Experimental Brain Research (2020) 238:1627–1636
https://doi.org/10.1007/s00221-020-05792-0

REVIEW

Spastic movement disorder: should we forget hyperexcitable stretch reflexes and start talking about inappropriate prediction of sensory consequences of movement?

Jens Bo Nielsen[1,2] · Mark Schram Christensen[1] · Simon Francis Farmer[3,4] · Jakob Lorentzen[1,2]

Received: 19 January 2020 / Accepted: 18 March 2020 / Published online: 7 May 2020

Abstract
Spastic movement disorder is characterized by reduced ability to selectively activate muscles with significant co-activation of antagonist muscles. It has traditionally been thought that hyperexcitable stretch reflexes have a central role in the pathophysiology and the clinical manifestations of the disorder. Here we argue that the main functional challenges for persons with spastic movement disorder are related to contractures, paresis, weak muscles and inappropriate central motor commands, whereas hyperexcitable reflexes play no or only an insignificant functional role. Co-activation of antagonist muscles and stiff posture and gait may rather be adaptations that aim to ensure joint and postural stability due to insufficient muscle strength. Aberrant (involuntary) muscle activity is likely related to an inadequate prediction of the sensory consequences of movement and a resulting impairment of muscle coordination. We argue that improvement of functional muscle strength and muscle coordination following central motor lesions may be achieved by optimizing integration of somatosensory information into central feedforward motor programs, whereas anti-spastic therapy that aims to reduce reflex activity may be less efficient. This opens for novel investigations into new treatment strategies that may improve functional control of movement and prevent reduced joint mobility in people with brain lesions.

Keywords Spastic paresis · Neurological disorders

Introduction

In 1980, William Landau made the following statement at a Ciba-Geigy symposium:

> However, useful to clinical diagnosis may be the increase of excitablity at anterior horn cells, and to some extent muscle spindles, these phenomena have little more relation to the patients disability than does insertion of the rectal thermometer in pneumonia. [(Landau 1980); p. 20].

Subsequent research on the relation between stretch reflexes and the functional disabilities associated with spastic movement disorder has provided ample evidence to support Landau's statement, but the idea that hyper-reflexia is of primary pathological significance still lingers in much of the literature. Therefore, for the sake of clear argument, here we will take a chance, and state clearly our belief that *stretch reflexes are not—and cannot be—responsible for spastic movement disorder.* As Landau pointed out, they are a useful sign of altered excitability of spinal motor neurons in people with central motor lesions, but they play no role in the pathophysiology of the movement disorder that these people experience and should, therefore, not—by themselves—be a target for treatment. It is the purpose of this review to convince the reader that this statement is correct. When we (hopefully) have accomplished this, we will present an alternative understanding of the pathophysiology of spastic

Communicated by Winston D. Byblow.

✉ Jens Bo Nielsen
jbnielsen@sund.ku.dk

[1] Department of Neuroscience, University of Copenhagen, Copenhagen, Denmark

[2] Elsass Foundation, Charlottenlund, Denmark

[3] Department of Clinical and Movement Neurosciences, Institute of Neurology, University College London, London, UK

[4] Department of Clinical Neurology, National Hospital for Neurology and Neurosurgery, London, UK

movement disorder, which opens up for new approaches to neuro-rehabilitation of people with central motor lesions.

First, a few clarifications are necessary. By spastic movement disorder, we understand the functional disabilities that characterize people who have had an acquired or genetically-determined lesion of the motor cortex or the descending motor tracts early or late in life. This includes the characteristic stiff gait with significant co-contraction of antagonists, reduced movement range and slow, badly coordinated movements with aberrant muscle activity. We have tried to avoid the term spasticity as much as possible, since there is considerable controversy about the proper definition of the term. However, this controversy is to some extent at the heart of the discussion that we take up later in this paper. Spasticity is usually defined in research papers as an exaggerated resistance of a muscle to passive stretch, but it is used in a much broader sense in the clinic and may have come to be synonymous with spastic movement disorder as described above. This is the key problem that we are raising here: To what an extent is the evaluation of increased muscle tone and muscle resistance to passive stretch as part of a neurological examination relevant for the spastic movement disorder of the examined person (Fig. 1)?

There are two distinct problems in relation to the idea that hyperexcitable stretch reflexes are of significance for the functional disability of people with central motor lesions. One is that it is not only stretch reflexes, but also other neural and non-neural factors that contribute to muscle resistance and muscle 'tone' (Lorentzen et al. 2010; Mirbagheri et al. 2008, 2005; Pandyan et al. 2005b; Sinkjaer and Magnussen 1994; Willerslev-Olsen et al. 2013; Wood et al. 2005). These different factors are difficult—if not impossible—to distinguish from each other without adequate biomechanical and electrophysiological techniques. Hyperexcitable reflexes have, therefore, wrongly been made responsible for functional deficits following brain and spinal cord lesion as pointed out in a number of publications (Geertsen et al. 2015; Landau 2004; Lorentzen et al. 2010; Malhotra et al. 2009; Nielsen et al. 2005; Pandyan et al. 2005b; Salazar-Torres Jde et al. 2004). Secondly, tendon jerks, muscle tone and resistance to stretch of muscles are generally evaluated (with or without the help of biomechanical and electrophysiological techniques) at rest rather than during the movements, which the hyperexcitable stretch reflexes are supposed to interfere with. However, four decades of research have shown that reflex measurements at rest have little relevance for how sensory activity from stretch receptors in the muscles is used by the nervous system during movement (Ibrahim et al. 1993; Nielsen et al. 2005; Sinkjaer and Magnussen 1994).

We will discuss these two issues in turn.

Distinguishing different causes of increased muscle resistance (or 'muscle tone')

The clinician has to rely on his or her hands and eyes during the neurological examination to determine whether muscles show pathologically increased muscle resistance or muscle tone. This may be sufficient to determine that something is wrong, but unfortunately research indicates that it is not sufficient to determine exactly what it is that is wrong (Lorentzen et al. 2010; Lorentzen et al. 2018; Malhotra et al. 2008; Pandyan et al. 2005a; Pandyan et al. 2005b; Willerslev-Olsen et al. 2013). Hyperexcitable stretch reflexes may cause increased resistance to passive movement, increased tendon jerks and clonus. In addition, alterations in the elastic properties of joints, muscle and connective tissue as well

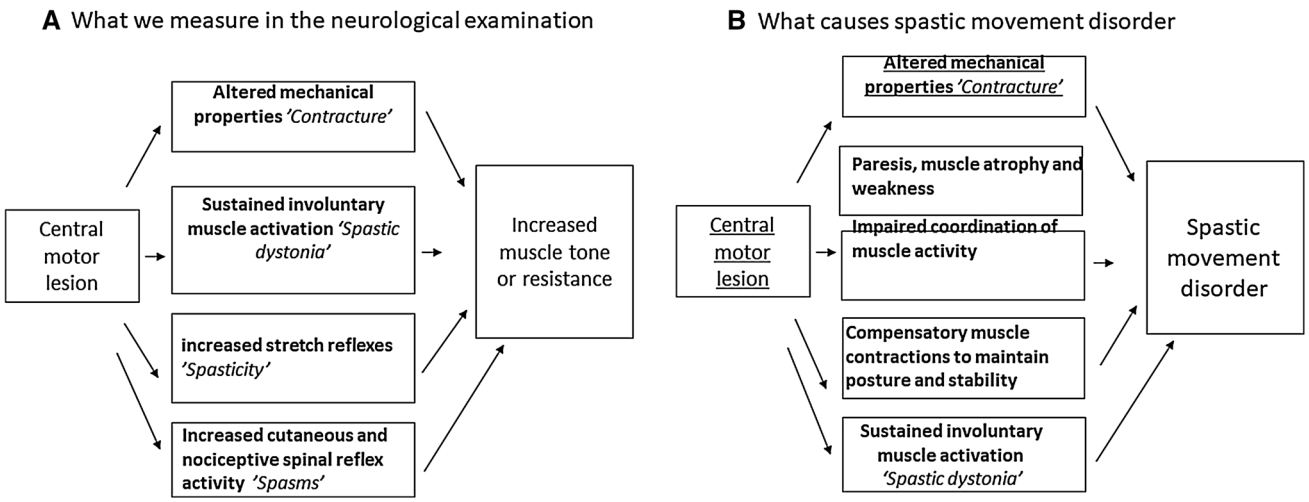

Fig. 1 Schematic diagram showing different factors that contribute to the muscle tone and muscle resistance, which is measured during neurological examination (**a**) and factors that contribute to spastic movement disorder (**b**)

as neural factors other than hyperexcitable stretch reflexes (Lorentzen et al. 2010; Mirbagheri et al. 2008, 2005; Pandyan et al. 2005b; Sinkjaer and Magnussen 1994; Willerslev-Olsen et al. 2013; Wood et al. 2005) have been shown to contribute to the resistance perceived by the clinician (Fig. 1). These may be distinguished with adequate electrophysiological and biomechanical instruments, but are difficult or nearly impossible to tell apart by simple observation or manual handling (Alibiglou et al. 2008; Lorentzen et al. 2010; Mirbagheri et al. 2005, 2007; Wood et al. 2005). These different factors, therefore, contribute to clinicians' perception of 'spasticity' and also influence clinical scores such as the Ashworth score and the Tardieu score (Alibiglou et al. 2008; Biering-Sorensen et al. 2006). Changes in non-neural tissue are seen within weeks following central motor lesions and are often measurable before any sign of hyperexcitable reflexes (Ada et al. 2006; Gao and Zhang 2008; Malhotra et al. 2011; Malouin et al. 1997; Urso et al. 2007). These changes are in all likelihood a response to the lack of neural activity, immobilization in shortened position, lack of mechanical loading and metabolic changes (Mathewson and Lieber 2015; Pingel et al. 2017). Instrumented evaluation of stretch reflex mediated muscle resistance consequently also often fails to confirm the presence of spasticity from the neurological examination such that alterations in non-neural tissue are generally overlooked as a cause of muscle resistance during the neurological examination (Burridge et al. 2005; Lorentzen et al. 2010; Malhotra et al. 2011; Pandyan et al. 2005b; Wood et al. 2005). Determination of possible changes in non-neural tissue as a cause of disability is important to initiate efficient treatment, but also because anti-spastic medication may be contra-indicated. Relatively simple methods such as portable dynamometers integrated with EMG measurements, which can distinguish neural from non-neural causes of increased muscle resistance, have now been validated and made available for clinical use (Yamaguchi et al. 2018).

Measurement of reflexes at rest has little functional relevance

Adequate and reliable evaluation of muscle resistance as part of the neurological examination depends crucially on the ability of the examined person to stay at rest during the examination. If this is not the case, then it is impossible to determine whether the reflexes are larger than normal because of abnormal motoneuronal excitability or simply because the examined person has been unable to relax and has inadvertently depolarized the motor neurons to a state, where they are more excitable than those of a relaxed person. The examined person thus has to 'actively' remain relaxed during the examination, which is a somewhat artificial situation. Research has also demonstrated unequivocally that measurements of stretch reflexes in that situation has little relevance during movement of the examined person. One of the first studies to suggest this was (Ibrahim et al. 1993), but studies with similar findings and conclusions have been published later by different groups (Dietz and Sinkjaer 2007, 2012; Schindler-Ivens et al. 2008; Sinkjaer and Magnussen 1994). Ibrahim et al (1993) measured stretch reflexes in elbow flexors of healthy subjects and on the lesioned and non-lesioned sides in hemiplegic stroke patients at rest and during voluntary elbow flexion. Whereas stretch reflexes were strongly exaggerated on the lesioned side, when measurements were made at *rest*, no significant difference between the reflexes of the two sides or when the reflexes were compared to healthy subjects was found during the elbow flexion. Hyperreflexia was only present in the resting situation, but not during actual movement. This is not surprising and may in fact be predicted from the known regulation of stretch reflex activity during movement (Nielsen 2016; Nielsen et al. 2005). At rest, motor neurons are below their firing threshold and presynaptic inhibition which diminishes transmitter release from sensory afferents is pronounced (Hultborn et al. 1987). During movement, motor neurons are depolarized and presynaptic inhibition is removed (Hultborn et al. 1987; Nielsen 2016). Stretch reflexes, therefore, normally increase in size during movement and attain the same size as reflexes in people with central motor lesions. In the latter people, the normal regulation of the stretch reflex is impaired, but since the reflexes are already increased at rest and are not further modulated during movement, the result is that there is no lesion-induced difference in the size of reflexes during movement (Nielsen et al. 2005).

The above considerations lack an important point. Stretch reflexes, whether elicited by a tendon tap or by a quick passive movement of a joint, are not representative of the way that the neural circuitry underlying the reflex operates during normal conditions. It is after all seldom that a doctor suddenly pops up, while we are happily out for our evening walk and taps us on the patella tendon with a hammer. A tendon tap by a hammer or a quick passive movement differs from the activation of the stretch reflex circuit under normal conditions in three important ways: First, when we move, sensory afferents from muscle spindles discharge at relatively low rates and the discharges are dispersed in time (Burke et al. 1978a; Edin and Vallbo 1990; Vallbo 1974; Wessberg and Vallbo 1995). The afferent activity alone is not sufficient to discharge the motor neurons but rather contributes to depolarization of motor neurons together with other inputs (e.g., activity in descending motor pathways). Second, during movement, the sensitivity of muscle spindles is regulated by gamma motor neuron activity which compensates for the shortening of muscle fibres during movement

(Burke et al. 1978a; Vallbo 1970a, b, 1971). When the muscle is shortened by an external movement, such as during a neurological examination, the muscle spindle afferents reduce their discharge (Burke et al. 1978b). Third, during movement the activity in sensory afferents is predicted by the nervous system and is, therefore, incorporated into the central motor program and the descending central drive to the motor neurons is adjusted accordingly (Nielsen 2016; Nielsen and Sinkjaer 2002a, b; Sinkjaer et al. 2000; Wolpert and Flanagan 2001; Wolpert and Ghahramani 2000). It is suggested that the external perturbation that is part of the neural examination is to some extent unexpected and harder for the nervous system to predict and it is, therefore, rather treated as an error signal (Nielsen and Sinkjaer 2002a, b). We shall discuss this further in the next section.

The differences between normal somatosensory feedback as part of active movements and the somatosensory activity elicited by external stimuli makes it difficult if not impossible to interpret the contribution of sensory input from muscle spindles to the active muscle based on observations of stretch reflex sizes either at rest or during the actual movement. Exaggerated stretch reflexes, therefore, tell us little about the activity in the stretch reflex neural circuitry during movement in patients with central motor lesions. Experiments which study the contribution of afferent inflow during movement through sudden removal of the afferent sensory activity suggest that the sensory drive is at the same level or maybe even smaller than normal in people with lesions of central motor pathways (Frisk et al. 2017; Mazzaro et al. 2007; Willerslev-Olsen et al. 2014). This indicates that individuals with central motor lesions may be unable to make use of sensory feedback drive to the spinal motor neurons to the same extent as healthy people and it speaks strongly against a simple reflex exaggeration as the cause of their functional problems.

What are the functional problems in people with central motor lesions?

If hyperexcitable stretch reflexes are not the problem, what is then the cause of the functional deficits that we clinically describe as spastic movement disorder? First of all, it is evident that the central motor lesion leaves the person with some degree of impaired ability to voluntarily activate muscles, i.e., paresis. Secondary to the paresis, muscles atrophy develops and the muscles become weaker, which adds to the functional impairment (English et al. 2010; Lang et al. 2013; Patten et al. 2004). This creates a challenge during movement: If muscles are weak and not easy to activate, joint stability and posture are threatened. One solution to this is to stabilize the joints through co-activation of antagonist muscles (Nielsen et al. 1994). This central feature of spastic movement disorder is usually seen as a maladaptation, since the co-activation of antagonists is an obstacle for normal flexion–extension movement and especially during gait (Arene and Hidler 2009). What we propose is that the co-activation of antagonists is not necessarily part of the problem, but rather a part of the solution that the injured nervous system has developed to obtain some degree of functionality when confronted with weak muscles that are difficult to activate with appropriate timing. The 'over-activity' of antagonists may not be caused by impaired transmission in spinal control circuitries, although this has been implied by earlier studies (Crone et al. 1994; Morita et al. 2001; Nielsen et al. 1995). Changes in transmission in spinal cord circuitries may rather be a necessary adaptation to ensure joint stability. The traditional thinking, i.e., that reduced spinal inhibition between antagonists contributes to an inability to coordinate antagonist muscles appropriately so that people with central motor lesions develop a stiff gait and stiff posture (Crone et al. 1994; Morita et al. 2001; Nielsen et al. 1995), may thus have to be inverted. It may be that spinal inhibition is reduced as an adaptation to co-activation and thus may be seen as a beneficial adaptation that helps the person to co-activate antagonist muscles more easily and thereby maintain posture despite of relatively weak muscles.

In addition to 'co-contraction by necessity', people with spastic movement disorder are also challenged by their reduced ability to use the descending pathways that are normally involved in movement control and have to find alternative ways of moving their body (Swayne et al. 2008). Reorganization of the cortical areas involved in muscle activation has been studied using imaging and electrophysiological techniques in people following stroke and spinal cord injury as well as people with cerebral palsy (Bestmann et al. 2010; Condliffe et al. 2019; Grefkes and Ward 2014; Kuppuswamy et al. 2015a; Lundell et al. 2011; Swayne et al. 2008; Ward et al. 2003a, b; Ward and Cohen 2004). As an example of one of the general findings in these studies, Fig. 2 shows an image of the BOLD response in the motor cortex of persons with spinal cord injury when performing a simple ankle movement (Lundell et al. 2011). Note the activation of large parts of both the primary, supplementary and premotor cortices bilaterally to perform the simple task of extending and flexing the ankle rhythmically. This may be a neural correlate to the over-activation of muscles that would normally not need to be activated as part of this task. However, with impaired transmission in the appropriate pathways the person inadvertently activates other cortical areas and pathways so that muscles in the whole limb and on both sides of the body are (un-necessarily) activated. Furthermore, this finding also provides an explanation why people with central motor lesions are quickly exhausted when performing movements that typically involve very little metabolic demand (De Doncker et al. 2018; Kuppuswamy et al.

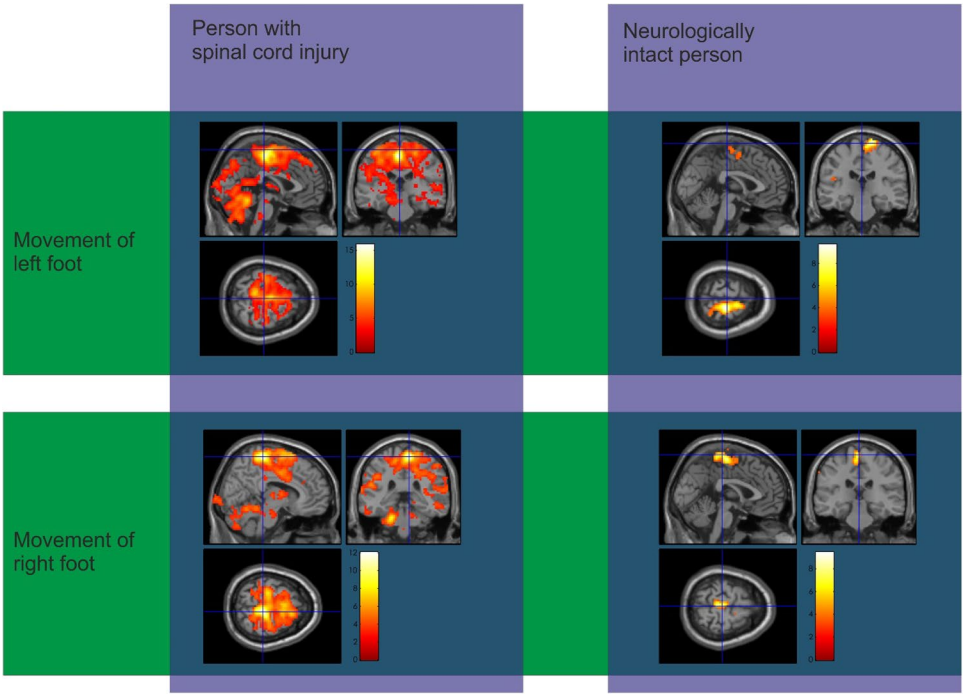

Fig. 2 Blood oxygenation level dependent (BOLD) signal changes measured by fMRI during performance of alternating ankle dorsiflexion and plantarflexion movements in a person with spinal cord injury (left column) and a neurologically intact person (right column). In the upper row, movements were performed with the left foot in the lower row movements were performed with the right foot. BOLD activation maps were obtained after fitting a general linear model of the movement and rest periods to the data and then threshold the statistical parametric maps at $p < 0.001$ uncorrected. Data adapted from the study by Lundell et al. 2011)

2015c). Even small movements require activation of large parts of the brain, which likely produces an experience of fatigue (Kuppuswamy et al. 2015a, b, c).

Correct prediction of sensory feedback as a basis for motor learning

Such findings also lead to an alternative interpretation for reduced ability to selectively activate muscles and unwanted muscle activity in people with central motor lesions. If we abandon the idea of stretch reflexes as separate entities and accept that somatosensory feedback is normally integrated into central motor commands (Fig. 3), we then need to understand what the brain lesion does to this integration and how it may affect movement. The healthy nervous system uses sensory information and efference copies of motor commands to ensure that a movement was performed according to the plan computed by an internal model (Frey et al. 2011; Shadmehr et al. 2010; Wolpert 1997; Wolpert et al. 2011; Wolpert and Flanagan 2016; Wolpert and Ghahramani 2000). If the sensory consequences of the movement do not correspond to the predicted sensory consequences, then the central motor program needs to be updated so that the execution of the movement is optimized through repetition and gradual reduction of the difference between the predicted and actual consequences of movement (Shadmehr et al. 2010; Wolpert 1997; Wolpert et al. 2011; Wolpert and Flanagan 2016; Wolpert and Ghahramani 2000). There is now very convincing evidence indicating that motor learning and adaptation rely on internal models. One role of the internal model is to make a prediction of the sensory consequences of movements. These predictions are then compared with the actual sensory consequences of the movements, and if there an error then the motor command can then be adjusted, hence motor learning and adaptation can be achieved. Internal models are the foundation of our normal ability to perform movements effortlessly and with great precision, and motor skill improve with our repeated performance of movements day after day (Wolpert 1997; Wolpert et al. 2011; Wolpert and Flanagan 2016; Wolpert and Ghahramani 2000). Through our daily sensory experience when we move, the nervous system builds this internal model of our body and its interaction with the world, which enables it to perform movements quickly and precisely without having to wait for sensory information to perform most movements. Sensory information is instead integrated into the motor command as an expectation of a given sensory input (i.e., for instance a stretch reflex) at a given time during a movement. A deviation from this expected sensory feedback will be computed as an error signal and used to update the motor program, so that future movements can be performed adequately with a more precise prediction of the sensory input. Without somatosensory information to update the predictive model, the ability to adapt movement effectively to the environment is impaired as illustrated by the case of I.W. ('the deafferented man'), who has been intensely studied by Jonathan Cole, John Rothwell and others (Yousif et al. 2015).

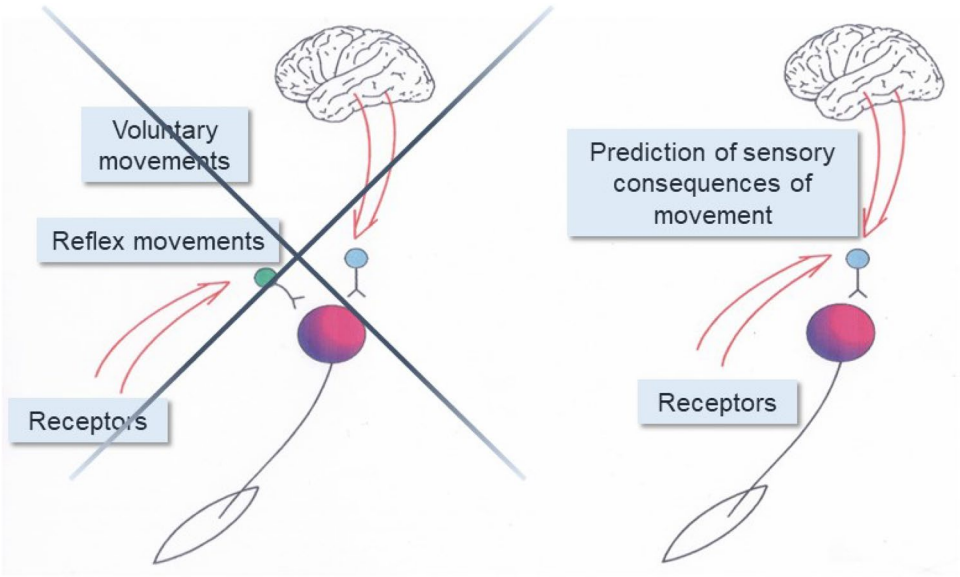

Fig. 3 Schematic illustration of the changing view of the role of sensory information during voluntary movement and in relation to spastic movement disorder. The idea that it is possible to separate reflexes and voluntary movements into separate entities has been abandoned a long time ago in the realization that descending motor pathways and sensory afferents converge on the same premotoneuronal neurons (left side of figure). Sensory information may instead be seen as an integrated part of central motor commands, if the nervous system optimizes movements by minimizing the error between the *predicted* and the *actual* sensory consequences of movements (right side of figure). It follows that spastic movement disorder may be seen as the consequence of an inadequate prediction of the sensory consequences of movements

Difficulty in establishing predictive model following central motor lesion

Within this theoretical framework, people with lesions that affect descending or ascending pathways in the brain or spinal cord are presented with a fundamental challenge in establishing consistent relationships between movements and their outcomes. Without a firm coupling between motor activity and sensory outcome it becomes difficult and maybe even impossible for the internal model to develop an adequate prediction of the sensory consequences of the movement. Movements become relatively random guesses without any way of telling what works and what does not work. In the face of this uncertainty, we might conceive of a spastic movement disorder as resulting from the nervous system's attempt at controlling excess degrees of freedom for the movement when confronted with a variable somatosensory input. The late onset of hyperexcitability following central lesions (Katoozian et al. 2018; Nam et al. 2019) may in this view reflect a gradual upregulation of somatosensory input (i.e., increasing the signal to noise ratio) to facilitate the establishment of the internal model. Without a firm prediction of somatosensory feedback from the moving limb, a person with a central motor lesion will experience reduced ability to optimize movement adequately and is forced to make relatively gross movements that are slow and imprecise. A strategy that involves co-contraction of the muscles around the joints may, therefore, be the most optimal solution to minimize the degrees of freedom and create a somewhat stable movement (Franklin et al. 2007; Heald et al. 2018). There is indeed evidence that initial paresis predicts spasticity (Picelli et al. 2014), suggesting that spastic movement disorder is related to a learned compensation for muscle weakness.

Difficulty in establishment of predictive model during maturation in children with cerebral palsy

Following Nikolai Bernstein (Bernstein 1967) we propose that muscle co-contraction in spastic cerebral palsy and other spastic movement disorders may assist motor learning; especially within a developmental context. Muscle co-contraction freezes a joint's degrees of freedom aiding motor learning. An example of this is the increased co-contraction around the ankle joint in late swing and early stance during gait in children with Cerebral Palsy (CP) (Lorentzen et al. 2019). In contrast, typically developing children acquire a predictive feedforward program in late childhood, which allows them to walk on toes with little co-activation of antagonistic muscles, children with cerebral palsy continue to stabilize the ankle joint by co-activation of antagonistic muscles at ground contact without a clear developmental

progression at least within the age group 2–12 years (Fig. 4) (Lorentzen et al. 2019). Again following Bernstein's concept of 'freezing' and 'freeing' degrees of freedom during motor learning our data have shown that, in contrast to children with cerebral palsy, typically developing subjects having first 'frozen' the degrees of freedom, then 'free' the degrees of freedom as they approach maturity. For subjects with CP, co-contraction may be an attempt to minimize the degrees of freedom and stabilize the joint position at the critical moment of ground contact and may, therefore, be the best attempt at making a coordinated movement for an internal model that is dealing with a too low somatosensory signal-to-noise ratio. We hypothesize that this solution for the internal model may be rather firmly established in children with CP around the age of 10–12 years based on two observations: First, it has been found that intensive gait training improves gait function significantly only in children below this age (Willerslev-Olsen et al. 2015). This suggests that the internal model for the particular gait pattern in children with CP has not yet been firmly established and may, therefore, more easily be influenced by specific training procedures. The developmental period up to 10–12 years of age should be considered a sensitive period for targeted training. Second, Selective Dorsal Rhizotomy (SDR; partial surgical lesion of dorsal roots) has been shown to improve gait function in children with CP with moderately affected spastic gait (Gross motor Function Classification Scale (GMFCS: 2–3) below the age of 10 years (MacWilliams et al. 2011). In people with severe CP (GMFCS: 4–5) SDR has no benefit on function and undertaken above the age of 15 years, regardless of CP severity it may be detrimental (MacWilliams et al. 2011). A possible explanation is that SDR in CP artificially reduces co-contraction at several lower limb joints (cf. Fig. 4), improves the signal to noise ratio and 'unfreezes' the degrees of freedom. This would allow internal models to adapt better during an important developmental window for young people with CP.

Is noisy somatosensory feedback a fundamental problem in spastic movement disorder?

Noise is inherent in any biological system and noise is, therefore, also a parameter that influences the learning process significantly. Some noise is seen as a good thing, since it allows flexibility and adaptability in the system (Wu et al. 2014). Without noise humans would not be able to explore alternative solutions to the performance of the optimized movement and would be constrained to one way of performing simple and complex motor tasks. Actually, large initial variation in movement execution has been shown to lead to faster learning despite similar feedback noise (Wu et al. 2014). However, too much noise is a serious problem and has been shown to decrease learning rates during sensorimotor adaptation learning (Wei and Kording 2010). People with spastic movement disorder are likely to have to deal with noise in both the motor output and the somatosensory input, which will slow down the learning process considerably.

There are at least two reasons for the increase in noise following brain lesion: One is that a lesion involving the motor areas might make it impossible to use the normal pathways that would produce a specific movement with an associated and predictable somatosensory consequence. The movements, therefore, are less coordinated to begin with and somatosensory information becomes less clearly associated to the movement, as it was originally planned. Secondly, since restriction of vascular supply in stroke or the forces

Fig. 4 Age-related changes in ankle co-contraction within 200 ms prior to ground contact during normal heel walking in typically developing (TD) children (**a**), toe walking in TD children (**b**) and (involuntary toe walking in children with Cerebral Palsy (CP) (**c**). The amount of anterior tibial EMG activity was calculated in the period 200 ms prior to ground contact and divided by the amount of Soleus EMG activity in the same period. Each symbol indicates data from one child. Full lines indicate regression lines calculated for the populations of children. Dashed lines indicate 95% confidence intervals. Correlation coefficients and level of statistical significance are given in the upper left corner of each graph. [Reproduced from (Lorentzen et al. 2019)]

induced by trauma are not restricted to motor areas, central motor lesions are seldom pure motor lesions, but also affect somatosensory information. If proprioceptive information is severely affected, then the signal to noise ratio is likely to be small and it may become difficult to tell signal from noise and optimize movements.

Towards a new treatment approach for spastic movement disorder

If this way of thinking is correct, it follows that a goal of future (re)habilitation strategies for people with spastic movement disorder, rather than to simply suppress reflex activity, must be to find ways of improving the somatosensory signal to noise ratio to most efficiently establish and maintain an accurate predictive model. This might involve technologies that thorough offering enhanced motivation, challenge the patients to increase their movement range, but also allow them to incorporate strategies that their central nervous system adapt to (like co-contraction) rather than applying supportive strategies, where the adaptation is to activate muscles less. To help rehabilitate people with central motor lesions we argue that it makes sense to find ways of helping them to obtain a clearer sensory signal through other less-affected sensory modalities with less variability that they can use to optimize movement. This suggests that a goal of future therapy would be to train patients using techniques or devices that can facilitate accuracy and precision of sensory information and help them to make accurate predictions of the sensory consequences of their movements. It is our suggestion that this will allow somatosensory feedback to be better integrated into the central motor command, allowing the subject to perform movements with greater ease and less mental effort. Stretch reflexes—measured at rest or during movement—may remain hyperactive or not. What matters is the development of sensorimotor integration that can assure optimal movement control in a variable environment—not whether a reflex which has little or no functional significance is hyperexcitable or not.

Acknowledgements JBN acknowledges funding from the Elsass foundation and the Danish Medical Research Council (Forskningsrådet for Sundhed og Sygdom). SFF acknowledges funding support from the UCLH Biomedical Research Centre. The authors acknowledge the careful reading and helpful comments of Dr. Lucinda Carr.

References

Ada L, O'Dwyer N, O'Neill E (2006) Relation between spasticity, weakness and contracture of the elbow flexors and upper limb activity after stroke: an observational study. Disabil Rehabil 28:891–897

Alibiglou L, Rymer WZ, Harvey RL, Mirbagheri MM (2008) The relation between Ashworth scores and neuromechanical measurements of spasticity following stroke. J Neuroeng Rehabil 5:18

Arene N, Hidler J (2009) Understanding motor impairment in the paretic lower limb after a stroke: a review of the literature. Top Stroke Rehabil 16:346–356

Bernstein NA (1967) The co-ordination and regulation of movements. Pergamon Press, Oxford

Bestmann S, Swayne O, Blankenburg F, Ruff CC, Teo J, Weiskopf N, Driver J, Rothwell JC, Ward NS (2010) The role of contralesional dorsal premotor cortex after stroke as studied with concurrent TMS-fMRI. J Neurosci 30:11926–11937

Biering-Sorensen F, Nielsen JB, Klinge K (2006) Spasticity-assessment: a review. Spinal Cord 44:708–722

Burke D, Hagbarth KE, Lofstedt L (1978a) Muscle spindle activity in man during shortening and lengthening contractions. J Physiol 277:131–142

Burke D, Hagbarth KE, Lofstedt L (1978b) Muscle spindle responses in man to changes in load during accurate position maintenance. J Physiol 276:159–164

Burridge JH, Wood DE, Hermens HJ, Voerman GE, Johnson GR, van Wijck F, Platz T, Gregoric M, Hitchcock R, Pandyan AD (2005) Theoretical and methodological considerations in the measurement of spasticity. Disabil Rehabil 27:69–80

Condliffe EG, Jeffery DT, Emery DJ, Treit S, Beaulieu C, Gorassini MA (2019) Full activation profiles and integrity of corticospinal pathways in adults with bilateral spastic cerebral palsy. Neurorehabil Neural Repair 33:59–69

Crone C, Nielsen J, Petersen N, Ballegaard M, Hultborn H (1994) Disynaptic reciprocal inhibition of ankle extensors in spastic patients. Brain 117(Pt 5):1161–1168

De Doncker W, Dantzer R, Ormstad H, Kuppuswamy A (2018) Mechanisms of poststroke fatigue. J Neurol Neurosurg Psychiatry 89(3):287–293

Dietz V, Sinkjaer T (2007) Spastic movement disorder: impaired reflex function and altered muscle mechanics. Lancet Neurol 6:725–733

Dietz V, Sinkjaer T (2012) Spasticity. Handbook Clin Neurol 109:197–211

Edin BB, Vallbo AB (1990) Muscle afferent responses to isometric contractions and relaxations in humans. J Neurophysiol 63:1307–1313

English C, McLennan H, Thoirs K, Coates A, Bernhardt J (2010) Loss of skeletal muscle mass after stroke: a systematic review. Int J Stroke 5:395–402

Franklin DW, Liaw G, Milner TE, Osu R, Burdet E, Kawato M (2007) Endpoint stiffness of the arm is directionally tuned to instability in the environment. J Neurosci 27:7705–7716

Frey SH, Fogassi L, Grafton S, Picard N, Rothwell JC, Schweighofer N, Corbetta M, Fitzpatrick SM (2011) Neurological principles and rehabilitation of action disorders: computation, anatomy, and physiology (CAP) model. Neurorehabil Neural Repair 25:6S–20S

Frisk RF, Jensen P, Kirk H, Bouyer LJ, Lorentzen J, Nielsen JB (2017) Contribution of sensory feedback to plantar flexor muscle activation during push-off in adults with cerebral palsy. J Neurophysiol 118:3165–3174

Gao F, Zhang LQ (2008) Altered contractile properties of the gastrocnemius muscle poststroke. J Appl Physiol 105:1802–1808

Geertsen SS, Kirk H, Lorentzen J, Jorsal M, Johansson CB, Nielsen JB (2015) Impaired gait function in adults with cerebral palsy is associated with reduced rapid force generation and increased passive stiffness. Clin Neurophysiol 126:2320–2329

Grefkes C, Ward NS (2014) Cortical reorganization after stroke: how much and how functional? Neuroscientist 20:56–70

Heald JB, Franklin DW, Wolpert DM (2018) Increasing muscle co-contraction speeds up internal model acquisition during dynamic motor learning. Sci Rep 8:16355

Hultborn H, Meunier S, Pierrot-Deseilligny E, Shindo M (1987) Changes in presynaptic inhibition of Ia fibres at the onset of voluntary contraction in man. J Physiol 389:757–772

Ibrahim IK, Berger W, Trippel M, Dietz V (1993) Stretch-induced electromyographic activity and torque in spastic elbow muscles. Differential modulation of reflex activity in passive and active motor tasks. Brain 116(Pt 4):71–989

Katoozian L, Tahan N, Zoghi M, Bakhshayesh B (2018) The onset and frequency of spasticity after first ever stroke. J Natl Med Assoc 110:547–552

Kuppuswamy A, Clark EV, Sandhu KS, Rothwell JC, Ward NS (2015a) Post-stroke fatigue: a problem of altered corticomotor control? J Neurol Neurosurg Psychiatry 86:902–904

Kuppuswamy A, Clark EV, Turner IF, Rothwell JC, Ward NS (2015b) Post-stroke fatigue: a deficit in corticomotor excitability? Brain 138:136–148

Kuppuswamy A, Rothwell J, Ward N (2015c) A model of post-stroke fatigue based on sensorimotor deficits. Curr Opin Neurol 28:582–586

Landau WM (1980) Spasticity: what is it? What is it not? In: Feldman RG, Koella WP (eds) Spasticity: disordered motor control. Cibageigy Coporation, Chicago, pp 17–25

Landau WM (2004) Spasticity after stroke: why bother? Stroke 35:1787–1788 **(author reply 1787–1788)**

Lang CE, Bland MD, Bailey RR, Schaefer SY, Birkenmeier RL (2013) Assessment of upper extremity impairment, function, and activity after stroke: foundations for clinical decision making. J Hand Ther 26:104–114 **(quiz 115)**

Lorentzen J, Grey MJ, Crone C, Mazevet D, Biering-Sorensen F, Nielsen JB (2010) Distinguishing active from passive components of ankle plantar flexor stiffness in stroke, spinal cord injury and multiple sclerosis. Clin Neurophysiol 121:1939–1951

Lorentzen J, Pradines M, Gracies JM, Bo NJ (2018) On Denny-Brown's 'spastic dystonia'—what is it and what causes it? Clin Neurophysiol 129:89–94

Lorentzen J, Willerslev-Olsen M, Huche Larsen H, Farmer SF, Nielsen JB (2019) Maturation of feedforward toe walking motor program is impaired in children with cerebral palsy. Brain 142:526–541

Lundell H, Christensen MS, Barthelemy D, Willerslev-Olsen M, Biering-Sorensen F, Nielsen JB (2011) Cerebral activation is correlated to regional atrophy of the spinal cord and functional motor disability in spinal cord injured individuals. NeuroImage 54:1254–1261

MacWilliams BA, Johnson BA, Shuckra AL, D'Astous JL (2011) Functional decline in children undergoing selective dorsal rhizotomy after age 10. Dev Med Child Neurol 53:717–723

Malhotra S, Cousins E, Ward A, Day C, Jones P, Roffe C, Pandyan A (2008) An investigation into the agreement between clinical, biomechanical and neurophysiological measures of spasticity. Clin Rehabil 22:1105–1115

Malhotra S, Pandyan AD, Day CR, Jones PW, Hermens H (2009) Spasticity, an impairment that is poorly defined and poorly measured. Clin Rehabil 23:651–658

Malhotra S, Pandyan AD, Rosewilliam S, Roffe C, Hermens H (2011) Spasticity and contractures at the wrist after stroke: time course of development and their association with functional recovery of the upper limb. Clin Rehabil 25:184–191

Malouin F, Bonneau C, Pichard L, Corriveau D (1997) Non-reflex mediated changes in plantarflexor muscles early after stroke. Scand J Rehabil Med 29:147–153

Mathewson MA, Lieber RL (2015) Pathophysiology of muscle contractures in cerebral palsy. Phys Med Rehabil Clin N Am 26:57–67

Mazzaro N, Nielsen JF, Grey MJ, Sinkjaer T (2007) Decreased contribution from afferent feedback to the soleus muscle during walking in patients with spastic stroke. J Stroke Cerebrovasc Dis 16:135–144

Mirbagheri MM, Rymer WZ, Tsao C, Settle K (2005) Evolution of reflexive and muscular mechanical properties in stroke-induced spasticity. Conf Proc IEEE Eng Med Biol Soc 4:4393–4395

Mirbagheri MM, Settle K, Harvey R, Rymer WZ (2007) Neuromuscular abnormalities associated with spasticity of upper extremity muscles in hemiparetic stroke. J Neurophysiol 98:629–637

Mirbagheri MM, Alibiglou L, Thajchayapong M, Rymer WZ (2008) Muscle and reflex changes with varying joint angle in hemiparetic stroke. J Neuroeng Rehabil 5:6

Morita H, Crone C, Christenhuis D, Petersen NT, Nielsen JB (2001) Modulation of presynaptic inhibition and disynaptic reciprocal Ia inhibition during voluntary movement in spasticity. Brain 124:826–837

Nam KE, Lim SH, Kim JS, Hong BY, Jung HY, Lee JK, Yoo SD, Pyun SB, Lee KM, Lee KJ, Kim H, Han EY, Lee KW (2019) When does spasticity in the upper limb develop after a first stroke? A nationwide observational study on 861 stroke patients. J Clin Neurosci 66:144–148

Nielsen JB (2016) Human spinal motor control. Annu Rev Neurosci 39:81–101

Nielsen JB, Sinkjaer T (2002a) Afferent feedback in the control of human gait. J Electromyogr Kinesiol 12:213–217

Nielsen JB, Sinkjaer T (2002b) Reflex excitation of muscles during human walking. Adv Exp Med Biol 508:369–375

Nielsen J, Sinkjaer T, Toft E, Kagamihara Y (1994) Segmental reflexes and ankle joint stiffness during co-contraction of antagonistic ankle muscles in man. Exp Brain Res 102:350–358

Nielsen J, Petersen N, Crone C (1995) Changes in transmission across synapses of Ia afferents in spastic patients. Brain 118(Pt 4):995–1004

Nielsen JB, Petersen NT, Crone C, Sinkjaer T (2005) Stretch reflex regulation in healthy subjects and patients with spasticity. Neuromodulation 8:49–57

Pandyan AD, Cousins E, van Wijck F, Barnes MP, Johnson GR (2005a) Spasticity research: some common catches. Arch Phys Med Rehabil 86:845 **(author reply 845–846)**

Pandyan AD, Gregoric M, Barnes MP, Wood D, Van Wijck F, Burridge J, Hermens H, Johnson GR (2005b) Spasticity: clinical perceptions, neurological realities and meaningful measurement. Disabil Rehabil 27:2–6

Patten C, Lexell J, Brown HE (2004) Weakness and strength training in persons with poststroke hemiplegia: rationale, method, and efficacy. J Rehabil Res Dev 41:293–312

Picelli A, Tamburin S, Dambruoso F, Midiri A, Girardi P, Santamato A, Fiore P, Smania N (2014) Topical distribution of initial paresis of the limbs to predict clinically relevant spasticity after ischemic stroke: a retrospective cohort study. Eur J Phys Rehabil Med 50:489–494

Pingel J, Bartels EM, Nielsen JB (2017) New perspectives on the development of muscle contractures following central motor lesions. J Physiol 595:1027–1038

Salazar-Torres Jde J, Pandyan AD, Price CI, Davidson RI, Barnes MP, Johnson GR (2004) Does spasticity result from hyperactive stretch reflexes? Preliminary findings from a stretch reflex characterization study. Disabil Rehabil 26:756–760

Schindler-Ivens S, Brown DA, Lewis GN, Nielsen JB, Ondishko KL, Wieser J (2008) Soleus H-reflex excitability during pedaling post-stroke. Exp Brain Res 188:465–474

Shadmehr R, Smith MA, Krakauer JW (2010) Error correction, sensory prediction, and adaptation in motor control. Annu Rev Neurosci 33:89–108

Sinkjaer T, Magnussen I (1994) Passive, intrinsic and reflex-mediated stiffness in the ankle extensors of hemiparetic patients. Brain 117(Pt 2):355–363

Sinkjaer T, Andersen JB, Ladouceur M, Christensen LO, Nielsen JB (2000) Major role for sensory feedback in soleus EMG activity in the stance phase of walking in man. J Physiol 523(Pt 3):817–827

Swayne OB, Rothwell JC, Ward NS, Greenwood RJ (2008) Stages of motor output reorganization after hemispheric stroke suggested by longitudinal studies of cortical physiology. Cereb Cortex 18:1909–1922

Urso ML, Chen YW, Scrimgeour AG, Lee PC, Lee KF, Clarkson PM (2007) Alterations in mRNA expression and protein products following spinal cord injury in humans. J Physiol 579:877–892

Vallbo AB (1970a) Discharge patterns in human muscle spindle afferents during isometric voluntary contractions. Acta Physiol Scand 80:552–566

Vallbo AB (1970b) Response patterns of human muscle spindle endings to isometric voluntary contractions. Acta Physiol Scand 80:43A

Vallbo AB (1971) Time difference between onset of spindle acceleration and skeletomotor activation in isometric voluntary contractions in man. Acta Physiol Scand 82:15A–16A

Vallbo AB (1974) Afferent discharge from human muscle spindles in non-contracting muscles. Steady state impulse frequency as a function of joint angle. Acta Physiol Scand 90:303–318

Ward NS, Cohen LG (2004) Mechanisms underlying recovery of motor function after stroke. Arch Neurol 61:1844–1848

Ward NS, Brown MM, Thompson AJ, Frackowiak RS (2003a) Neural correlates of motor recovery after stroke: a longitudinal fMRI study. Brain 126:2476–2496

Ward NS, Brown MM, Thompson AJ, Frackowiak RS (2003b) Neural correlates of outcome after stroke: a cross-sectional fMRI study. Brain 126:1430–1448

Wei K, Kording K (2010) Uncertainty of feedback and state estimation determines the speed of motor adaptation. Front Comput Neurosci 4:11

Wessberg J, Vallbo AB (1995) Human muscle spindle afferent activity in relation to visual control in precision finger movements. J Physiol 482(Pt 1):225–233

Willerslev-Olsen M, Lorentzen J, Sinkjaer T, Nielsen JB (2013) Passive muscle properties are altered in children with cerebral palsy before the age of 3 years and are difficult to distinguish clinically from spasticity. Dev Med Child Neurol 55:617–623

Willerslev-Olsen M, Andersen JB, Sinkjaer T, Nielsen JB (2014) Sensory feedback to ankle plantar flexors is not exaggerated during gait in spastic hemiplegic children with cerebral palsy. J Neurophysiol 111:746–754

Willerslev-Olsen M, Petersen TH, Farmer SF, Nielsen JB (2015) Gait training facilitates central drive to ankle dorsiflexors in children with cerebral palsy. Brain 138:589–603

Wolpert DM (1997) Computational approaches to motor control. Trends Cogn Sci 1:209–216

Wolpert DM, Ghahramani Z (2000) Computational principles of movement neuroscience. Nat Neurosci 3(Suppl):1212–1217

Wolpert DM, Flanagan JR (2001) Motor prediction. Curr Biol 11:R729–732

Wolpert DM, Flanagan JR (2016) Computations underlying sensorimotor learning. Curr Opin Neurobiol 37:7–11

Wolpert DM, Diedrichsen J, Flanagan JR (2011) Principles of sensorimotor learning. Nat Rev Neurosci 12:739–751

Wood DE, Burridge JH, van Wijck FM, McFadden C, Hitchcock RA, Pandyan AD, Haugh A, Salazar-Torres JJ, Swain ID (2005) Biomechanical approaches applied to the lower and upper limb for the measurement of spasticity: a systematic review of the literature. Disabil Rehabil 27:19–32

Wu HG, Miyamoto YR, Gonzalez Castro LN, Olveczky BP, Smith MA (2014) Temporal structure of motor variability is dynamically regulated and predicts motor learning ability. Nat Neurosci 17:312–321

Yamaguchi T, Hvass Petersen T, Kirk H, Forman C, Svane C, Kofoed-Hansen M, Boesen F, Lorentzen J (2018) Spasticity in adults with cerebral palsy and multiple sclerosis measured by objective clinically applicable technique. Clin Neurophysiol 129:2010–2021

Yousif N, Cole J, Rothwell J, Diedrichsen J (2015) Proprioception in motor learning: lessons from a deafferented subject. Exp Brain Res 233:2449–2459