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Journal of Muscle Health

Review Article

Spasticity and the Human Pyramidal Tracts

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Submitted: 02 June 2017

Accepted: 08 September 2017

Published: 10 September 2017

Keywords

- Extrapyramidal system
- Pyramidal syndrome
- Pyramidal tracts
- Reticulospinal tracts
- Sign of Babinski
- Spasticity

Abstract

After a long and tortuous history spanning over a century of clinicoanatomical and experimental observations, the concept of spasticity has assumed its current form as a velocity-dependent increase of tone in a group of passively stretched muscles. However, several gaps have remained in the understanding of spasticity as a clinical and experimental phenomenon. A long-standing controversy concerns the critical neural pathways that must be damaged for the production of spasticity. Two general explanations have been offered as a way out of this conundrum. The clinicoanatomical tradition (human) contends that spasticity is one of the four cardinal symptoms of pyramidal tract damage, whereas the experimental school (experimental animals) regards spasticity as a symptom of injury of extrapyramidal pathways, particularly the reticulospinal tracts. This review provides evidence that both claims are valid for different animal species. Thus, while spasticity (or its experimental equivalent) is a symptom of extrapyramidal injury in all mammals, including nonhuman primates, in humans it is a legitimate symptom of pyramidal tract lesion or dysfunction.

ABBREVIATIONS

PyrT: Pyramidal Tract; PyrTs: Pyramidal Tracts

INTRODUCTION

Spasticity has a long and tortuous history. *As a symptom of brain damage*, it was slowly distinguished from other actual (e.g., parkinsonian rigidity, dystonia) and apparent (e.g., fixed joints due to arthrosis) increases in muscle tone [1]. *As a descriptive term*, influential authors gave different names to spasticity as we currently recognize it, including "rigidity", "spasm" and "contracture" [2]. In the early decades of the twentieth century, descriptions of spasticity gradually began to assume its current the form, namely, a distinctive type of hypertonia that is usually found in patients with cerebral hemiplegia and spinal cord injuries [3,4].

For our present purposes, spasticity will be defined as a velocity-dependent increase of tone in a passively stretched group of muscles [5]. More precisely, it is the proprioceptive impression that is framed in the mind of the examiner as he briskly moves the body segments of the patient at different rates; in a spastic muscle, this manoeuver elicits an initial resistance that quickly reaches a peak and suddenly melts away (the clasp-knife phenomenon). In severe cases, spasticity assumes the form of a sustained contraction that imposes a relatively fixed attitude to the affected body parts—typically, the Wernicke-Mann attitude—which is most evident on standing and walking. Spasticity primarily affects the muscles of the trunk, limb girdles and limbs in unequal proportions. It tends to be most evident in the adductors of the arm, and in the flexors of forearm, hand and fingers; in the lower limbs, spasticity affects the extensors and adductors of the leg and the dorsiflexors of the foot [6]. Over time, secondary mechanical changes in the viscoelastic properties of muscles, collagen and tendinous tissues eventually add to the primary neurogenic mechanisms to produce the phenomenon of spasticity as commonly met with in clinical practice [7]. Hemiplegic spasticity has little observable counterpart in the muscles of the eyes, face, jaw, tongue, throat, and voice; however, spasticity of these muscles is the rule in cases of bilateral hemiplegia or bilateral suprabulbar paralysis [8]. Although in clinical practice weakness and spasticity often share a similar body distribution, there is no obligatory correlation between their respective body topography and magnitude in individual cases. For example, spasticity not uncommonly overrides the residual power in one leg, thus representing a major impediment to walking; when it is attenuated by surgical or pharmacological means, the gait is much improved or even made possible. In other patients in whom paralysis would prevent independent mobility, the onset of spasticity provides the necessary antigravity support for standing and walking.

The mesoscopic underpinnings of spasticity

The mesoscopic level, or "macrolevel", of experience corresponds to the ordinary apprehension of reality that falls within the sensorimotor resolution of our unarmed senses [9]. In the nervous system, the mesoscopic level encompasses entire structural-functional systems and fiber pathways that are discernible with the naked eye [10]. An accurate mesoscopic

description is mandatory for the analysis of submesoscopic phenomena, such as the chemistry of neurotransmission. Over the past century, two mesoscopic-level explanations for human spastic hemiplegia have been advanced. According to the clinicoanatomical tradition [11], the cardinal signs of spastic hemiplegia are caused by an injury of the contralateral pyramidal tracts (PyrTs) at any level from the precentral gyrus to the medullary pyramids [12-14]; conversely, lesions that spare the PyrTs never cause spastic hemiplegia although they may result in different types of disorders of movement (e.g., hemiballismus). This double dissociation was established early by clinicoanatomical studies [15] and repeatedly confirmed ever since [16], thus closing a protracted cycle of inquiry covering over two millennia [17]. The other neural correlate of spastic hemiplegia is represented by the *theoretical* extension of animal experiments to humans [18]. These experiments have led to the assertion that the only true correlate of PyrT damage in humans is the sign of Babinski and a paretic impairment of the deftness of the hands, fingers and toes in the execution of skilled movements [19]. The experimental school has additionally proposed that paralysis of trunk and limbs, hyperreflexia and spasticity is a product of injury of the extrapyramidal pathways that is inevitably associated with PyrT damage, a view that still permeates our medical books [20]. Following the experimental tradition, then, most of what is classically considered to result from a PyrT injury is actually caused by an injury of certain fiber tracts that by definition belong to the extrapyramidal system [21]. Finding out the truth between these alternatives has both theoretical and practical implications. For example, considering the fact that different neurotransmitters are released by extrapyramidal and pyramidal axons, knowing their exact neurochemistry is a critical requisite for the development of rational drug therapies [22].

In the following section I will argue that, in contrast to what happens with non-human primates and other experimental animals, damage to structures that belong to the extrapyramidal system plays little, if any, role in the determination of *human* spastic hemiplegia. A corollary of this assumption is that *human spastic hemiplegia and the human pyramidal syndromeof the classical authors are the same clinicopathological entity*.

The human pyramidal syndrome (viz. spastic hemiplegia) is caused by injury of the pyramidal tracts

The human pyramidal syndrome encompasses four cardinal signs: paralysis, spasticity, hyperactive phasic muscle ("tendon") reflexes, and the sign of Babinski [23]. Paralysis is the only negative symptom, the remaining three standing for positive symptoms of segmental reorganization, release from supraspinal descending pathways, or both [24].

The lack of reciprocal correlations among the cardinal signs of spastic hemiplegia [25] points to different neural substrates enrolled in the PyrTs [26]. One testable possibility is that damage to fibers of different sizes gives rise to different symptoms. For example, diseases that course with progressive degeneration of the thin PyrT fibers eventually lead to spasticity and hyperreflexia, but not to paralysis [27]; when the thicker fibers also degenerate, paralysis sets in [28]. These findings are consistent with the average diameter of PyrT axons, which roughly cluster into three or four fiber spectra [29]. Over 85% of PyrT fibers are ''thin'' (diameters ≤ 4 μ), the diameter of the remaining (''thick'') fibers varying from 4-10 μ (10%) to 10-20 μ (< 1.5 %). The thin fibers probably originate from Brodmann's area (BA) 6 and BA 4 (medial and lateral), whereas the thick ones originate from BA 4 only [30,31]. PyrT fibers tend to sort in three or four tracts in the spinal cord: the crossed PyrT (which runs in the dorsolateral region of the lateral column after decussating at the medullary pyramids), the ventral PyrT (which descends in the ventromedial region of the anterior columns and is primarily uncrossed), and the ipsilateral PyrT, which is composed of a smaller contingent of PyrT fibers that also run in the dorsolateral region of the lateral column interspersed with the fibers of the lateral PyrT; in an unknown number of individuals a ventrolateral tract (also uncrossed) descends in the ventrolateral region of the lateral column [32]. Axons from BA 4 typically descend in the lateral (crossed) PyrT, while those from the premotor cortex (BA 6) descend in the ipsi and contralateral ventral columns and terminate in the motoneuron pools of both sides of the cord [33]. The thickest PyrT fibers are the axons of Betz cells, which sustain direct connections with the spinal α-motoneurons [34,35] as far down as the lumbosacral segments [36]. Cases of focal brain lesions lend further support to the idea that the heterogeneous fiber composition of the PyrTs underpins particular combinations of symptoms in individual patients. Thus, some patients develop a severe hemiplegia without spasticity [37], while in others a severe spastic hemiplegia settles down from apparently similar injuries of one medullary pyramid [38]; in still others the symptoms of PyrT damage are so meager as to go nearly unnoticed [39].

Postmortem observations indicate that two main factors account for the apparent contradictions in the clinical manifestation of PyrT injury. Firstly, is the considerable interindividual variation in the number and course of PyrT fibers between the subthalamus and the medullary pyramids. As a rule, several slender fascicles leave off the main tract along its ventral brainstem course and turn backwards into the tegmentum; they then head for (i) the motor nuclei of cranial nerves III-VII and IX-XII, (ii) the motoneurons of the medullary reticular formation responsible for the automatic innervation of the diaphragm ("respiratory center") [40,41], and (iii) the motoneurons of the midcervical (C3-C5) cord (the "phrenic nucleus"), which mediate the voluntary control of respiration through the phrenic nerves [42]. These are the "aberrant" fascicles originally described in postmortem material [43,44], and which are now partially accessible to current *in vivo* imaging techniques [45]. A corollary of this organization is that a lesion restricted to the medullary pyramids or, for that matter, to any level of the ventral brainstem, may spare aberrant PyrT fibers and explain the absence of symptoms of PyrT damage [46].

The second apparent contradiction is the sparing or recovery of fine motor skills in the hand and fingers after unilateral injuries of the PyrT [47]. Postmortem studies reveal that such injuries seldom destroy all fibers of the PyrT; they have also shown that less than 15% of residual PyrT fibers suffice to promote recovery from PyrT damage [48,49] *provided the contralateral PyrT is intact* [50]. Therefore, the puzzling recovery of motor function in

some patients with seemingly discrete damage to the PyrTs still depends on the functional reorganization of the remaining ipsi and contralateral pyramidal fibers [51]. Two additional lines of evidence support the view that spasticity and the other cardinal signs of human spastic hemiplegia are genuine symptoms of PyrT damage. The first is a unique clinicoanatomical report of a patient who presented a virtually complete destruction of the lower brainstem tegmentum with sparing of the PyrTs; he showed no evidence of paralysis or other signs of PyrT damage over the course of his illness [52]. The second source of evidence is anatomical and refers to an overall reduction of the extrapyramidal pathways in humans, which is reciprocated by an increase of the pyramidal and propriospinal systems [53]. Therefore, the human pyramidal-propriospinal system takes over most of the functions that belong to the realm of the extrapyramidal system in nonhuman mammals (Figure 1).

CONCLUSIONS AND OPPORTUNITIES FOR RESEARCH

The evidence briefly reviewed above and in more detail in previous publications indicate that spasticity is a legitimate symptom of PyrT damage in man. This assertion is only true for humans and may apply in part if at all to non-human primates and the other vertebrates [54]. It also provides compelling arguments for the hypothesis that the heterogeneity of PyrT axons and their cells of origin has both functional and pathophysiological significance. More specifically, the differential destruction and sparing of particular clusters of PyrT fibers or motor cortical neurons may explain each cardinal symptom of PyrT injury that were originally assembled in a unitary syndrome by the classical authors. However, much research is still needed to ascertain the exact areal and cellular origin of the human PyrTs as well as their clinicoanatomical correlates. Ideally, this will lead to the determination of the neurotransmitters involved in paralysis and spasticity. Transcranial magnetic stimulation is an important tool that should be more actively integrated with current experimental and clinical protocols that assess the PyrTs *in vivo*, since it can detect even subclinical impairments of the corticomotoneuronal pathway [57] as well as critical recovery mechanisms [58]. It is now clear that results from animal experiments cannot squarely

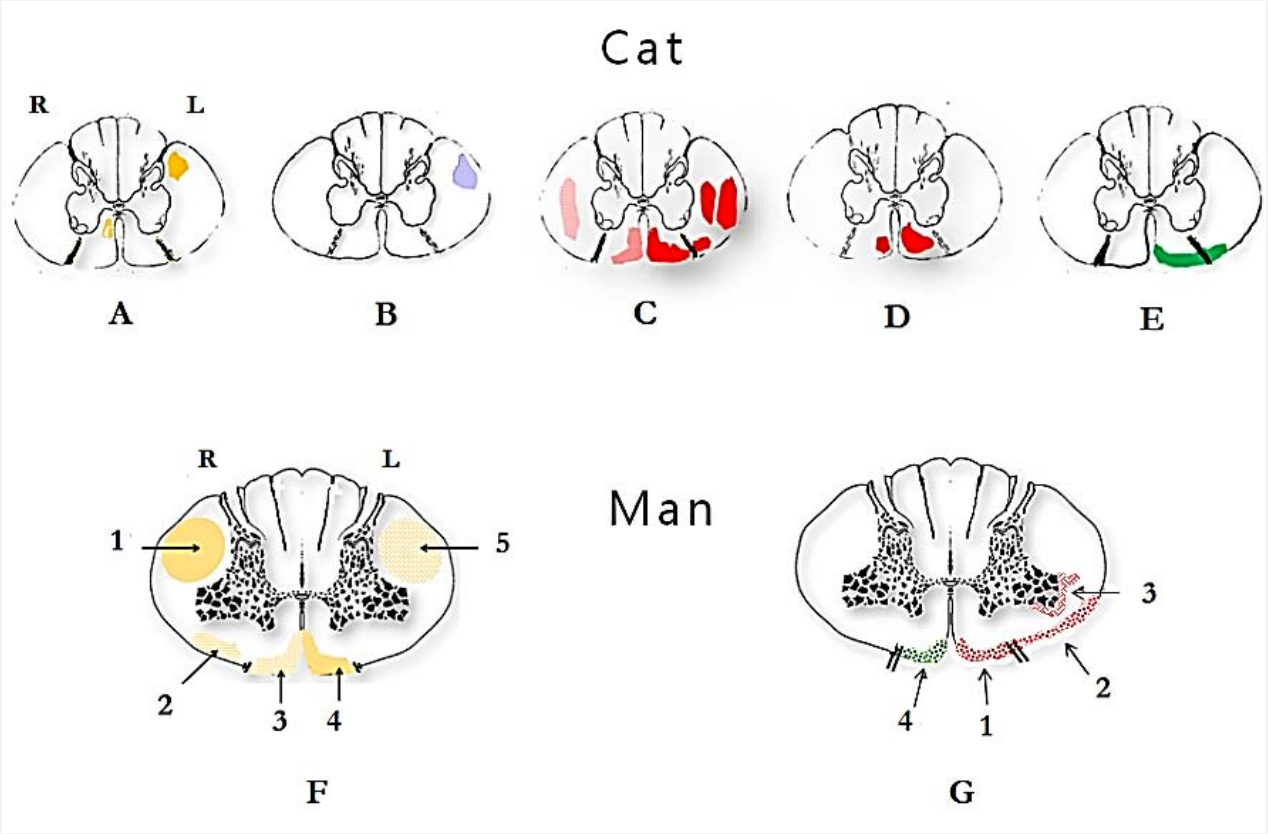

Figure 1 Schematic comparison of pyramidal and extrapyramidal pathways in the midcervical cord of a representative quadrupedal mammal (upper row) and man. A. Lateral (crossed) pyramidal tract in the dorsolateral column and ventral (uncrossed) pyramidal tract in anterior column (yellow). B. Left rubrospinal tract (blue) originating in right red nucleus. C. Reticulospinal tracts (red) originating in the left nucleus reticularis gigantocellularis (bilateral, mostly uncrossed). D. Reticulospinal tracts originating in the left nucleus reticularis pontis caudalis (mostly uncrossed). E. Vestibulospinal tracts (green) originating in the left lateral vestibular (Deiter's) nucleus (mostly uncrossed). Note the obvious predominance of the ipsilaterality of the extrapyramidal projections. F. Pyramidal tracts originating in human left hemisphere: 1. Lateral (crossed) pyramidal tract in dorsolateral region of lateral column; 2. Barnes ventrolateral pyramidal tract (uncrossed); 3. Anterior (uncrossed) pyramidal tract; 4. Anterior (crossed) pyramidal tract; and 5. Homolateral pyramidal tract. G. 1-3. Areas of the anterior and lateral columns traversed by reticulospinal, and 4. vestibulospinal fibers. The human reticulospinal and vestibulospinal fibers are mainly ipsilateral; they are so scant in comparison to those of the other mammals that they seldom assemble into "tracts"; therefore, these areas indicate only where their axons are most probably found. Extrapyramidal tracts in the cat adapted from reference 55; pyramidal tracts and extrapyramidal regions of human spinal cord adapted from reference 56.

be translated into the human condition without indulging in serious conceptual inconsistencies. The astonishing advances in the *in vivo* analysis of the human nervous system that took place in the past two decades should not obscure the plain fact that our knowledge of the anatomical and functional organization of the human PyrTs is still full of gaps and deceitfully complete [16].

ACKNOWLEDGEMENTS

The author is indebted to Professor Omar da Rosa Santos (Federal University of the State of Rio de Janeiro) for institutional support, and to librarians José Ricardo Pinheiro and Jorge Baçal *(in memoriam*), of the Oswaldo Cruz Institute, Rio de Janeiro, for their invaluable help in the retrieval of rare articles and books.

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Cite this article

de Oliveira-Souza R (2017) Spasticity and the Human Pyramidal Tracts. J Muscle Health 1(2): 1008.