Framework for the Treatment of Spasticity and Muscle Stiffness

8

Preeti Raghavan

New frameworks are like climbing a mountain - the larger view encompasses rather than rejects the more restricted view.
– Albert Einstein, 1879–1955.

- This chapter provides a brief overview of a framework for the treatment of spasticity and muscle stiffness in the context of the overall rehabilitation plan for patients with spastic paresis. A key aspect of any treatment of spasticity and muscle stiffness is to restore mobility and function as early as possible, and to the greatest extent possible, to mitigate the negative effects of weakness, immobility, and inactivity.
- Central to the framework is a comprehensive evaluation including a patient-centered history and physical examination, as well as a five-step assessment which incorporates upper and lower limb functional ability, passive range of motion, and active range of motion with repetition of movement.
- The purpose of the assessment is to set collaborative patient-centered goals for treatment and to evaluate the treatment response in a consistent and repeatable manner. The history and physical should enable the assessment of medical conditions exacerbating spasticity that must be treated first and include body diagrams to determine the degree to which the symptoms are generalized or focal for appropriate selection of treatment(s).

P. Raghavan (✉)
Departments of Physical Medicine and Rehabilitation and Neurology, The Johns Hopkins University School of Medicine, Baltimore, MD, USA
e-mail: praghavan@jhmi.edu

P. Raghavan (ed.), *Spasticity and Muscle Stiffness*,
https://doi.org/10.1007/978-3-030-96900-4_8

- The assessment can aid in distinguishing between generalized hyperexcitability amenable to intervention with oral spasmolytics and intrathecal baclofen in severe cases, predominantly neural muscle overactivity that can be treated with focal neurolysis and/or chemodenervation using botulinum toxins, and predominantly non-neural muscle shortening that can be treated with focal pharmacologic release using hyaluronidase injections.

Introduction

Damage to the central nervous system (CNS) leads to negative symptoms such as weakness and loss of selective control of muscles, limb segments, and finger dexterity [1]. In addition, positive symptoms of hyperreflexia and spasticity are hallmarks of the movement dysfunction [2]. The co-existence of weakness and spasticity make the syndrome of spastic paresis particularly challenging to treat as the treatment of the positive symptoms can exacerbate the negative symptoms [3, 4].

Weakness, immobility, and inactivity affect several organ systems adversely, including the skin, vascular, and musculoskeletal systems [5], and individuals with spasticity are not protected from these adverse effects [6–8]. Immobility and inactivity produce secondary musculoskeletal changes including muscle atrophy, fatty infiltration, weakness, osteoporosis, muscle stiffness, and contractures through complex biophysical and endocrine interactions [9]. Furthermore, the degree to which patients are mobile influences decision-making about how to treat spasticity and the ensuing spastic movement disorder as discussed in Chap. 2. In turn, spasticity and muscle stiffness contribute to persistent motor dysfunction and impaired motor control [10]. Early mobilization after neurological stability has been found to be beneficial in promoting motor recovery, for example, after stroke [11, 12]. Even individuals who are severely impaired and in the chronic stage poststroke benefit from frequent therapy provided over long durations [13, 14]. Therefore, to reduce the complications related to weakness, immobility, and inactivity, rehabilitation therapy is the cornerstone of treatment after CNS injury due to stroke, traumatic brain injury, spinal cord injury, cerebral palsy, and multiple sclerosis [7, 8, 15–17].

Rehabilitation Based on Principles of Motor Learning

The goal of rehabilitation is to restore function which requires recovery of movement and performance to the extent possible. The management of spasticity and/or muscle stiffness should thus aim to facilitate the process of rehabilitation, i.e., facilitate therapy and caregiving and restore function [18]. Functional training with task-specific practice also requires sensory feedback for task-appropriate intra- and interlimb coordination [19, 20], which is frequently impaired in individuals with spastic movement disorder as discussed in Chap. 2. Individuals with severe motor impairment generally demonstrate greater spasticity and/or muscle stiffness [21]. However, even in these individuals skill acquisition can be accomplished based on

the principles of motor learning using a stepwise logical approach. The focus should first be on recovery of the movement components composing functional tasks, such as: muscle activation in synergy, then single joint movements in synergy, followed by single joint movements out of synergy to restore full isolated movement, first in one direction and then using alternating joint movements in both directions, progressing to task component practice, and then eventually to full functional task practice [14, 22, 23]. Attempting to engage severely impaired patients in complex functional task practice early on invariably leads to the use of compensatory strategies [24], which if reinforced can be detrimental to long-term recovery [25]. Therefore, it may not be productive to practice complex functional tasks at the beginning of treatment. However, individual movement components, including finger extension and somatosensory function, have been shown to continue to recover over the long term [26, 27]. As isolated movements of the scapula, shoulder, elbow, forearm, wrist, fingers, and thumb improve, they can be incorporated into functional task components and subsequently into whole task practice. The idea is to practice movements that are as close to normal as possible [28], and to gradually increase the ability to repeat the movements without compromising movement quality [29–31]. It is also important to allow room for variability in practice to enable self-correction based on explicit knowledge about the task and sensory feedback [32–37].

Operationalizing motor learning strategies for recovery of movement and skill in the context of spasticity and/or muscle stiffness requires setting small accomplishable goals, and education of and partnership with patients and their caregivers to achieve these goals. Technology can be used to aid this process using the A3E framework which stands for Accessibility, Adaptability, Accountability, and Engagement [38] (Fig. 8.1). Accessibility encompasses awareness of the benefits of rehabilitation, access to the appropriate frequency of visits, intensity of prescribed activities, duration of therapy, availability of technological resources needed, and affordability of rehabilitation services. Adaptability refers to the ability of

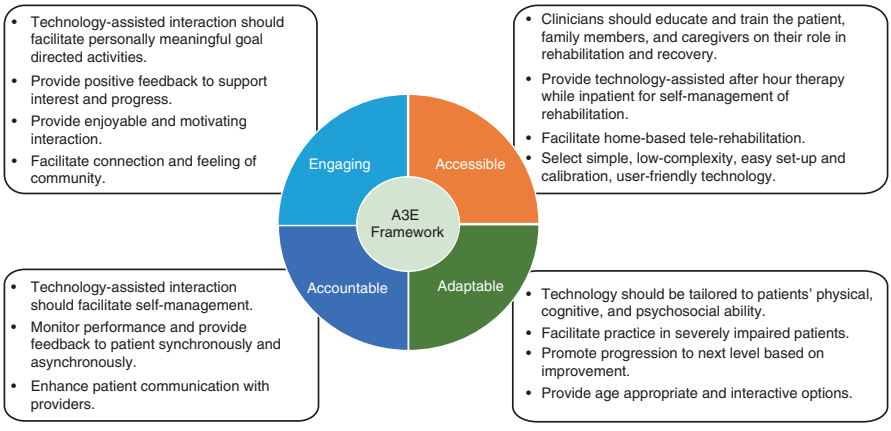

Fig. 8.1 The A3E framework for technology-aided rehabilitation can extend rehabilitation services beyond conventional care settings. (From Jayasree-Krishnan (2020), with permission)

technological solutions to serve patients with varying impairment levels in the physical, cognitive, and psychosocial domains. Accountability refers to patients' willingness to accept responsibility to continue rehabilitation even when they are not in direct contact with the provider, and engagement represents all the efforts that patients make during rehabilitation to derive benefit. Regardless of the specific technology used, a staged stepwise approach should target preservation of muscle length and range of motion, muscle strengthening, and functional performance, with frequent evaluation of progress to address any barriers that arise [39]. One example of a patient-provider partnership is the use of guided self-rehabilitation contracts (GSCs), a diary-based rehabilitation strategy where specific muscles are identified for self-stretching. A combination treatment using GSC for stretching and botulinum toxin injections for muscle overactivity demonstrated high compliance with GSC and improvement in composite active range of motion in adults with chronic spastic paresis [40]. In this study, the GSCs did not use any specific technology to aid stretching. Also, no direct comparisons were made between treatment with injections alone, GSCs alone, and the combined approach. However, the results favor the argument that the purpose of pharmacologic and technologic approaches in the treatment of spasticity and muscle stiffness should be to facilitate the process of rehabilitation beyond the clinic, and that patient education and engagement are key aspects in doing so. This study also points to the usefulness of the five-step assessment for selection of the appropriate treatment and for post-treatment evaluations as discussed below and detailed in Chap. 3 [41].

Medical and Pharmacologic Treatment Algorithm

As described above, the first line of treatment for individuals with spasticity and muscle stiffness is rehabilitation to restore and maintain movement capability. Medical and pharmacologic interventions are an adjunct to facilitate mobility and function. Figure 8.2 outlines a medical and pharmacologic treatment algorithm. Central to the algorithm is evaluation of the patient by a careful history and physical examination and the setting of collaborative patient-centered SMART (specific, measurable, achievable, relevant, and timely) goals based on the patient's experience of their symptoms and limitations [42].

The Patient's Experience

It is important to understand the patient's experience of spasticity and muscle stiffness as it has been shown to differ from the clinician's assessment [43–46]. For example, the vocabulary used to describe the symptoms of 'muscle tightness' by patients includes words such as 'tight', 'stiff', 'sore', and 'tender'. Patients may use metaphorical descriptors such as 'rock feeling', 'Charlie horse', and 'locked feeling' that contain pain and sensory experiences. On the other hand, clinicians may

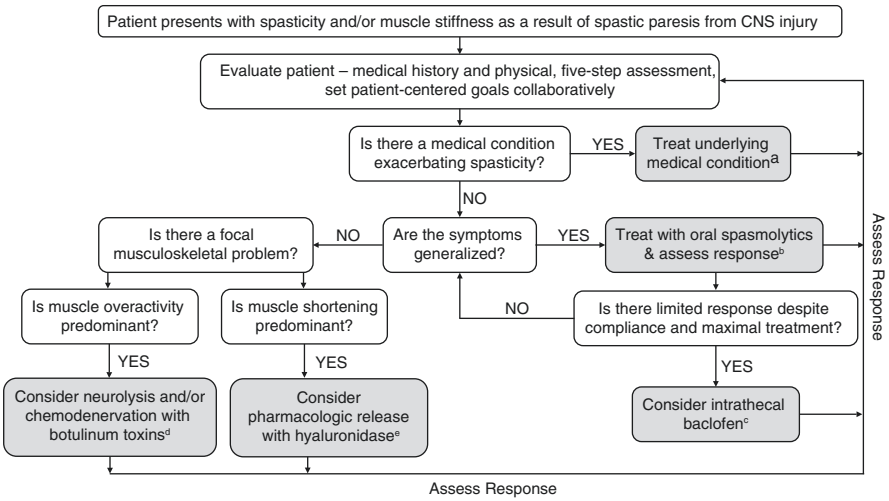

Fig. 8.2 Medical and pharmacologic algorithm for clinical decision-making regarding treatment. *CNS* central nervous system; [a]see Chap. 9; [b]see Chap. 10; [c]see Chap. 11; [d]see Chap. 12; [e]see Chap. 13

describe muscle tightness from a functional perspective using words such as 'restricted range of motion', 'contracted muscles', 'soreness', and 'fibrous band' which contain few descriptors of pain and sensory input. Overlapping vocabulary across patients and clinicians includes words such as 'stiffness', 'inflexible', 'spasm', 'tingling', 'knots', 'hard', and 'movement restrictions' [47]. Understanding the symptoms from the patient's perspective can enable appropriate goal setting, shared decision-making, and a successful response to treatment. A body diagram (Fig. 8.3) may assist in determining whether the symptoms are generalized or localized.

The medical history and physical should also include a thorough review of systems to determine whether a medical condition, such as a pressure sore, urinary tract infection, or constipation could be exacerbating spasticity and need to be treated first. Chapter 9 provides details on the medical exacerbation of spasticity and its treatment.

Many patients with spasticity, for example those with multiple sclerosis, may have multiple co-morbidities and interrelated symptoms such as fatigue, pain, and difficulty sleeping that may have to be assessed carefully to develop an individualized treatment strategy [48, 49]. It is also critical to reconcile medications as a sudden change in dose or frequency of spasmolytics can lead to symptoms of withdrawal and exacerbation of spasticity, as detailed in Chap. 10. Patients may also use non-medicinal cannabinoids via various routes such as smoking, vaping, topicals, tinctures and oils, and/or edibles, including foods, chocolate, and candy that may influence their symptoms and their treatment [50].

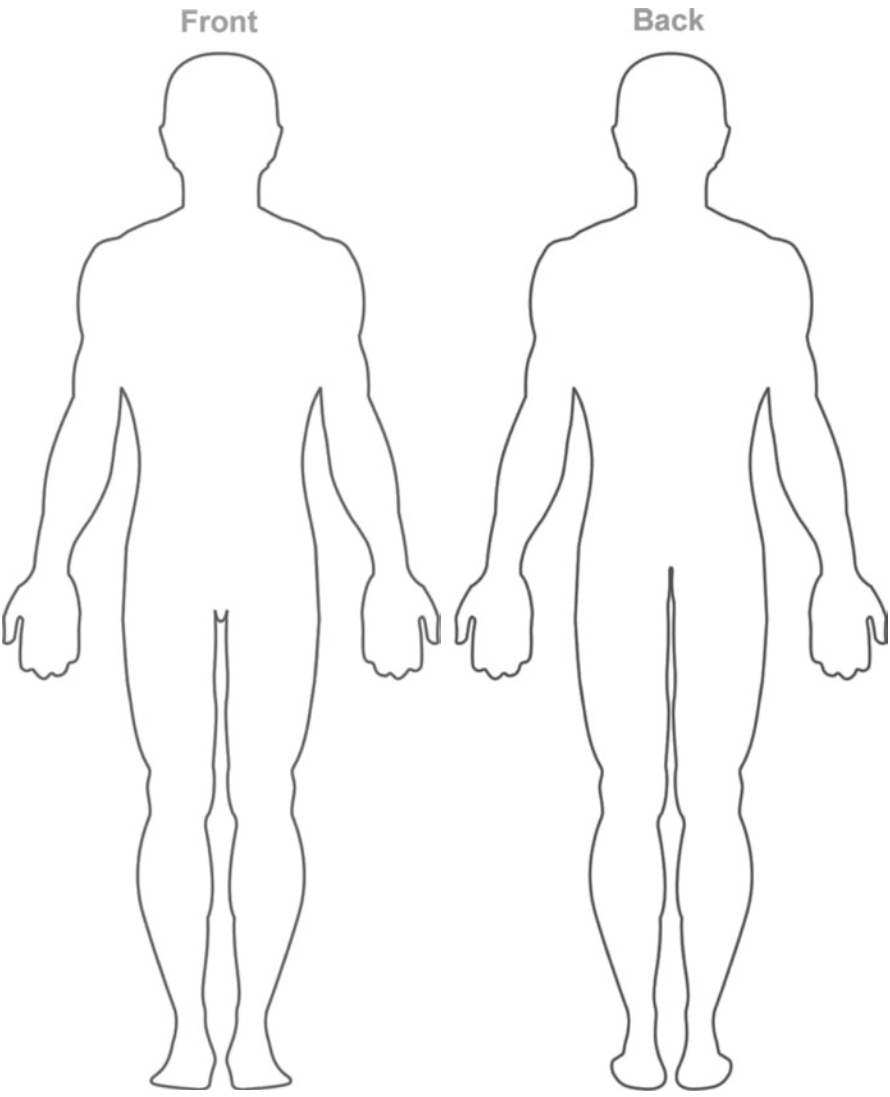

Fig. 8.3 A body diagram can be used to indicate areas of pain, discomfort, tightness or restriction to determine the degree to which the symptoms are generalized or localized for appropriate goal setting, shared decision-making, and assessment of treatment response. A blank body diagram is provided here as an example for the patient to fill out

Spasticity Versus Muscle Stiffness

Since the syndrome of spastic paresis consists of both neural and non-neural components as detailed in Chaps. 1, 2, 3, 4, 5, 6 and 7 in Part I of this book, accurate identification of the dominant component can assist with effective treatment. Spasticity is a neural phenomenon which can have both generalized manifestations such as hyperexcitability to sensory stimuli, exaggerated stretch reflexes, muscle spasms, and clonus, as well as focal manifestations such as overactivity of the antagonist muscle and/or hypoactivity of the agonist muscle across a joint, which together limit active movement. In contrast, muscle stiffness is a non-neural consequence of spasticity characterized by loss of extensibility of the muscle tissue due to increased muscle viscosity, which if untreated can eventually lead to contracture as detailed in Chap. 6. The affected muscles become physically shortened and demonstrate increased resistance to both active and passive movement [51], often producing deforming after-effects that are described in Chap. 7. Distinguishing between symptoms related predominantly to spasticity versus those related predominantly to muscle stiffness can be helpful to optimize focal treatment.

The Five-Step Assessment

Traditionally, the Modified Ashworth Scale (MAS) has been used to assess spasticity at the bedside and in the clinic. Although widely used, the MAS is limited in both inter- and intra-rater reliability, and cannot differentiate between the neural and non-neural components underlying the movement limitation, as demonstrated in Chap. 4. The five-step clinical assessment proposed by Gracies et al. is a comprehensive assessment that incorporates functional assessments as well as the Tardieu test and attempts to distinguish between predominantly neural and non-neural focal components contributing to the functional limitation [41]. *Step 1* assesses function using a standard test such as the 10 m walk test for the lower limb or the Modified Frenchay Scale for the upper limb. *Steps 2 and 3* assess passive range of motion at slow and fast speeds to differentiate between muscle shortening/stiffness (non-neural resistance at slow speed, X_{V1}) and spasticity (neural resistance at fast speed, X_{V3}) relative to the expected total range of motion at a given joint (X_N). *Steps 4 and 5* assess maximal active range of motion, X_A (due to neural weakness), and the decrement in range of motion with repetition X_R (due to fatigability and/or mild non-neural resistance). Coefficients of impairment can be derived based on these measurements to provide clinical guidance regarding treatment as detailed in Chap. 3 and summarized in Table 8.1.

Although these coefficients are theoretically derived, they provide a means to test the effect of specific treatments on the various coefficients of impairment. For example, the baseline coefficient of shortening was used to create a guided self-stretching program that resulted in increased passive range of motion in the stretched versus non-stretched muscles and increased ambulation speed [52]. However, there are a few caveats to bear in mind with the five-step assessment in the context of the quantitative data presented in Chap. 4. For example, the speed of elbow joint rotation did not clearly

Table 8.1 Coefficients of impairment derived from the five-step assessment, their interpretation, and implications for treatment

Coefficient of impairment	Interpretation	Treatment implication
Coefficient of shortening	Represents greater limitation in passive range of motion at slow speed suggesting non-neural passive resistance	Consider stretching, pharmacologic release of shortened/ stiff muscles, or surgical release in case of contracture
Coefficient of spasticity	Represents greater limitation in passive range of motion at fast speed likely due to neural muscle overactivity	Consider nerve (phenol or alcohol) or muscle (botulinum toxin) blocks to overactive muscles
Coefficient of weakness	Represents reduced active range of motion due to weakness	Consider strengthening using rehabilitation therapy and/or electrical stimulation
Coefficient of fatigability	Represents movement fatigability due to a combination of weakness and mild non-neural resistance	Consider combination treatment to strengthen appropriate muscle groups and reduce resistance/ stiffness by pharmacologic release

distinguish between passive resistance arising from neurally driven EMG overactivity versus non-neural stiffness associated with a minimal EMG response (see Chap. 4). This may make it difficult to differentiate between the coefficients of shortening and spasticity. In fact, patients who showed an EMG response showed a decreased catch angle as a function of joint rotation speed (i.e., the catch angle became smaller indicating greater extension with increasing speed of joint rotation), which is contrary to what is expected with spasticity. The acquisition of EMG signals along with joint motion data may provide a better understanding of the origins of the perceived resistance as demonstrated in Chap. 7, although it is highly likely that both neurally driven muscle overactivity and non-neural muscle stiffness coexist in most patients as they reinforce each other as explained in Chap. 6. Hence, consistent and periodic assessments of the response to treatment using objective measurements of function and active and passive range of motion may be the most practical manner of delineating neural and non-neural contributions to the movement restriction, and planning the next course of treatment in a staged manner. Diagnostic short-acting local anesthetic nerve blocks can also be a valuable screening tool in deciding whether to treat with longer-acting nerve blocks or botulinum toxin injections [53, 54]. New guidelines for the use of these agents in the treatment of spasticity have recently been released [55].

Generalized and Focal Treatments

Should the patient's symptoms be generalized, treatment may be initiated with oral spasmolytics individually or in combination. Chapter 10 details the various classes of medication, their mechanisms of action, clinical use, dosing and pharmacology, side-effect profile, and case studies to highlight salient aspects of treatment. Should symptoms remain generalized and severe despite compliance with maximal oral

treatment, intrathecal baclofen may be considered. Chapter 11 details the components of intrathecal baclofen therapy, patient selection, the advantages, and disadvantages of the treatment, as well as the intrathecal baclofen trial, pump implantation, maintenance, troubleshooting, and pump explantation. Generalized treatments alone may be insufficient if there are focal musculoskeletal symptoms that contribute to discomfort and/or dysfunction, such as those described in Chap. 7.

If symptoms are localized to specific limb(s) or muscle group(s), it is helpful to ask if the symptoms can be attributed predominantly to muscle overactivity or to muscle shortening using the five-step assessment or its equivalent, measurement of EMG and resistance using instrumented tools, and/or screening using short-acting local anesthetics. Although these may be difficult to do precisely for several reasons discussed above, a consistent set of assessments will be most helpful to test the treatment hypothesis. If muscle overactivity is found to be a key driver of the focal symptoms, the treating clinician must decide if treatment-induced focal muscle weakness could potentially exacerbate the dysfunction as outlined in Chap. 2. Here, collaborative patient-centered decision-making may be helpful [42]. Partial nerve blocks using phenol or alcohol and/or chemodenervation using botulinum toxin injections to partially weaken overactive muscles may be appropriate. Details on the use of neurolysis using phenol and alcohol and newer techniques are outside the scope of this book, although the reader is referred to several pertinent sources [56–62]. Chapter 12 provides details on the use and guidelines for botulinum toxin injections.

Muscle shortening can be caused by immobility and inactivity, but also by muscle overactivity as discussed in detail in Chap. 6. Pharmacologic release of shortened stiff muscles using hyaluronidase injections is a new tool that shows promise in increasing passive and active range of motion in the upper limb [63, 64]. Chapter 13 provides details on the selection of patients and the available evidence using this new tool. Here, the treating clinician must decide if the muscle shortening is reversible. Should the patient already have irreversible contracture, referral for surgical treatment with or without serial casting in combination with other focal treatments may be warranted [65, 66].

Emerging Non-Pharmacologic Treatments

As our understanding of the neural basis and pathophysiology of spasticity and its consequences such as muscle stiffness and contracture continue to evolve, new treatments are likely to emerge. Chapter 14 discusses the many potentially promising emerging non-pharmacologic treatments available. These include peripheral electrical stimulation at the level of the skin (transcutaneous electrical nerve stimulation, TENS) and muscle (neuromuscular electrical stimulation, NMES; functional electrical stimulation, FES; breathing-controlled electrical stimulation, BreEStim), spinal cord stimulation (SCS), transcranial direct current stimulation (tDCS), transcranial magnetic stimulation (TMS), acupuncture, whole body vibration, and extracorporeal shockwave therapy, which have been studied in various populations such as stroke, spinal cord injury, multiple sclerosis, and cerebral palsy.

Conclusion

A key aspect of the framework for the treatment of spasticity and/or muscle stiffness from CNS injury is the stepwise restoration of movement and function to mitigate the negative effects of weakness, immobility, and inactivity. This requires a comprehensive evaluation including a patient-centered history and physical examination, as well as a five-step assessment which incorporates upper and lower limb functional ability, passive range of motion, and active range of motion with repetition of movement to determine the degree to which the symptoms are generalized or focal for appropriate selection of treatment(s). The evaluation may help distinguish between neural muscle overactivity versus non-neural muscle shortening for clinical decision-making about focal treatment with chemodenervation using neurolytic agents and botulinum toxins versus pharmacologic release with hyaluronidase injections, and assess the treatment response in a consistent and repeatable manner.

References

1. Kuypers HGJM. Anatomy of the descending pathways. In: Brooks VB, editor. Handbook of physiology. Bethesda: American Physiological Society; 1981.
2. Lance JW. Symposium synopsis. In: Feldman RG, Young RR, Koella WP, editors. Spasticity: disordered motor control. Chicago: Year Book Medical Publishers; 1980.
3. Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, Burridge J, et al. Spasticity: clinical perceptions, neurological realities and meaningful measurement. Disabil Rehabil. 2005;27(1–2):2–6.
4. Li S, Francisco GE, Rymer WZ. A new definition of poststroke spasticity and the interference of spasticity with motor recovery from acute to chronic stages. Neurorehabil Neural Repair. 2021;35:601. https://doi.org/10.1177/15459683211011214.
5. Kortebein P. Rehabilitation for hospital-associated deconditioning. Am J Phys Med Rehabil. 2009;88(1):66–77.
6. Jaul E, Factor H, Karni S, Schiffmiller T, Meiron O. Spasticity and dementia increase the risk of pressure ulcers. Int Wound J. 2019;16(3):847–51.
7. de Bruin M, Smeulders MJ, Kreulen M. Why is joint range of motion limited in patients with cerebral palsy? J Hand Surg Eur. 2013;38(1):8–13.
8. Qin W, Bauman WA, Cardozo C. Bone and muscle loss after spinal cord injury: organ interactions. Ann N Y Acad Sci. 2010;1211:66–84.
9. Herrmann M, Engelke K, Ebert R, Muller-Deubert S, Rudert M, Ziouti F, et al. Interactions between muscle and bone-where physics meets biology. Biomol Ther. 2020;10(3):432.
10. Pundik S, McCabe J, Skelly M, Tatsuoka C, Daly JJ. Association of spasticity and motor dysfunction in chronic stroke. Ann Phys Rehabil Med. 2019;62(6):397–402.
11. Oyanagi K, Kitai T, Yoshimura Y, Yokoi Y, Ohara N, Kohara N, et al. Effect of early intensive rehabilitation on the clinical outcomes of patients with acute stroke. Geriatr Gerontol Int. 2021;21(8):623–8.
12. Yen HC, Jeng JS, Chen WS, Pan GS, Chuang Pt Bs WY, Lee YY, et al. Early mobilization of mild-moderate intracerebral hemorrhage patients in a stroke center: a randomized controlled trial. Neurorehabil Neural Repair. 2020;34(1):72–81.
13. Boissoneault C, Grimes T, Rose DK, Waters MF, Khanna A, Datta S, et al. Innovative Long-dose neurorehabilitation for balance and mobility in chronic stroke: a preliminary case series. Brain Sci. 2020;10(8):555.

14. Daly JJ, McCabe JP, Holcomb J, Monkiewicz M, Gansen J, Pundik S. Long-dose intensive therapy is necessary for strong, clinically significant, upper limb functional gains and retained gains in severe/moderate chronic stroke. Neurorehabil Neural Repair. 2019;33(7):523–37.
15. Gaber TA. Significant reduction of the risk of venous thromboembolism in all long-term immobile patients a few months after the onset of immobility. Med Hypotheses. 2005;64(6):1173–6.
16. Hagen EM. Acute complications of spinal cord injuries. World J Orthop. 2015;6(1):17–23.
17. LaBan MM, Martin T, Pechur J, Sarnacki S. Physical and occupational therapy in the treatment of patients with multiple sclerosis. Phys Med Rehabil Clin N Am. 1998;9(3):603–14, vii.
18. Galea MP. Physical modalities in the treatment of neurological dysfunction. Clin Neurol Neurosurg. 2012;114(5):483–8.
19. Logan LR. Rehabilitation techniques to maximize spasticity management. Top Stroke Rehabil. 2011;18(3):203–11.
20. Dietz V. Proprioception and locomotor disorders. Nat Rev Neurosci. 2002;3(10):781–90.
21. Andringa A, Meskers C, van de Port I, van Wegen E, Kwakkel G. Time course of wrist hyperresistance in relation to upper limb motor recovery early post stroke. Neurorehabil Neural Repair. 2020;34(8):690–701.
22. Daly JJ, McCabe JP, Gansen J, Rogers J, Butler K, Brenner I, et al. Gait coordination protocol for recovery of coordinated gait, function, and quality of life following stroke. J Rehabil Res Dev. 2012;49(8):xix–xxviii.
23. McCabe J, Monkiewicz M, Holcomb J, Pundik S, Daly JJ. Comparison of robotics, functional electrical stimulation, and motor learning methods for treatment of persistent upper extremity dysfunction after stroke: a randomized controlled trial. Arch Phys Med Rehabil. 2015;96(6):981–90.
24. van Kordelaar J, van Wegen EE, Nijland RH, Daffertshofer A, Kwakkel G. Understanding adaptive motor control of the paretic upper limb early poststroke: the EXPLICIT-stroke program. Neurorehabil Neural Repair. 2013;27(9):854–63.
25. Raghavan P. Upper limb motor impairment after stroke. Phys Med Rehabil Clin N Am. 2015;26(4):599–610.
26. Winters C, Kwakkel G, Nijland R, van Wegen E. Consortium EX-s. When does return of voluntary finger extension occur post-stroke? A prospective Cohort Study. PLoS One. 2016;11(8):e0160528.
27. Zandvliet SB, Kwakkel G, Nijland RHM, van Wegen EEH, Meskers CGM. Is recovery of somatosensory impairment conditional for upper-limb motor recovery early after stroke? Neurorehabil Neural Repair. 2020;34(5):403–16.
28. Levin MF, Kleim JA, Wolf SL. What do motor "recovery" and "compensation" mean in patients following stroke? Neurorehabil Neural Repair. 2009;23(4):313–9.
29. Butefisch C, Hummelsheim H, Denzler P, Mauritz KH. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. J Neurol Sci. 1995;130(1):59–68.
30. Kitago T, Krakauer JW. Motor learning principles for neurorehabilitation. Handb Clin Neurol. 2013;110:93–103.
31. Plautz EJ, Milliken GW, Nudo RJ. Effects of repetitive motor training on movement representations in adult squirrel monkeys: role of use versus learning. Neurobiol Learn Mem. 2000;74(1):27–55.
32. Halsband U, Lange RK. Motor learning in man: a review of functional and clinical studies. J Physiol Paris. 2006;99(4–6):414–24.
33. Vidoni ED, Boyd LA. Achieving enlightenment: what do we know about the implicit learning system and its interaction with explicit knowledge? J Neurol Phys Ther. 2007;31(3):145–54.
34. Stanley J, Krakauer JW. Motor skill depends on knowledge of facts. Front Hum Neurosci. 2013;7:503.
35. Subramanian SK, Massie CL, Malcolm MP, Levin MF. Does provision of extrinsic feedback result in improved motor learning in the upper limb poststroke? A systematic review of the evidence. Neurorehabil Neural Repair. 2010;24(2):113–24.

36. Ranganathan R, Lee MH, Newell KM. Repetition without repetition: challenges in understanding behavioral flexibility in motor skill. Front Psychol. 2020;11:2018.
37. Lee TD, Swanson LR, Hall AL. What is repeated in a repetition? Effects of practice conditions on motor skill acquisition. Phys Ther. 1991;71(2):150–6.
38. Jayasree-Krishnan V, Ghosh S, Palumbo A, Kapila V, Raghavan P. Developing a framework for designing and deploying technology-assisted rehabilitation after stroke: a qualitative study. Am J Phys Med Rehabil. 2021;100(8):774–9.
39. Richardson D. Physical therapy in spasticity. Eur J Neurol. 2002;9(Suppl 1):17–22. discussion 53-61
40. Gracies JM, Francisco GE, Jech R, Khatkova S, Rios CD, Maisonobe P, et al. Guided self-rehabilitation contracts combined with AbobotulinumtoxinA in adults with spastic paresis. J Neurol Phys Ther. 2021;45(3):203–13.
41. Gracies JM. Coefficients of impairment in deforming spastic paresis. Ann Phys Rehabil Med. 2015;58(3):173–8.
42. Turner-Stokes L, Ashford S, Esquenazi A, Wissel J, Ward AB, Francisco G, et al. A comprehensive person-centered approach to adult spastic paresis: a consensus-based framework. Eur J Phys Rehabil Med. 2018;54(4):605–17.
43. Bhimani RH, Peden-McAlpine C, Gaugler J, Anderson LC. Spasticity over time during acute rehabilitation: a study of patient and clinician scores. Appl Nurs Res. 2016;30:16–23.
44. Bhimani RH, McAlpine CP, Henly SJ. Understanding spasticity from patients' perspectives over time. J Adv Nurs. 2012;68(11):2504–14.
45. Mahoney JS, Engebretson JC, Cook KF, Hart KA, Robinson-Whelen S, Sherwood AM. Spasticity experience domains in persons with spinal cord injury. Arch Phys Med Rehabil. 2007;88(3):287–94.
46. Morley A, Tod A, Cramp M, Mawson S. The meaning of spasticity to people with multiple sclerosis: what can health professionals learn? Disabil Rehabil. 2013;35(15):1284–92.
47. Bhimani RH, Gaugler JE, Skay C. Understanding symptom experiences of muscle tightness from patients' and clinicians' perspectives. J Clin Nurs. 2017;26(13–14):1927–38.
48. Barin L, Salmen A, Disanto G, Babacic H, Calabrese P, Chan A, et al. The disease burden of Multiple Sclerosis from the individual and population perspective: which symptoms matter most? Mult Scler Relat Disord. 2018;25:112–21.
49. Gustavsen S, Olsson A, Sondergaard HB, Andresen SR, Sorensen PS, Sellebjerg F, et al. The association of selected multiple sclerosis symptoms with disability and quality of life: a large Danish self-report survey. BMC Neurol. 2021;21(1):317.
50. Rice J, Hildebrand A, Spain R, Senders A, Silbermann E, Wooliscroft L, et al. A cross-sectional survey of cannabis use by people with MS in Oregon and Southwest Washington. Mult Scler Relat Disord. 2021;55:103172.
51. Baude M, Nielsen JB, Gracies JM. The neurophysiology of deforming spastic paresis: a revised taxonomy. Ann Phys Rehabil Med. 2019;62(6):426–30.
52. Pradines M, Baude M, Marciniak C, Francisco G, Gracies JM, Hutin E, et al. Effect on passive range of motion and functional correlates after a Long-term lower limb self-stretch program in patients with chronic spastic paresis. PM R. 2018;10(10):1020–31.
53. Picelli A, Battistuzzi E, Filippetti M, Modenese A, Gandolfi M, Munari D, et al. Diagnostic nerve block in prediction of outcome of botulinum toxin treatment for spastic equinovarus foot after stroke: a retrospective observational study. J Rehabil Med. 2020;52(6):jrm00069.
54. Gracies JM, Elovic E, McGuire J, Simpson DM. Traditional pharmacological treatments for spasticity. Part I: local treatments. Muscle Nerve Suppl. 1997;6:S61–91.
55. Yelnik AP, Hentzen C, Cuvillon P, Allart E, Bonan IV, Boyer FC, et al. French clinical guidelines for peripheral motor nerve blocks in a PRM setting. Ann Phys Rehabil Med. 2019;62(4):252–64.
56. Karri J, Zhang B, Li S. Phenol neurolysis for management of focal spasticity in the distal upper extremity. PM R. 2020;12(3):246–50.

57. Kaymak B, Kara M, Gurcay E, Aydin G, Ozcakar L. Selective peripheral neurolysis using high frequency ultrasound imaging: a novel approach in the treatment of spasticity. Eur J Phys Rehabil Med. 2019;55(4):522–5.
58. Gonnade N, Lokhande V, Ajij M, Gaur A, Shukla K. Phenol versus Botulinum toxin a injection in ambulatory cerebral palsy spastic Diplegia: a comparative study. J Pediatr Neurosci. 2017;12(4):338–43.
59. Ploypetch T, Kwon JY, Armstrong HF, Kim H. A retrospective review of unintended effects after single-event multi-level Chemoneurolysis with botulinum toxin-A and phenol in children with cerebral palsy. PM R. 2015;7(10):1073–80.
60. Kocabas H, Salli A, Demir AH, Ozerbil OM. Comparison of phenol and alcohol neurolysis of tibial nerve motor branches to the gastrocnemius muscle for treatment of spastic foot after stroke: a randomized controlled pilot study. Eur J Phys Rehabil Med. 2010;46(1):5–10.
61. Elovic EP, Esquenazi A, Alter KE, Lin JL, Alfaro A, Kaelin DL. Chemodenervation and nerve blocks in the diagnosis and management of spasticity and muscle overactivity. PM R. 2009;1(9):842–51.
62. Zafonte RD, Munin MC. Phenol and alcohol blocks for the treatment of spasticity. Phys Med Rehabil Clin N Am. 2001;12(4):817–32, vii.
63. Raghavan P, Lu Y, Mirchandani M, Stecco A. Human recombinant hyaluronidase injections for upper limb muscle stiffness in individuals with cerebral injury: a case series. EBioMedicine. 2016;9:306–13.
64. Harlaar J. Diagnosis and treatment of` spasticity and stiff muscles. EBioMedicine. 2016;9:23–4.
65. Long JT, Cobb L, Garcia MC, McCarthy JJ. Improved clinical and functional outcomes in Crouch gait following minimally invasive hamstring lengthening and serial casting in children with cerebral palsy. J Pediatr Orthop. 2020;40(6):e510–e5.
66. Leung J, King C, Fereday S. Effectiveness of a programme comprising serial casting, botulinum toxin, splinting and motor training for contracture management: a randomized controlled trial. Clin Rehabil. 2019;33(6):1035–44.