Neuropsychologia ∎ (∎∎∎∎) ∎∎∎–∎∎∎

Contents lists available at ScienceDirect

Neuropsychologia

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

Sensory-motor integration in focal dystonia

Laura Avanzino [a], Michele Tinazzi [b], Silvio Ionta [c], Mirta Fiorio [b,*]

[a] Department of Experimental Medicine, Section of Human Physiology and Centro Polifunzionale di Scienze Motorie, University of Genoa, 16132 genoa, Italy
[b] Department of Neurological and Movement Sciences, University of Verona, 37131 Verona, Italy
[c] Laboratory for Investigative Neurophysiology, Department of Radiology and Department of Clinical Neurosciences, University Hospital Center and University of Lausanne, Lausanne, Switzerland

ARTICLE INFO

Article history:
Received 10 February 2015
Received in revised form
4 June 2015
Accepted 7 July 2015

Keywords:
Focal dystonia
Sensory-motor integration
Proprioception
Transcranial magnetic stimulation

ABSTRACT

Traditional definitions of focal dystonia point to its motor component, mainly affecting planning and execution of voluntary movements. However, focal dystonia is tightly linked also to sensory dysfunction. Accurate motor control requires an optimal processing of afferent inputs from different sensory systems, in particular visual and somatosensory (e.g., touch and proprioception). Several experimental studies indicate that sensory-motor integration – the process through which sensory information is used to plan, execute, and monitor movements – is impaired in focal dystonia. The neural degenerations associated with these alterations affect not only the basal ganglia–thalamic–frontal cortex loop, but also the parietal cortex and cerebellum. The present review outlines the experimental studies describing impaired sensory-motor integration in focal dystonia, establishes their relationship with changes in specific neural mechanisms, and provides new insight towards the implementation of novel intervention protocols. Based on the reviewed state-of-the-art evidence, the theoretical framework summarized in the present article will not only result in a better understanding of the pathophysiology of dystonia, but it will also lead to the development of new rehabilitation strategies.

1. Introduction

Dystonia is a syndrome characterized by prolonged muscle contractions causing involuntary repetitive twisting movements and abnormal postures. In focal dystonia, the dystonic pattern can involve single body parts in isolation and may occur at rest or during the performance of intended movements (Fahn et al., 1998). Cervical and hand dystonia are the most common forms of late-onset primary focal dystonia (Jankovic, 2009), but little is known about their etiopathogenesis and treatment. Historically, dystonia has been considered a disorder of the basal ganglia, mainly affecting planning and execution of voluntary movements. This notion comes from the observation that most lesions responsible for secondary dystonia involve the basal ganglia (Bhatia and Marsden, 1994). However, recent research highlights that dystonia is linked to the dysfunction of a complex neural network comprising basal ganglia–thalamic–frontal regions, as well as the somatosensory cortex and cerebellum. Indeed, patients with dystonia display not only motor symptoms, but also a number of disturbances in the sensory domain (reviewed in: Avanzino and Fiorio (2014), Konczak and Abbruzzese (2013), Perruchoud et al. (2014) and Tinazzi et al. (2009)) and in cognitive processing of movements, such as movement simulation and prediction (Avanzino et al., 2013; Fiorio et al., 2006; Perruchoud et al., 2014).

In this review, starting from the neurophysiological and the neuroanatomical aspects of sensory-motor integration processes, we will provide robust evidence consistent with the hypothesis that dystonia is a sensory and/or a sensory-motor rather than a motor disorder. To this aim first we will start by summarizing the available behavioral data on abnormalities in sensory functions, cognitive representation of movements, and sensory-motor integration in focal dystonia. Then, we will review the large amount of experimental evidence on the neural correlates of these aberrant functions. Furthermore, we will discuss novel therapeutic approaches aiming at promoting the reorganization of sensory-motor regions inspired by the reported findings. Finally, on the basis of the available data, we will strongly support the "network"

Abbreviations: CNS, central nervous system; fMRI, functional magnetic resonance imaging; LAI, long-latency afferent inhibition; M1, primary motor cortex; MEP, motor evoked potential; PET, positron emission tomography; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; PPC, posterior partietal cortex; ppTMS, paired pulse transcranial magnetic stimulation; rCBF, regional cerebral blood flow; rTMS, repetitive transcranial magnetic stimulation; SAI, short-latency afferent inhibition; SI, primary somatosensory cortex; SII, secondary somatosensory cortex; SDT, spatial discrimination threshold; SMA, supplementary motor area; TDT, temporal discrimination threshold; TMS, transcranial magnetic stimulation; TVR, tonic vibration reflex; VBM, voxel-based morphometry

* Correspondence to: Department of Neurological and Movement Sciences, University of Verona, via Casorati 43, 37131 Verona, Italy. Fax: +39 0 458425131.
E-mail address: mirta.fiorio@univr.it (M. Fiorio).

http://dx.doi.org/10.1016/j.neuropsychologia.2015.07.008
0028-3932/© 2015 Elsevier Ltd. All rights reserved.

hypothesis at the basis of the pathophysiology of dystonia. In addition, some limitations to this hypothesis will be discussed, like the inability, so far, to establish which specific neural structure is primarily altered and which instead is altered for compensatory and not pathophysiological reasons.

2. Sensory-motor integration: neurophysiological and neuroanatomical aspects

Optimal movement execution requires accurate processing of sensory information from the environment and from the body. Different sensory systems contribute to motor control by encoding both such external and internal sources of information. For example, one of the most obvious interaction between senses and movements is visuo-motor integration, in which visual information about objects in the external world is converted from extrinsic/allocentric coordinates into intrinsic/egocentric coordinates (Pouget and Sejnowski, 1997). This transformation underlies the planning of goal-directed actions (Rizzolatti et al., 1997; Wolpert et al., 1995, 1998). Also the somatosensory systems, and in particular touch and proprioception, help movement execution. The interaction between the tactile and motor systems is revealed by the fact that the lack of afferent information (because of deafferentation or local anesthesia) strongly and selectively impairs motor control (Taub, 1976). Hence, even if the motor pathway is preserved, the absence of tactile information from the skin receptors undermines movement execution. In a similar vein, proprioception – the perception of the position and movements of our limbs and trunk – is strictly linked to motor control. Specialized receptors on the joints and muscle spindles signal the size and speed of muscle length changes (Goodwin et al., 1972; Matthews, 1972) and contribute to movement perception and processing (review in Proske and Gandevia, 2012). Yet, in 1996 Prochazka elegantly characterized the dependence of motor control mechanisms on sensory signals stating "*you can only control what you sense*" (Prochazka, 1996). This concept well explains the process of sensory-motor integration. It is worth noting that prior to sensory-motor integration, the brain operates a multisensory integration process, in which inputs from different sensory modalities are combined together. Internal sources of information emanate from the body (e.g. somatosensory and vestibular input), whereas external sources are perceived by special senses (e.g. visual and auditory systems). Two multisensory integration processes proceed in parallel: the first dealing with body representation; the second with the representation of the external world. Both processes exploit the complementarities provided by multiple sensory modalities in order to produce (i) body awareness and self-consciousness and (ii) a coherent multimodal representation of the external world.

Finally, for action execution, the two processes need to be integrated (sensory-motor integration), i.e. sensory data are mapped onto volitional motor commands. In general, the term sensory-motor integration describes all the processes where sensory information is used to plan and execute volitional movement, as well as the sensory counterpart of each executed movement. It is worth noting that sensory-motor integration is requested even when movement processing is done in absence of sensory feedback (cognitive representation of movement). Indeed, movement processing, prediction, and planning involve the activation of higher order sensory areas and motor areas (Tin and Poon, 2005).

A complex cerebral network seems to be involved in sensory-motor integration, including the sensorimotor cerebral cortex, the basal ganglia and the cerebellum (Fig. 1). Cortical frontal and parietal areas are strongly interconnected and function together for many aspects of action planning. Starting from sensory parietal

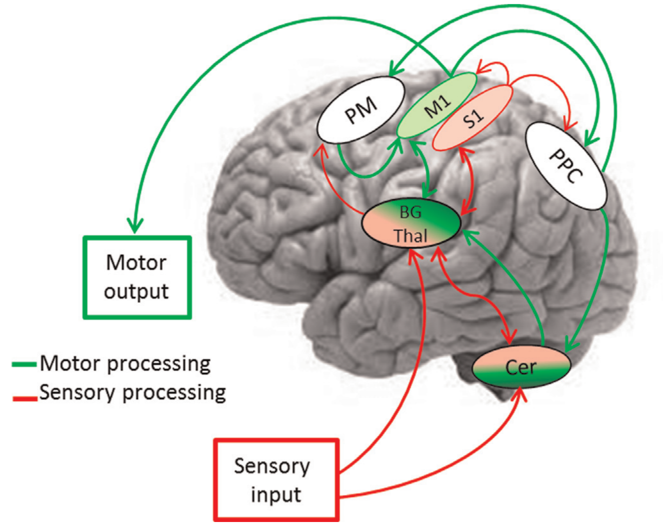

Fig. 1. Schematic representation of the complex brain network involved in sensory-motor integration. Sensory input (red) is elaborated by subcortical (firstly Thal, Cer and then BG) and cortical (SI) regions and integrated with the motor plan (green) through associative areas (PPC and PM). Deficits of sensory-motor integration in dystonia could arise from dysfunctions at different levels of this network. BG = basal ganglia; Thal = thalamus; Cer = cerebellum; SI = primary somatosensory cortex; PM = premotor cortex; PPC = posterior parietal cortex; M1 = primary motor cortex.

areas, the primary somatosensory cortex (SI) consists of the postcentral gyrus of the parietal lobe, which corresponds to Brodmann areas 3a, 3b, 1, 2. Axons from the thalamic neurons receiving somatic sensations terminate in somatotopically corresponding regions of the primary somatosensory cortex. The primary somatosensory cortex projects to the secondary somatosensory cortex (SII), located on the superior border of the lateral fissure.

The posterior parietal cortex (PPC) is involved in spatial attention, spatial awareness, and multisensory integration (Colby and Goldberg, 1999). Furthermore, recent studies suggest that PPC plays also an important role in different action-related functions, including movement intention (together with frontal areas) (Andersen and Buneo, 2002). Thus, PPC is a crucial node for sensory-motor integration, in that it integrates extrinsic (from the "external" world) and intrinsic (from the body) sensory inputs in order to create a cognitive representation of movement for motor planning and understanding.

Regarding frontal structures, the premotor area is of particular importance for the sensory guidance of movement. In humans, strong evidence has been provided for a dissociation between the role of the ventral premotor (PMv) and the dorsal premotor cortex (PMd) (Davare et al., 2006). PMv seems crucial when hand movements are selected to grasp objects according to their visuospatial properties, playing a key role in visuomotor transformations required to generate grasping. PMd instead provides signals related to the final goal of the movement rather than the intermediate steps (Hoshi and Tanji, 2007). For the final motor output, integrated signals from the premotor areas are sent to the primary motor cortex (M1), which consists of the precentral gyrus of the frontal lobe and corresponds to Brodmann area 4.

Not only the cerebral cortex, but also subcortical structures are involved in sensory-motor integration. The cerebellum plays a major role in modulating sensorimotor, premotor and posterior parietal areas for better fine-tuning motor control. In addition, it has been proposed that the cerebellum acts as a processor of sensory information, combining ascending input from the spinocerebellar pathway and descending visual input from the parietal