voluntary effort directed to the agonist, aggravated by antagonist stretch; it is primarily due to misdirection of the supraspinal descending drive and contributes to reducing movement amplitude; and the third is spasticity, one form of hyperreflexia, defined by an enhancement of the velocity-dependent responses to phasic stretch, detected and measured at rest (another form of hyperreflexia is "nociceptive spasms", following flexor reflex afferent stimulation, particularly after spinal cord lesions). The 3 main forms of overactivity, spastic dystonia, spastic cocontraction and spasticity, share the same motor neuron hyperexcitability as a contributing factor, all being predominant in the muscles that are more affected by spastic myopathy. The fourth component of the neurologic disorder affects the agonist: it is stretch-sensitive paresis, which is a decreased access of the central command to the agonist, aggravated by antagonist stretch. Improved understanding of the pathophysiology of deforming spastic paresis should help clinicians select meaningful assessments and refined treatments, including the utmost need to preserve muscle tissue integrity as soon as paresis sets in.

1. Introduction – Historical perspective

Despite decades of research and clinical efforts, patients with paresis of central origin invariably end up with an altering and shortening muscle disorder, only days or weeks after paresis has set in. This disorder worsens in the following months and years. In children with infant paresis, these muscle changes are of greater and even sometimes massive proportions. The mechanisms by which an initially trivial neurologic disorder transforms into a pathological duo of both a muscular and a nervous disease, the 2 potentiating each other, must be better understood for a better chance of achieving more than relentlessly repeated measurements of "increased tone" in paretic patients.

Many lesions of the central nervous system may lead to a syndrome of deforming spastic paresis with 2 main components: the first is a neurologic insult with a default in voluntary motor command. This quantitative lack of descending motor command accessing motor neurons leads to motor behavioral hypoactivity, which corresponds to a state of sensorimotor restriction [1]. Among other consequences, motor hypoactivity leads to rapid muscle deconditioning, with deleterious structural and functional adaptations. Clinically, this muscle disorder manifests by a gradual decrease in muscle extensibility — which, for example, has been clinically identified as soon as 25 to 30 months of age in children with brain lesions at birth [2] but has been shown to genetically

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start as soon as a few hours after the hypo-mobilization onset in animal models [3]. The lack of muscle extensibility enforces a dramatic change in the pattern of afferent signals that are chronically sent to the central nervous system. These permanently increased afferent signals affect and aggravate the neurologic disorder, with the emergence of different types of stretch-sensitive muscle overactivity in the antagonist [3,4] and the transformation of simple agonist paresis into stretch-sensitive paresis [3]. Concomitantly, uncorrected motor hypoactivity (i.e., insufficiently counteracted sensorimotor restriction) also leads to further deterioration of the motor command to the underused limb segments (i.e., paresis aggravation) [5].

The combination of these 2 disorders, muscular and neurologic, leads to early neuro-orthopedic body deformities that are visible during movements only in very mild cases (e.g., during the swing phase of gait just before foot landing and at initial contact of stance) or simply during spontaneous resting postures in more severe cases.

The term "spasm", from the Greek spasmos (spasm, convulsion), is ancient — used by Hippocrates to describe an epileptic seizure — but the English adjective "spastic", derived via Latin from the Greek spastikos ("drawing in"), may have been first used in the 16th century to describe contraction of muscles around wounds. In 1829, Good described "a spastic wryneck as an excess of muscular action on the contracted side" [6]. Little, in 1843, brought the word closer to its current meaning in describing the deformities in cases of spastic diparesis; his name would later be given to this deforming spastic disorder [7]. Later, the noun spasticity (in German Spastizität) was probably first used by Erb in 1875 [8].

The term then became largely overused in the medical literature, with no unanimous definition, a situation that created much confusion among researchers and clinicians. In 1954, Tardieu proposed a definition of spasticity as 'è an increase in stretch reflexes that could be characterized and measured by the speed required to elicit the reflexes" [9]. Following his own definition and to assess this phenomenon, Tardieu developed a clinical method to measure spasticity, through the angle of the muscle reaction to stretch at various speeds (5 different speeds initially) [10]. In 1980, a complex consensus definition of the word spasticity was then proposed as "...a motor disorder, characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyper-excitability of the stretch reflex as one component of the upper motor neuron (UMN) syndrome" [11]. Precise investigation of this long definition shows how confusing, and in some ways inaccurate, it may be; for example, the term "velocity-dependent increase" is an unfortunate misnomer because it describes the opposite of what occurs in patients with spasticity: the increase in stretch reflexes is actually slowness-dependent in spastic patients. The reflexes themselves are velocity-dependent but their pathological increase, as compared with healthy subjects, becomes less and less obvious as one stretches faster [12]. Along the lines of Tardieu's thinking and to make the definition of the word as precise and objective as possible, spasticity has been more recently defined as "an increase in the velocity-dependent reflexes to phasic stretch, detected and measured at rest" [13].

In the meantime, Ashworth had published an easy-to-use, simple ordinal scale to grossly rate resistance to passive movement in individuals with spastic paresis [14]. Through another common misconception, this scale was later used by many authors as a tool evaluating spasticity, rather than a mere measurement of global resistance to passive movement (i.e., tone). In fact, when keeping the strict "stretch reflex enhancement" definition of spasticity, several authors have shown that resistance to passive movement depends on a number of factors other than spasticity, such as soft-tissue contracture including spastic myopathy, or spastic dystonia [15–17]. In recent years, the Ashworth scale has come under vehement criticism, first because it does not evaluate spasticity and second for its poor functional relevance and validity [18–20]. Nevertheless, this scale is still used in many current studies to "measure spasticity" [21].

The name deforming spastic paresis was then proposed to describe the clinical syndrome caused by lesions involving the corticospinal pathways [17]. This syndrome involves 2 disorders: a muscle disorder called spastic myopathy combining muscle shortening and loss of extensibility and a neurologic disorder comprising 4 main components:

- spastic dystonia defined as an unwanted, involuntary muscle activity at rest, in the absence of any phasic stretch or voluntary effort, but sensitive to tonic stretch;
- spastic cocontraction, defined as unwanted, involuntary muscle activity in the antagonist, during voluntary effort directed to the agonist, aggravated by antagonist stretch;
- spasticity, an enhancement of the velocity-dependent responses to phasic stretch, detected and measured at rest;
- and stretch-sensitive paresis, corresponding to a decreased central command to the agonist, aggravated by antagonist stretch [17].

In pursuing Tardieu's pioneering work, we first developed a two-speed clinical assessment tool to measure spasticity by using a spasticity angle as its key parameter (difference between the angle of movement arrest at slow speed of stretch and the angle of catch at fast speed), which we called the Tardieu Scale [22,23]. The tool was then refined and expanded into a Five-Step Assessment, to reflect as many aspects of deforming spastic paresis as seemed clinically possible, with the calculation of separate coefficients of impairment, designed to measure particular aspects of the neurologic disease independent of raw muscle extensibility [17,24].

To indeed design meaningful measures of deforming spastic paresis and to treat the whole syndrome adequately, its pathophysiology must be clarified. This is the aim of this article, in which each component of the syndrome is revisited (Table 1).

Table 1
Main features of spastic paresis, with their deforming and disabling properties and their clinical measurability. FRA, flexor reflex afferents.

	Symptom name	Condition of detection	Trigger	Deforming capacity	Disabling level	Measurability at bed side
Muscle disorder	Spastic Myopathy	Rest	N/A	High	High	Estimation possible
Neurological disorder						
Paresis	Stretch-sensitive paresis	Effort	N/A	None	Moderate	No
Muscle overactivity types	Spasticity	Rest	Phasic stretch	None	Low	Yes
	Spastic Dystonia	Rest	None	High	High	No
	Spastic Cocontraction	Effort	Effort directed to agonist	None	High	No
	Extrasegmental cocontraction (synkinesis)	Effort	Effort	Moderate	Moderate	No
	Nociceptive (FRA) spasms	Rest or effort	FRA stimulation	Moderate	High	No

2. The muscle disorder: spastic myopathy

This muscle disorder starts with the hypo-mobilization (complete or partial) of some muscles in short position, which acts as a true mechanical aggression of muscle tissue. Such hypo-mobilization typically begins with the onset of paresis (at which time point the muscle tissue is initially normal), and persists as paresis lingers [25–28]. This hypo-mobilization is often insufficiently compensated by healthcare teams. A muscle disease then develops via acute modifications of gene transcription in the muscle fibers immobilized in short position, with deleterious quantitative and qualitative changes [26–28]. Overall reduced rates of protein synthesis and induced expression of genes for disuse atrophy promoters (REDD1, REDD2, MAFbx, MuRF1) represent unseen changes when the muscle fiber is immobilized in long position [28]. Investigating mechanical and histological characteristics of spastic and healthy muscle biopsies taken from the same part of the flexor carpi ulnaris muscle, De Bruin et al. showed thickening of tertiary perimysium in cross-sections of fascicles, suggesting accumulation of collagen, also reinforcing major blood vessels, nerves and lymphatics [29]. These molecular, then biomechanical, physiological and finally clinical (see below) events follow an acute time course because most of the contracture has actually developed by the end of the acute/subacute period, within the days and weeks after hypo-mobilization onset [30]. This course of events constitutes a pathogenic entity termed spastic myopathy, which therefore is an evolving form of essentially avoidable myopathy that conditions and superimposes onto the neurologic disorder.

Clinically, spastic myopathy manifests as a loss of extensibility (stiffness) by increased muscle viscosity and elasticity, particularly obvious when applying high tension [30–37]. Spastic myopathy (classically and improperly called muscle contracture, as if this were a fixed phenomenon) becomes both the first factor of body deformity in patients with deforming spastic paresis [3] and, via increased spindle sensitivity in the contractured muscle [4], a factor greatly limiting passive and active movements (see below) [38,39].

3. The neurologic disorder

The neurologic disorder entails 2 main components, superimposed around each joint and acting synergistically to challenge active movements: muscle overactivity in antagonists (combining at least spastic dystonia, spastic cocontraction and spasticity) and stretch-sensitive paresis in agonists [3,13,39]. Spastic muscle overactivity comprises different forms of increased involuntary recruitment of motor units, of which the following 3 forms, most often co-existing with one another, are of particular importance.

4. Spastic dystonia

In 1966, Denny-Brown observed involuntary sustained muscle activity in monkeys with lesions restricted to the motor cortices. He further observed that such involuntary muscle activity persisted following abolition of sensory input to the spinal cord and concluded that a central mechanism rather than exaggerated stretch reflex activity had to be involved. He coined the term spastic dystonia to describe this involuntary tonic activity in the context of otherwise exaggerated stretch reflexes [40]. This phenomenon was later confirmed in humans [41]. Sustained involuntary muscle activity in the absence of any stretch or any voluntary command contributes to burdensome and disabling body deformities in patients with spastic paresis. Following Denny-Brown's work, a recent definition was proposed: an excessive, chronic, tonic muscle activation of supraspinal origin, detected and measured at rest, potentially reduced after maintained stretch of the dystonic muscle [42,43]. Spastic dystonia is likely related to increased involvement of brainstem descending pathways (rubro-, vestibulo-, tecto-, and ipsilateral reticulo-spinal pathways) undergoing abnormal branching onto deafferented hyperexcitable motor neurons following higher lesions [42–49]. Most of these brainstem descending pathways are excitatory and show reduced capacities of neuronal rest, as compared with the corticospinal pathway [50–52]. Within the most shortened muscles, spastic dystonia thus superimposes on spastic myopathy to represent the second major factor of deformity in patients with spastic paresis. In addition, recent studies propose the existence of persistent inward currents in spinal motoneurons, via upregulated Na and Ca channels following central motor lesions [53,54]. Contributions from altered synaptic inputs from surviving or abnormally branched sensory and descending fibers leading to overactivity and lack of motor coordination are also likely, as are alterations in motor cortical representational maps and basal ganglia lesions [43].

5. Spastic cocontraction

The phenomenon of abnormal antagonist cocontraction has long been noted in spastic paresis, even before the term spasticity was coined [55,56], but spastic cocontraction has recently been defined as an excessive degree of antagonistic activation elicited by voluntary agonist command, aggravated by antagonist stretch [13,57,58]. Hence, this type of overactivity is revealed and exclusively measured during voluntary command directed to the agonist; it has a mainly supraspinal origin and is aggravated by stretch of the cocontracting muscle [13,57,58]. Spastic cocontraction is a critical factor of limitation — sometimes reversal — of active movement in individuals with deforming spastic paresis [13,55–58]. Alterations in various physiological mechanisms have been associated with spastic cocontraction. These alterations include increased recurrent Renshaw inhibition [59], with associated reduction of Ia reciprocal inhibition exerted onto the antagonist during an agonist effort, as well as reduction of presynaptic inhibition and reduced increment of Ib inhibition [60–63]. Reduction of Ia reciprocal inhibition has been associated with poor motor performance, although the causal relation is unclear [62].

6. Spasticity

Spasticity is simply defined as an increase in the velocity-dependent reflexes to phasic stretch, detected and measured at rest [13]. With such a strict definition, spasticity is a useful construct to the clinician for being both a simple marker of this patient population and a clinical parameter quantifiable at the bedside (in contrast to functionally more important forms of muscle overactivity), provided a valid and precise measure is used [17,22,23]. In addition, spasticity may be mildly correlated with other forms of spastic muscle overactivity, because they may all partially reflect both motoneuronal hyperexcitability and spindle responsiveness [4,13,53,54,64,65]. However, spasticity per se is not the main factor limiting active movement in people with deforming spastic paresis, with the possible exception of attempts at fast or ballistic movements [13].

7. Stretch-sensitive paresis

Stretch-sensitive paresis is defined as a quantitative reduction of the voluntary recruitment of agonist motor units, further diminished by antagonist stretch [3,39]. In the most severe cases

(i.e., when the antagonist is a muscle with prominent shortening and spastic myopathy), full antagonist stretch may completely abolish (100% reduction) the ability of the motor command to bring agonist motor neurons to firing threshold, thus leading to full agonist plegia in that joint position [39]. This worsening of the agonist command disorder by antagonist stretch represents yet another incentive for clinicians not to let muscles follow the course of severe spastic myopathy in patients with paresis of central origin.

8. Conclusion

The elucidation of the pathophysiology of a disorder goes hand in hand with the selection of assessments and treatments used in this disorder. In 2018, it is probably time that we cease to use the easy term "spasticity" to encompass all the various pathophysiological features and complexities of deforming spastic paresis. The main beneficiary of such oversimplification is likely the pharmaceutical industry, which simply had to develop or promote synaptic blockers and ask clinicians to measure resistance to passive movement (which was affected at least by spasticity and spastic dystonia) before and after. It is less certain that the all-embracing concept of spasticity as one name fits all, has been useful for patients.

When reviewing the main pathophysiological features of the syndrome of deforming spastic paresis, which combines a neural disorder of motor command and a muscle disorder of extensibility loss, clearly, every single component of the neurologic disorder, whether it may affect the antagonist (spastic dystonia, spastic cocontraction, spasticity) or the agonist (stretch-sensitive paresis), is negatively affected by tension applied on the diseased antagonist muscle. For the clinician, this is a crucial observation because it may seem easier to treat the muscle with the objective to increase its extensibility than to directly improve the pathways of motor command.

Therefore, a better understanding of the pathophysiology of deforming spastic paresis syndrome should help in choosing appropriate and refined means to both measure the syndrome and adjust treatments. One should certainly research preventive therapies in the early stages of a central nervous system lesion, using techniques to prevent or minimize the emergence of spastic myopathy and its neural consequences.

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References

[1] Xerri C, Lacour M. [Compensation deficits in posture and kinetics following unilateral vestibular neurectomy in cats. The role of sensorimotor activity]. Acta Otolaryngol 1980;90:414–24.
[2] Herskind A, Ritterband-Rosenbaum A, Willerslev-Olsen M, Lorentzen J, Hanson L, Lichtwark G, et al. Muscle growth is reduced in 15-month-old children with cerebral palsy. Dev Med Child Neurol 2016;58:485–9.
[3] Gracies JM. Pathophysiology of spastic paresis. Part I: Paresis and soft tissue changes. Muscle Nerve 2005;31:514–35.
[4] Gioux M, Petit J. Effects of immobilising the cat peroneus longus muscle on the activity of its own spindles. J Appl Physiol 1993;75:2629–30.
[5] Mysoet J, Dupont E, Bastide B, Canu MH. Role of IGF-1 in cortical plasticity and functional deficit induced by sensorimotor restriction. Behav Brain Res 2015;290:117–23.
[6] Good JM. The study of medicine, Vol. 4. London: Baldwin, Cradock and Joy; 1829.
[7] Little W. Course of lectures on the deformities of the human frame. Lancet 1843;44 [5–7, 38–44, 70–74, 209–12, 230–3, 257–60, 290–3, 318–20, 346–9, 350–543].
[8] Erb WH. Spinaler Symptomenkomplex. Berliner Zeitschrift Psych 1875;32 [Über die spastische Spinal paralyse (tabès dorsal spasmodique Charcot)].
[9] Tardieu G, Shentoub S, Delarue R. À la recherche d'une technique de mesure de la spasticité. Rev Neurol 1954;91:143–4.
[10] Tardieu G. Évaluation et caractères distinctifs des diverses raideurs d'origine cérébrale. In: Chapitre VB1b Les feuillets de l'infirmité motrice cérébrale. Paris: Association Nationale des IMC Ed; 1966. p. 1–28.
[11] Lance JW, Feldman RG, Young RR, Koeller C. Spasticity: disorder of motor control. Chicago, IL: Year Book Medical; 1980. p. 485–94.
[12] Fellows SJ, Ross HF, Thilmann AF. The limitations of the tendon jerk as a marker of pathological stretch reflex activity in human spasticity. J Neurol Neurosurg Psychiatry 1993;56:531–7.
[13] Gracies JM. Pathophysiology of spastic paresis. Part II. The emergence of muscle overactivity. Muscle Nerve 2005;31:552–71.
[14] Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner 1964;192:540–2.
[15] Pandyan AD, Johnson GR, Price CI, Curless RH, Barnes MP, Rodgers H. A review of the properties and limitations of the Ashworth and modified Ashworth Scales as measures of spasticity. Clin Rehabil 1999;13:373–83.
[16] Patrick E, Ada L. The Tardieu Scale differentiates contracture from spasticity whereas the Ashworth Scale is confounded by it. Clin Rehabil 2006;20:173–82.
[17] Gracies JM. Coefficients of impairment in deforming spastic paresis. Ann Phys Rehabil Med 2015;58:173–8. http://dx.doi.org/10.1016/j.rehab.2015.04.004.
[18] Fleuren JF, Voerman GE, Erren-Wolters CV, Snoek GJ, Rietman JS, Hermens HJ, et al. Stop using the Ashworth Scale for the assessment of spasticity. J Neurol Neurosurg Psychiatry 2010;81:46–52.
[19] Ansari NN, Naghdi S, Moammeri H, Jalaie S. Ashworth Scales are unreliable for the assessment of muscle spasticity. Physiother Theory Pract 2006;22:119–25.
[20] Mutlu A, Livanelioglu A, Gunel MK. Reliability of Ashworth and Modified Ashworth Scales in Children with Spastic Cerebral Palsy. BMC Musculoskelet Disord 2008;9:44.
[21] Wein T, Esquenazi A, Jost WH, Ward AB, Pan G, Dimitrova R. Onabotulinumtoxin A for the treatment of post-stroke distal lower-limb spasticity: a randomized trial. PM&R 2018. http://dx.doi.org/10.1016/j.pmrj.2017.12.006 [pii: S1934-1482(17)30072-2].
[22] Gracies JM, Marosszeky JE, Renton R, Sandanam J, Gandevia SC, Burke D. Short-term effects of dynamic lycra splints on upper limb in hemiplegic patients. Arch Phys Med Rehabil 2000;81:1547–55.
[23] Gracies JM, Burke K, Clegg NJ, Browne R, Rushing C, Fehlings D, et al. Reliability of the Tardieu Scale for assessing spasticity in children with cerebral palsy. Arch Phys Med Rehabil 2010;91:421–8. http://dx.doi.org/10.1016/j.apmr.2009.11.017.
[24] Gracies JM, Bayle N, Vinti M, Alkandari S, Vu P, Loche CM, et al. Five-step clinical assessment in spastic paresis. Eur J Phys Rehabil Med 2010;46:411–21.
[25] Tabary JC, Tabary C, Tardieu C, Tardieu G, Goldspink G. Physiological and structural changes in cat's soleus muscle due to immobilization at different lengths by plaster casts. J Physiol (Lond) 1972;224:231–44.
[26] Giger JM, Bodell PW, Zeng M, Baldwin KM, Haddad F. Rapid muscle atrophy response to unloading: pretranslational processes involving MHC and actin. J Appl Physiol 2009;107:1204–12.
[27] Baptista IL, Leal ML, Artioli GG, Aoki MS, Fiamoncini J, Turri AO, et al. Leucine attenuates skeletal muscle wasting via inhibition of ubiquitin ligases. Muscle Nerve 2010;41:800–8.
[28] Kelleher AR, Gordon BS, Kimball SR, Jefferson LS. Changes in REDD1, REDD2, and atrogene mRNA expression are prevented in skeletal muscle fixed in a stretched position during hindlimb immobilization. Physiol Rep 2014;2:e00246.
[29] de Bruin M, Smeulders MJ, Kreulen M, Huijing PA, Jaspers RT. Intramuscular connective tissue differences in spastic and control muscle: a mechanical and histological study. PLoS One 2014;9:e101038.
[30] Diong J, Harvey LA, Kwah LK, Clarke JL, Bilston LE, Gandevia SC, et al. Gastrocnemius muscle contracture after spinal cord injury: a longitudinal study. Am J Phys Med Rehabil 2013;92:565–74.
[31] Tardieu C, Tardieu G, Colbeau-Justin P, Huet de la Tour E, Lespargot A. Trophic muscle regulation in children with congenital cerebral lesions. J Neurol Sci 1979;42:357–64.
[32] Baker JH, Hall-Craggs EC. Changes in sarcomere length following tenotomy in the rat. Muscle Nerve 1980;3:413–6.
[33] McLachlan EM. Rapid atrophy of mouse soleus muscles after tenotomy depends on an intact innervation. Neurosci Lett 1981;25:269–74.
[34] McLachlan EM, Chua M. Rapid adjustment of sarcomere length in tenotomized muscles depends on an intact innervation. Neurosci Lett 1983;35:127–33.
[35] McLachlan EM. Atrophic effects of proximal tendon transaction with and without denervation on mouse soleus muscles. Exp Neurol 1983;81:651–68.
[36] McLachlan EM. Modification of the atrophic effects of tenotomy on mouse soleus muscles by various hind limb nerve lesions and different levels of voluntary motor activity. Exp Neurol 1983;81:669–82.

[37] Kwah LK, Herbert RD, Harvey LA, Diong J, Clarke JL, Martin JH, et al. Passive mechanical properties of gastrocnemius muscles of people with ankle contracture after stroke. Arch Phys Med Rehabil 2012;93:1185–90.
[38] Dehail P, Simon O, Godard AL, Faucher N, Coulomb Y, Schnitzler A, et al. Acquired deforming hypertonia and contractures in elderly subjects: definition and prevalence in geriatric institutions (ADH survey). Ann Phys Rehabil Med 2014;57:11–23.
[39] Vinti M, Bayle N, Hutin E, Burke D, Gracies JM. Stretch-sensitive paresis and effort perception in hemiparesis. J Neural Transm (Vienna) 2015;122:1089–97.
[40] Denny-Brown D. The cerebral control of movement. Liverpool: Liverpool University Press; 1966 [p 124–3, 171–84].
[41] Laplane D, Talairach J, Meininger V, Bancaud J, Bouchareine A. Motor consequences of motor area ablations in man. J Neurol Sci 1977;31:29–49.
[42] Gracies JM, Simpson DM. Spastic dystonia. In: Brin MF, Comella C, Jankovic J, editors. Dystonia: etiology, classification, and treatment. Philadelphia: Lippincott Williams & Wilkins; 2004. p. 192–210.
[43] Lorentzen J, Pradines M, Gracies JM, Bo Nielsen J. On Denny-Brown's 'spastic dystonia' – What is it and what causes it? Clin Neurophysiol 2018;129:89–94.
[44] Gracies JM. Pathophysiology of impairment in spasticity, and use of stretch as a treatment of spastic hypertonia. Phys Med Rehabil Clin N Am 2001;12:747–68.
[45] Raineteau O, Fouad K, Bareyre FM, Schwab ME. Reorganization of descending motor tracts in the rat spinal cord. Eur J Neurosci 2002;16:1761–71.
[46] Sukal-Moulton T, Krosschell KJ, Gaebler-Spira DJ, Dewald JP. Motor impairments related to brain injury timing in early hemiparesis. Part II: abnormal upper extremity joint torque synergies. Neurorehabil Neural Repair 2014;28:24–35.
[47] Ellis MD, Drogos J, Carmona C, Keller T, Dewald JP. Neck rotation modulates flexion synergy torques, indicating an ipsilateral reticulospinal source for impairment in stroke. J Neurophysiol 2012;108:3096–104.
[48] Krainak DM, Ellis MD, Bury K, Churchill S, Pavlovics E, Pearson L, et al. Effects of body orientation on maximum voluntary arm torques. Muscle Nerve 2011;44:805–13.
[49] Miller DM, Klein CS, Suresh NL, Rymer WZ. Asymmetries in vestibular evoked myogenic potentials in chronic stroke survivors with spastic hypertonia: evidence for a vestibulospinal role. Clin Neurophysiol 2014;125:2070–8.
[50] Du Beau A, Shakya Shrestha S, Bannatyne BA, Jalicy SM, Linnen S, Maxwell DJ. Neurotransmitter phenotypes of descending systems in the rat lumbar spinal cord. Neuroscience 2012;227:67–79.
[51] Drew T, Cabana T, Rossignol S. Responses of medullary reticulospinal neurones to stimulation of cutaneous limb nerves during locomotion in intact cats. Exp Brain Res 1996;111:153–68.
[52] Drew T, Dubuc R, Rossignol S. Discharge patterns of reticulospinal and other reticular neurons in chronic, unrestrained cats walking on a treadmill. J Neurophysiol 1986;55:375–401.
[53] D'Amico JM, Murray KC, Li Y, Chan KM, Finlay MG, Bennett DJ, et al. Constitutively active 5-HT2/alpha1 receptors facilitate muscle spasms after human spinal cord injury. J Neurophysiol 2013;109:1473–84.
[54] D'Amico JM, Condliffe EG, Martins KJ, Bennett DJ, Gorassini MA. Recovery of neuronal and network excitability after spinal cord injury and implications for spasticity. Front Integr Neurosci 2014;8:36.
[55] Nothnagel H. Uber centrale Irradiation des Willensimpulses. Eur Arch Psychiatry Clin Neurosci 1872;214–8.
[56] Beaunis H. Recherches sur la contraction simultanée des muscles antagonistes (I et II). Gazette médicale de Paris 1885 [56e année, Série 7, T. 2, 11 juillet, no 28, pp. 325–8 ; no 29, 18 juillet, pp. 339–42].
[57] Gracies JM, Wilson L, Gandevia SC, Burke D. Stretched position of spastic muscles aggravates their co-contraction in hemiplegic patients. Ann Neurol 1997;42:438–9.
[58] Vinti M, Couillandre A, Hausselle J, Bayle N, Primerano A, Merlo A, et al. Influence of effort intensity and gastrocnemius stretch on co-contraction and torque production in the healthy and paretic ankle. Clin Neurophysiol 2013;124:528–35.
[59] Katz R, Pierrot-Deseilligny E. Recurrent inhibition of alpha-motoneurons in patients with upper motor neuron lesions. Brain 1982;105:103–24.
[60] Morita H, Crone C, Christenhuis D, Petersen NT, Nielsen JB. Modulation of presynaptic inhibition and disynaptic reciprocal Ia inhibition during voluntary movement in spasticity. Brain 2001;124:826–37.
[61] Crone C, Petersen NT, Gimenéz-Roldán S, Lungholt B, Nyborg K, Nielsen JB. Reduced reciprocal inhibition is seen only in spastic limbs in patients with neurolathyrism. Exp Brain Res 2007;181:193–7.
[62] Bhagchandani N, Schindler-Ivens S. Reciprocal inhibition post-stroke is related to reflex excitability and movement ability. Clin Neurophysiol 2012;123:2239–46.
[63] Morita H, Shindo M, Momoi H, Yanagawa S, Ikeda S, Yanagisawa N. Lack of modulation of Ib inhibition during antagonist contraction in spasticity. Neurology 2006;67:52–6.
[64] Gorassini M, Bennett DJ, Kiehn O, Eken T, Hultborn H. Activation patterns of hindlimb motor units in the awake rat and their relation to motoneuron intrinsic properties. J Neurophysiol 1999;82:709–17.
[65] Gorassini MA, Knash ME, Harvey PJ, Bennett DJ, Yang JF. Role of motoneurons in the generation of muscle spasms after spinal cord injury. Brain 2004;127:2247–50.