Clinical Neurophysiology 129 (2018) 89–94

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Review

On Denny-Brown's 'spastic dystonia' – What is it and what causes it?

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ARTICLE INFO

Article history:
Accepted 2 October 2017
Available online 4 November 2017

Keywords:
Spasticity
Spastic dystonia
Hypertonia

HIGHLIGHTS

- Stretch and effort-unrelated sustained involuntary muscle activity following central motor lesions may be caused by:
- Plastic changes at a spinal level involving upregulation and sprouting of surviving descending fibres and/or changes in intrinsic properties of motoneurones.
- Re-organization in the motor cortex.
- Lesions in basal ganglia.

ABSTRACT

In this review, we will work around two simple definitions of two different entities, which most often co-exist in patients with lesions to central motor pathways: Spasticity is "Enhanced excitability of velocity-dependent responses to phasic stretch at rest", which will not be the subject of this review, while Spastic dystonia is tonic, chronic, involuntary muscle contraction in the absence of any stretch or any voluntary command (Gracies, 2005). Spastic dystonia is a much less well understood entity that will be the subject this review.

Denny-Brown (1966) 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. 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. Yet, little has been done since Denny-Brown's studies to determine the pathophysiology of this non- stretch or effort related sustained involuntary muscle activity following motor lesions and there is a clear need for research studies in order to improve current therapy.

The purpose of the present review is to discuss some of the possible mechanisms that may be involved in the hope that this may guide future research. We discuss the existence of persistent inward currents in spinal motoneurones and present the evidence that the channels involved may be upregulated following central motor lesions. We also discuss a possible contribution from alterations in synaptic inputs from surviving or abnormally branched sensory and descending fibres leading to over-activity and lack of motor coordination. We finally discuss evidence of alterations in motor cortical representational maps and basal ganglia lesions.

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https://doi.org/10.1016/j.clinph.2017.10.023
1388-2457/

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1. Introduction

There has been considerable debate in the scientific literature in recent years regarding the proper definition of spasticity (Biering-Sorensen et al., 2006; Burridge et al., 2005; Gracies, 2005a, 2005b; Lorentzen et al., 2010; Malhotra et al., 2008; Pandyan et al., 2005a, 2005b; Sheean, 2002). Much of this debate stems from documented differences in the understanding of which clinical signs define spasticity as well as a presumed variability in the clinical use of the term (Pandyan et al., 2005a, 2005b). Without a clear consensus of what we understand by 'spasticity' there is a risk that research in the field remains confused and potentially leads to misunderstandings and wrong treatment decisions in the clinic.

Spasticity has commonly been linked to an increase in the velocity-dependent stretch responses of a muscle, manifested as a 'catch' that can be felt when stretching the muscle quickly enough (Gracies, 2005a; Lance, 1980; Sheean, 2002; Sheean and McGuire, 2009). The implicit assumption is that the 'catch' is caused by hyperactive stretch reflexes and several definitions, including that of Lance (1980), consequently include hyperactive stretch reflex activity as a central component (Lance, 1980) or the *only* component of the definition (Gracies, 2005b). Yet, research in the past 20–30 years has documented that hyperactive stretch reflexes generally do not cause functional problems and do not show any clear relation to the main clinical problems experienced by the patients and clinicians (Dietz and Sinkjaer, 2007, 2012; Lorentzen et al., 2010; Salazar-Torres Jde et al., 2004; Willerslev-Olsen et al., 2013). In the clinic, the term spasticity has in fact often been used much more broadly, also including spasms, involuntary movements, unwanted muscle activity and alterations of elastic muscle properties leading to reduced movement range and eventually contractures (Pandyan et al., 2005b). It has especially been a confounding factor that the alterations of elastic muscle properties are difficult to distinguish clinically from the muscle resistance caused by hyperactive stretch reflexes and many of the functional problems observed in patients with central motor lesions have therefore been falsely attributed to hyperactive stretch reflex activity (Dietz and Sinkjaer, 2007, 2012). Research through three decades have instead documented that it is the reduced movement range and lack of extensibility of the muscle and connective tissue, which are dominant causes of reduced functional capacity in "spastic" patients, particularly those with cerebral palsy (Berger et al., 1982; Geertsen et al., 2015; Willerslev-Olsen et al., 2014), but also with stroke (Pradines et al., 2015). Spasms are a frequent cause of painful muscle contractions, which may interfere with sleep (Biering-Sorensen and Biering-Sorensen, 2001). They are caused by activation of hyperactive spinal networks, which are distinct from the stretch reflex circuitry (Sheean and McGuire, 2009). Recent research has implicated altered persistent inward currents in both motoneurones and interneurons as important pathophysiological factors in the development of spasms (Bellardita et al., 2017; Gorassini et al., 2004; Kong et al., 2011; Murray et al., 2010, 2011).

Little is known of the involuntary movements and unwanted muscle activity, which are frequently observed in patients with central motor lesions and which constitute the core of what is also often called spastic movement disorder. There may be some kind of 'overactivity' causing unwanted muscle activity when the patient attempts to remain at rest. This clinical symptom is what has been named spastic dystonia (Denny-Brown, 1966; Gracies, 2005b). In addition to this involuntary resting activity, one can often observe in the same patients involuntary activation of antagonist muscles to the muscles targeted by the command, and of muscles other than those that the patient attempts to activate. These phenomena have been termed spastic co-contraction and extrasegmental co-contraction respectively (Gracies, 2005b). As Spastic Dystonia is caused by an actual brain lesion (vascular, traumatic, etc.), being usually accompanied by a number of other symptoms (spasticity, spastic cocontraction, etc.), Spastic Dystonia is one type of what has been labelled secondary dystonias (Gracies and Simpson, 2004).

The term 'spastic dystonia' may be seen as a misnomer by some, since it mixes terms that have traditionally been linked to either lesions of descending motor pathways or the basal ganglia. Despite these problems we have decided to maintain the term in this review, since it is already used widely in the literature and since an alternative term such as 'dystonic spasticity' would be equally misleading and would imply a false pathophysiological relationship with spasticity. We do not believe that it would add to clarity in the field if we were to introduce yet another term for which there is no general consensus and which in our opinion would not help in achieving what we aim for with this review, which is to point out that the sustained involuntary muscle activity observed in patients with central motor lesions should not be mistaken for spasticity. For that purpose spastic dystonia is a better term than dystonic spasticity. A descriptive term such as 'stretch- and effort-unrelated sustained involuntary muscle activity following central motor lesions' may avoid some of the confusion, but it is lengthy and awkward. The reader should therefore see our use of the term 'spastic dystonia' in this review as a convenient abbreviation for 'stretch- and effort-unrelated sustained involuntary muscle activity following central motor lesions'.

In humans, spastic dystonia is seen most conspicuously in the upper limb where it contributes to the so-called hemiparetic posture, particularly in subjects with stroke or cerebral palsy (Gracies, 2005b; Sheean, 2002, Sheean and McGuire, 2009). An aggravated expression of spastic dystonia may also be seen during standing and gait where the subject may adopt a posture with plantarflexion and/or inversion at the ankle, toe flexion, pronounced extension at the knee and associated flexion at the elbow (Gracies, 2005b; Sheean, 2002; Sheean and McGuire, 2009).