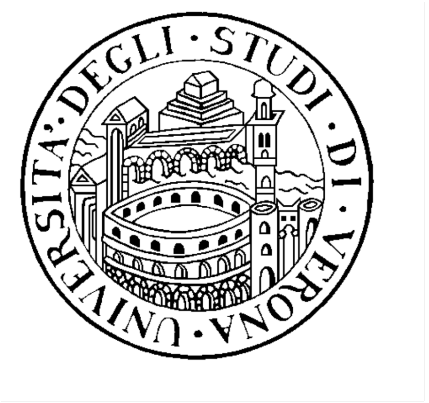
Sensory symptoms in dystonia

Michele Tinazzi



Department of Neurosciences, Biomedical and Movement Sciences, **University of Verona**

Received: 12 December 2012; **Revised:** 30 April 2013;
Accepted: 2 May 2013

REVIEW

Emerging Concepts in the Physiological Basis of Dystonia

Angelo Quartarone, MD,[1,2,3,4*] and Mark Hallett, MD[5]

- Work over the past 2 decades has led to substantial changes in our understanding of pathophysiology in dystonia.

- Neurophysiologic studies in humans have shown 3 abnormalities which may relate each other.

Introduction

➢Loss of inhibition: responsible for the **excess of movement** and for the **overflow** phenomena in dystonia.

➢Sensory dysfunction: related to **mild sensory findings** in focal dystonias responsible of the motor dysfunction.

➢Maladaptative plasticity: during **motor learning** it may lead to abnormal sensorimotor integration.

Sensory Dysfunction

The most dramatic symptoms in dystonia are motor, but somatosensory perceptual deficits are also present in this disease and might contribute to the generation of dystonic movements.

BG are involved not only in motor control but also in non-motor cognitive functions, such as sensory functions.

In these last decades, several **psychophysical, neurophysiological and neuroimaging studies** have shown that somatosensory functions are compromised in several forms of primary dystonia.

Movement Disorders
Vol. 18, No. 6, 2003, pp. 605–622

Research Review

Role of the Somatosensory System in Primary Dystonia

Michele Tinazzi, MD,* Tiziana Rosso, MD, and Antonio Fiaschi, MD

Review

Movement Disorders
Vol. 24, No. 10, 2009, pp. 1427–1436

Sensory Functions in Dystonia: Insights from Behavioral Studies

Michele Tinazzi, MD, PhD,[1,2] Mirta Fiorio, PhD,[1]* Antonio Fiaschi, MD,[1]
John C. Rothwell, PhD,[3] and Kailash P. Bhatia, MD[3]*

224 | APRIL 2019 | VOLUME 15 www.nature.com/nrneurol

The role of sensory information in the pathophysiology of focal dystonias

*Antonella Conte[1,2], Giovanni Defazio[3,4], Mark Hallett[5], Giovanni Fabbrini[1,2] and Alfredo Berardelli[1,2]**

Psychophysical Procedures

Spatial discrimination of tactile stimuli

Temporal discrimination and integration of sensory signals

Kinesthesia (vibration-induced illusion of movements)

Tactile diplopia or diplesthesia (Aristotle's illusion)

Neurophysiological Procedures

Somatosensory evoked potentials

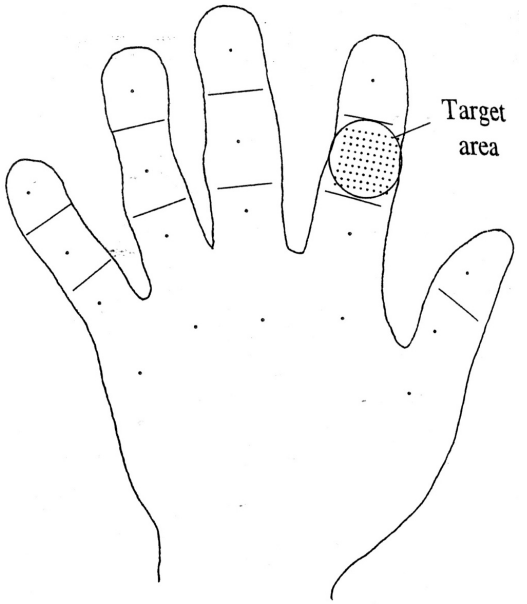
Somatosensory evoked fields

Neuroimaging Procedures

fMRI, MEG

Sensory Dysfunction - SD

Spatial Discrimination (SD) can be obtained by measuring the **shortest distance between two tactile stimuli which are perceived as separate when applied to the fingertip** or by measuring the sensitivity to the orientation of parallel-embossed gratings of various widths.



Bara–Jimenez et al. Neurology 2000

Table 1 | **Investigations on spatial discrimination threshold in patients with dystonia**

Study	Patients tested	Unaffected relatives tested	Effects on spatial discrimination threshold
Bara-Jimenez et al. (2000)[30]	17 with FHD	–	Increased
Sanger et al. (2001)[31]	9 with FHD	–	Increased
Molloy et al. (2003)[25]	9 with blepharospasm, 10 with cervical dystonia, 15 with FHD and 13 with DYT1 primary dystonia	–	Increased in blepharospasm, cervical dystonia and FHD but normal in DYT1 dystonia
Zeuner & Hallett (2003)[32]	10 with FHD	–	Increased
Walsh & Hutchinson (2007)[29]	20 with cervical dystonia	–	Increased
Walsh et al. (2007)[26]	20 with cervical dystonia	105	Increased in 5 of 20 patients with cervical dystonia and 24 of 105 unaffected relatives
Walsh et al. (2009)[27]	–	52 relatives of patients with cervical dystonia (28 familial and 24 sporadic)	Increased in 12 of 28 relatives of patients with familial cervical dystonia and 13 of 24 relatives of patients with sporadic cervical dystonia
Ganos et al. (2017)[28]	17 with cervical dystonia	–	Increased

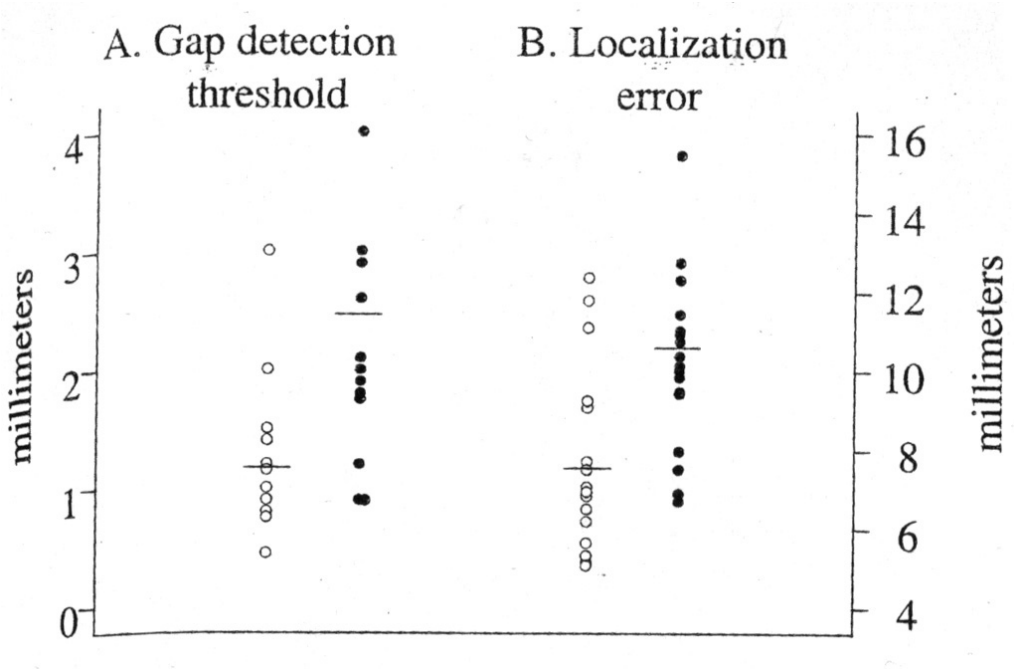
In all studies, the spatial discrimination threshold was tested in the hand. FHD, focal hand dystonia.

Conte et al. Nature Rev Neurol 2019

SD deficits in adult-onset dystonia

Abnormalities of SD have been found in focal dystonias, including blepharospasm, cervical and focal hand dystonia, also in body parts far from motor symptoms *(Bara–Jimenez et al. 2000; Sanger et al. 2001; Molloy et al. 2003)*.

It might be the clinical correlate of abnormal digit representations in SI documented in both humans and animals.



Bara–Jimenez et al. Neurology 2000

Sensory Dysfunction - TDT

TDT is the ability to process sequences of tactile stimuli over time and **is defined as the shortest time interval at which two stimuli are perceived as being temporally separate.**

Tinazzi et al. Mov Disord 2002

Table 2 | **Investigations on STDT in patients with dystonia**

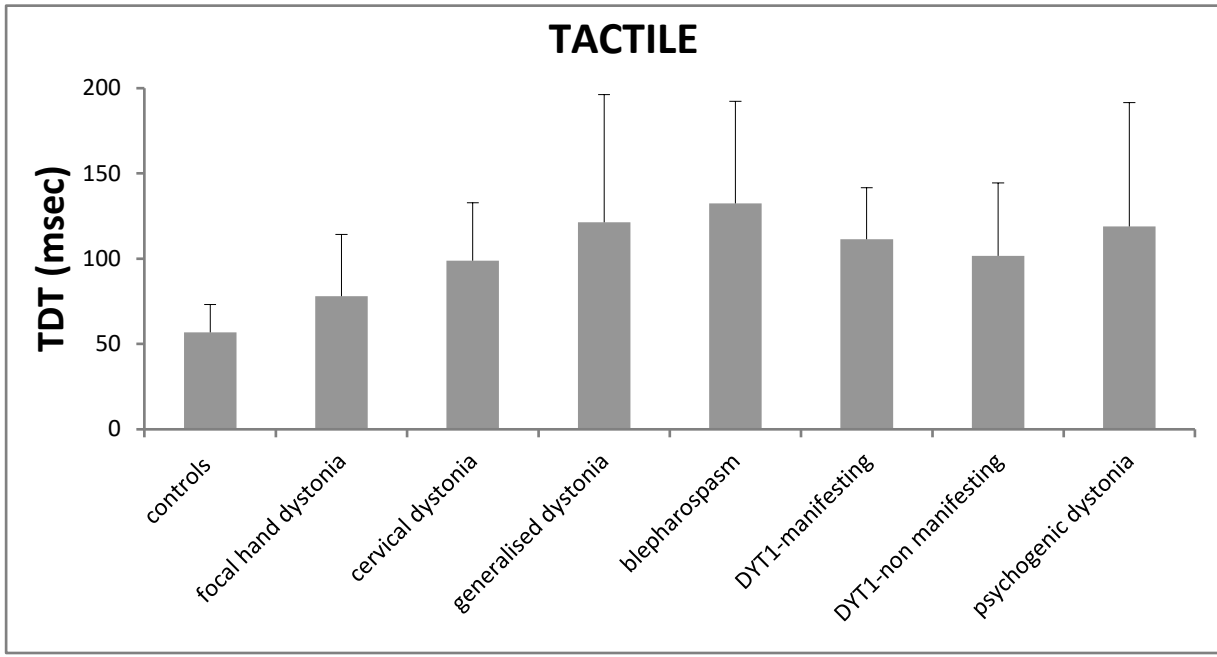
Study	Patients tested	Unaffected relatives tested	Body part tested	Effects on STDT
Fiorio et al. (2003)[42]	14 with FHD	–	Hand	Increased
Tinazzi et al. (2004)[43]	10 with cervical dystonia	–	Hand	Increased
Fiorio et al. (2007)[54]	9 with DYT1 primary dystonia	11 DYT1 carrier and 9 non-carrier relatives	Hand	Increased
Fiorio et al. (2008)[41]	19 with blepharospasm	–	Face and hand	Increased
Scontrini et al. (2009)[48]	35 with blepharospasm, 30 with cervical dystonia and 8 with FHD	–	Face, neck and hand	Increased
Bradley et al. (2009)[55]	20 with cervical dystonia and 13 with FHD	42 first-degree and 32 second-degree relatives	Hand	Increased
Scontrini et al. (2011)[57]	24 with cervical dystonia	–	Face, neck and hand	Increased
Bradley et al. (2012)[39]	9 with blepharospasm, 37 with cervical dystonia and 14 with FHD	–	Hand	Increased
Kimmich et al. (2011)[40]	30 with cervical dystonia	73 first-degree relatives	Hand	Increased in 27 of 30 patients with cervical dystonia and 32 of 73 first-degree relatives
Conte et al. (2013)[49]	24 with blepharospasm and 16 with increased blinking	–	Hand	Increased
Kagi et al. (2013)[85]	32 with cervical dystonia	–	Hand	Increased
Sadnicka et al. (2013)[51]	35 with cervical dystonia, 11 of whom had undergone DBS	–	Hand	Increased
Tinazzi et al. (2013)[66]	19 with cervical dystonia with tremor	–	Hand	Increased
Conte et al. (2014)[58]	12 with FHD	–	Hand	Increased
Kimmich et al. (2014)[56]	–	158 first-degree relatives of patients with cervical dystonia	Hand	Increased in 37 of 158 first-degree relatives
Antelmi et al. (2017)[53]	19 with cervical dystonia	–	Hand	Increased
Conte et al. (2017)[50]	11 with blepharospasm	–	Hand	Increased
Conte et al. (2017)[74]	15 with blepharospasm and 10 with cervical dystonia	–	Hand	Increased
Kägi et al. (2017)[52]	45 with cervical dystonia	14 first-degree relatives	Hand	Increased
Sadnicka et al. (2017)[35]	22 with cervical dystonia	–	Hand	Normal
Ganos et al. (2017)[28]	17 with cervical dystonia	–	Hand	Normal

DBS, deep brain stimulation; FHD, focal hand dystonia; STDT, somatosensory temporal discrimination threshold.

Conte et al. Nature Rev Neurol 2019

TDT deficits in adult-onset dystonia

Abnormalities of **tactile** in body parts affected and unaffected by dystonic spasms have been found in patients with generalized and focal dystonias, including blepharospasm cervical, focal hand dystonia and recently in psychogenic dystonia *(Tinazzi et al.1999, 2004; Bara–Jimenez et al. 2000; Sanger et al. 2001; Aglioti et al. 2003; Fiorio et al.2003; Tamura et al 2008; Scontrini et al. 2009; Morgante et al. in 2011)*.



A correlation between tactile deficits and severity of motor symptoms has been found only in patients with focal hand dystonia suggesting that **local somesthetic factors may be involved in this form.**

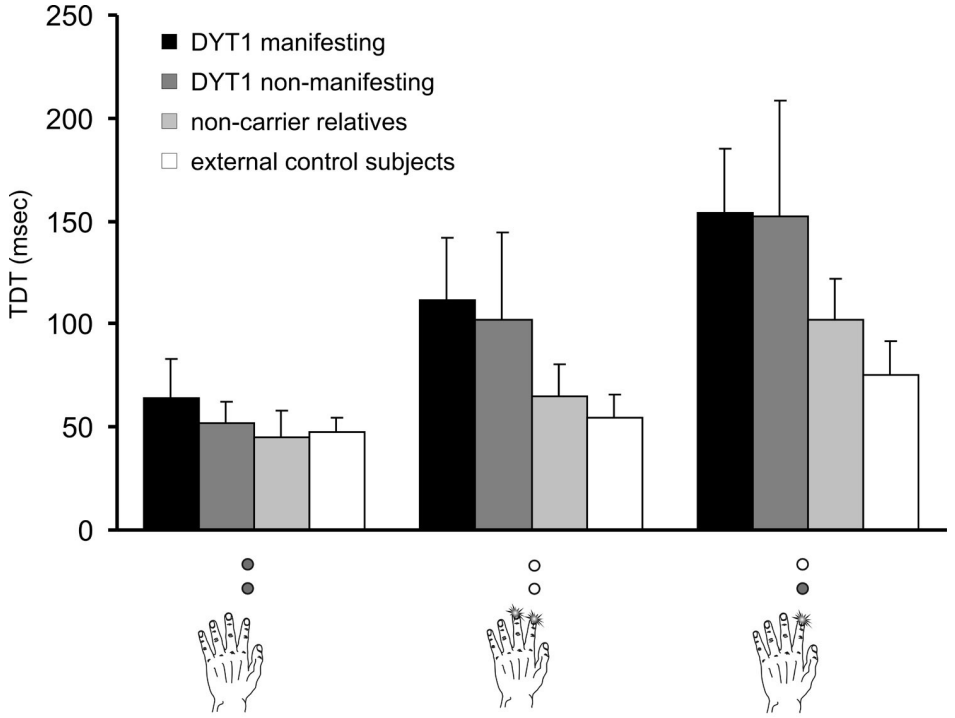
Tinazzi et al. Mov Disord et al. 2009

doi:10.1093/brain/awl283 *Brain* (2007), **130**, 134–142

Defective temporal processing of sensory stimuli in *DYT1* mutation carriers: a new endophenotype of dystonia?

Mirta Fiorio,[1] Mattia Gambarin,[1] Enza Maria Valente,[3] Paolo Liberini,[5] Mario Loi,[6] Giovanni Cossu,[6] Giuseppe Moretto,[2] Kailash P. Bhatia,[8] Giovanni Defazio,[7] Salvatore M. Aglioti,[4] Antonio Fiaschi[1] and Michele Tinazzi[1,2]

Both groups of DYT1 carriers (manifesting and non-manifesting) were significantly **more impaired** than non-carrier relatives and normal subjects in tactile and visuo-tactile TDT tasks.

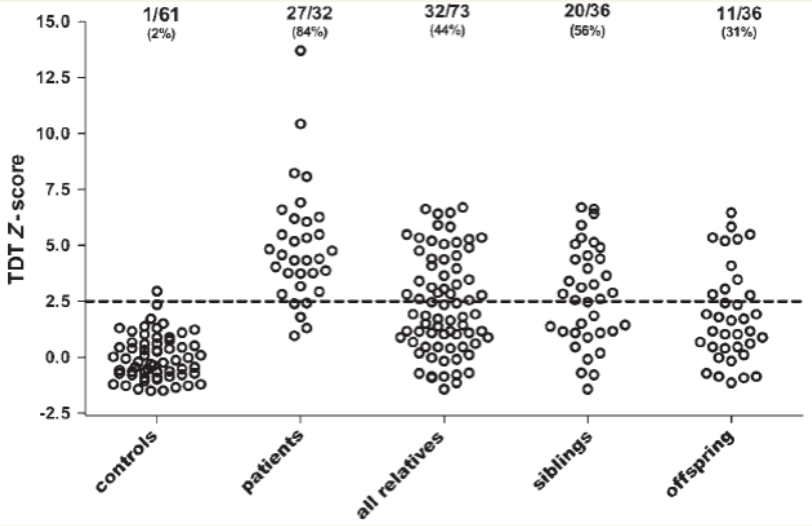


Brain Advance Access published August 11, 2011
doi:10.1093/brain/awr194 Brain 2011: Page 1 of 8 | 1

Sporadic adult onset primary torsion dystonia is a genetic disorder by the temporal discrimination test

Okka Kimmich,[1,*] David Bradley,[1,2,*] Robert Whelan,[2] Nicola Mulrooney,[1] Richard B. Reilly,[2] Siobhan Hutchinson,[1] Sean O'Riordan[1] and Michael Hutchinson[1]

When two or more relatives were tested in any one family, 22 of 24 families had at least one first-degree relative with an abnormal TDT. The frequency of abnormal TDT **in first-degree relatives of patients with sporadic AOPTD** is compatible with an autosomal dominant disorder.



Sensory Dysfunction - Proprioception

Obtained through vibration of the muscle tendon (the tonic vibration reflex). In this task, **subjects are asked to reproduce the direction and amplitude of the movement they perceive in the vibrated arm** by actively **moving the tracking arm**.

Tonic vibration task

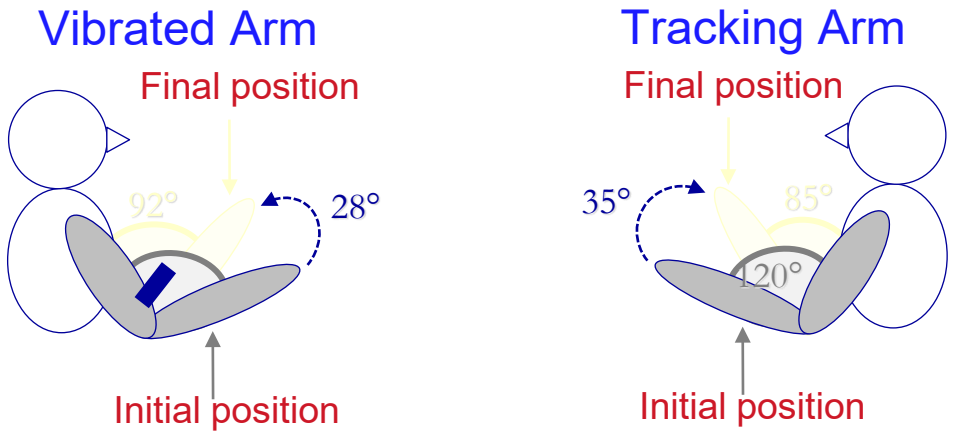


Table 3 | Studies on proprioceptive processing in patients with dystonia

Study	Patients tested	Effects on TVR
Kaji et al. (1995)[99]	15 with FHD	Abnormally increased TVR
Grunewald et al. (1997)[60]	2 with blepharospasm, 20 with cervical dystonia and 9 with FHD	Abnormal perception of TVR
Yoneda et al. (2000)[61]	2 with blepharospasm, 18 with cervical dystonia and 9 with FHD	Abnormal perception of TVR
Trompetto et al. (2006)[103]	10 with FHD	Abnormally increased TVR

In all studies, the tonic vibration reflex (TVR) was tested in the upper limb. FHD, focal hand dystonia.

Conte et al. Nature Rev Neurol 2019

Sensory Dysfunction - Proprioception

Abnormalities of limb perception have been found in patients with different forms of focal dystonia *(Grunewald et al. 1997; Yoneda et al. 2000)* and in asymptomatic first degree relatives of patients *(Frima et al. 2008).*

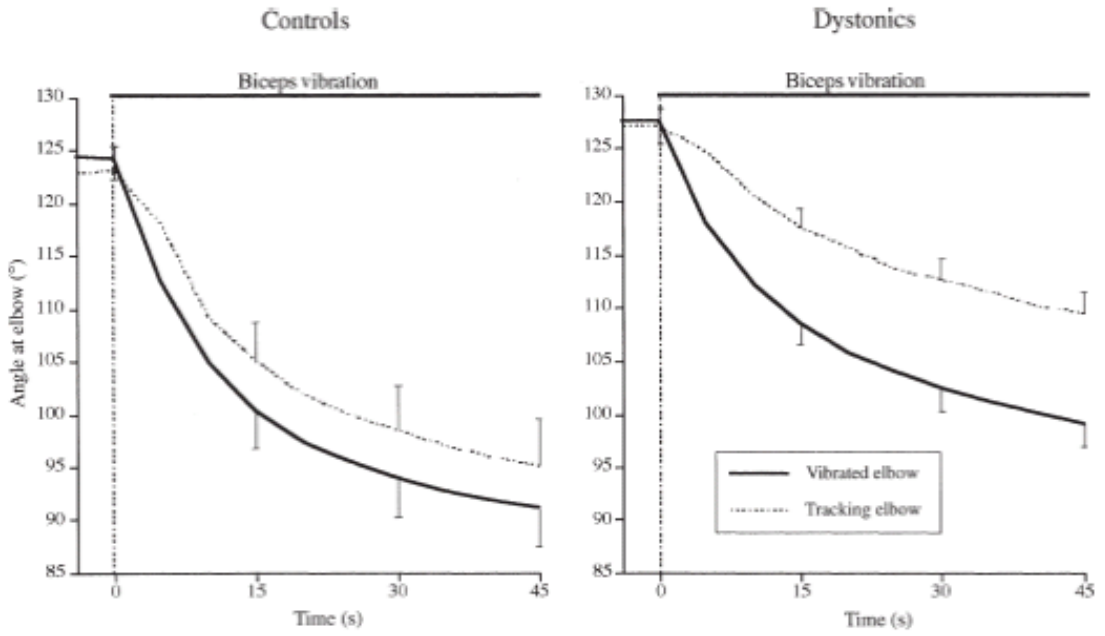


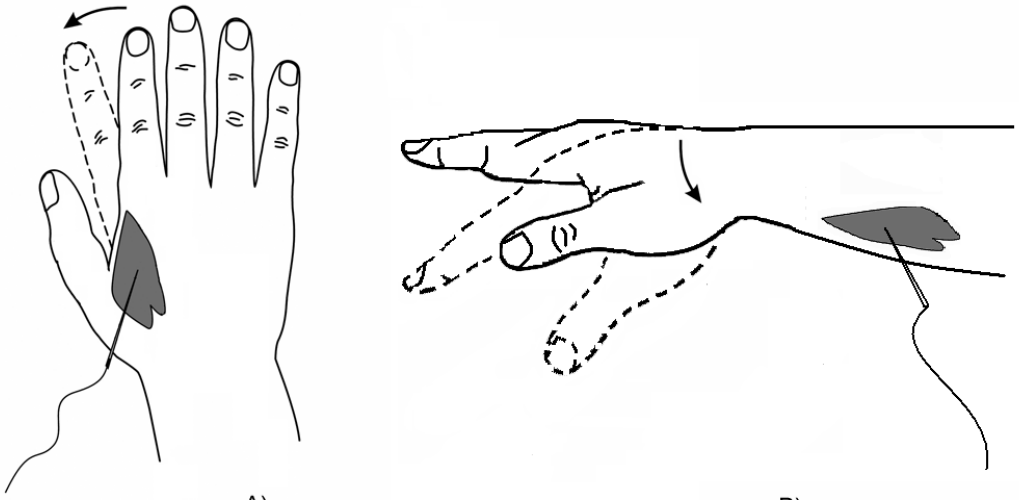
FIG. 2. Mean angular displacement of the elbow of the vibrated arm tracking in the groups of healthy control subjects (n = 16) and dystonic subjects (n = 13) on stimulation of biceps brachii tendon. The tonic vibration reflex is similar in both groups, but the tracking movements are smaller in the dystonic patients.[39]

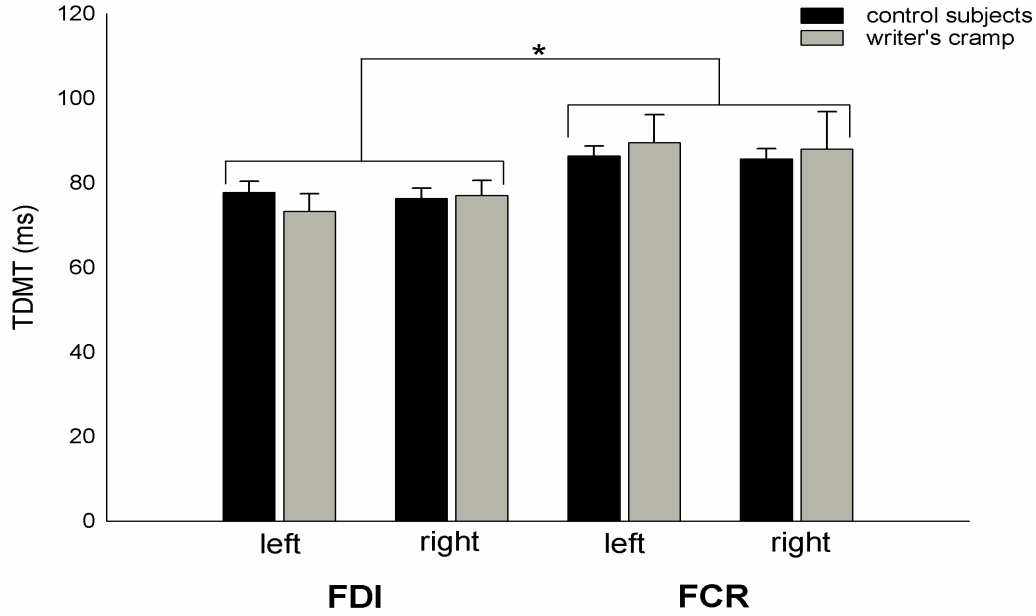
Grunewald et al. Brain 1997

Sensory Dysfunction - Proprioception

Temporal discrimination movement threshold

This can be obtained by delivering pairs of electrical stimuli to the motor point of hand or forelimb muscles. These stimuli produce muscle contraction and passive joint movement, and subjects have to indicate the shortest interval between two electrical stimuli at which they perceive two separate movements





(Tinazzi et al. 2006)

No deficits of timing processing of proprioceptive inputs in focal hand dystonia patients

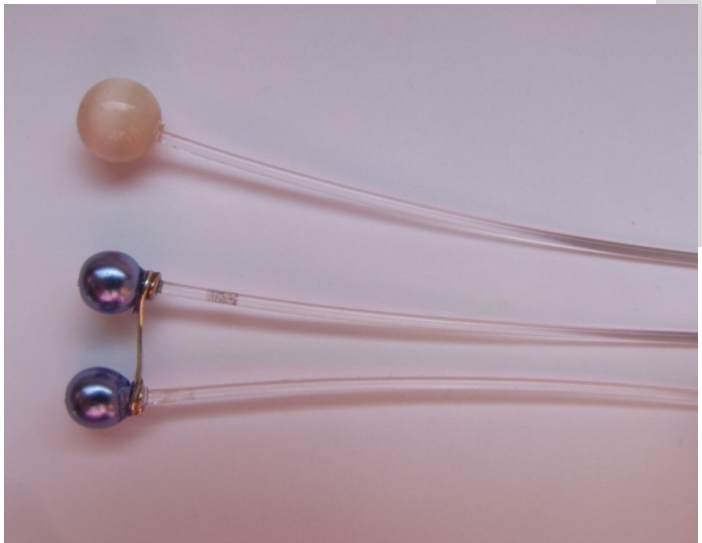
doi:10.1093/brain/aws372 Brain 2013: 136; 782–789 | 782

BRAIN
A JOURNAL OF NEUROLOGY

Aristotle's illusion reveals interdigit functional somatosensory alterations in focal hand dystonia

Michele Tinazzi,[1] Angela Marotta,[1] Alfonso Fasano,[2] Francesco Bove,[2] Anna Rita Bentivoglio,[2] Giovanna Squintani,[3,4] Lara Pozzer[1] and Mirta Fiorio[1]

When the subject crosses two adjacent fingers, and then the two crossed fingertips are touched by a small ball, the subject will experience a sensation of touching two balls *(Ponzo 1910, Benedetti 1985)*.So, there are cutaneous areas where the fusion of two cutaneous "images" into a single object occurs (functionally correlated), and areas where the fusion does not (nonfunctionally correlated).



Resting

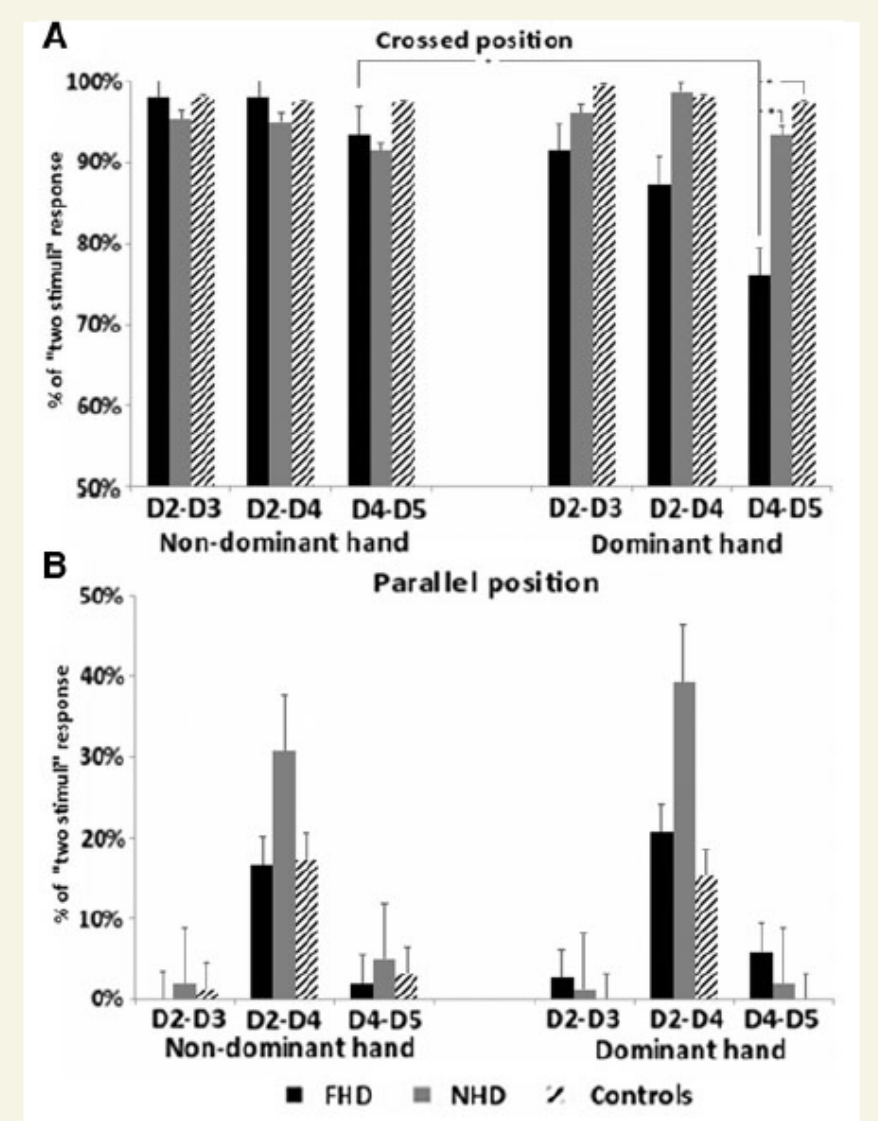
Crossed

Diplesthesia in focal hand dystonia

15 Control subjects

15 FHD Patients

Patients with focal hand dystonia, only for the **affected hand** and only for **the crossed condition 4-5 fingers** (but not for the conditions 2-3 and 2-4), showed a lower percentage of double stimulus detection than normal subjects. This might be consistent with recent data reported by Nelson et al. 2009.



Tinazzi et al. Brain 2013

Diplesthesia in focal hand dystonia

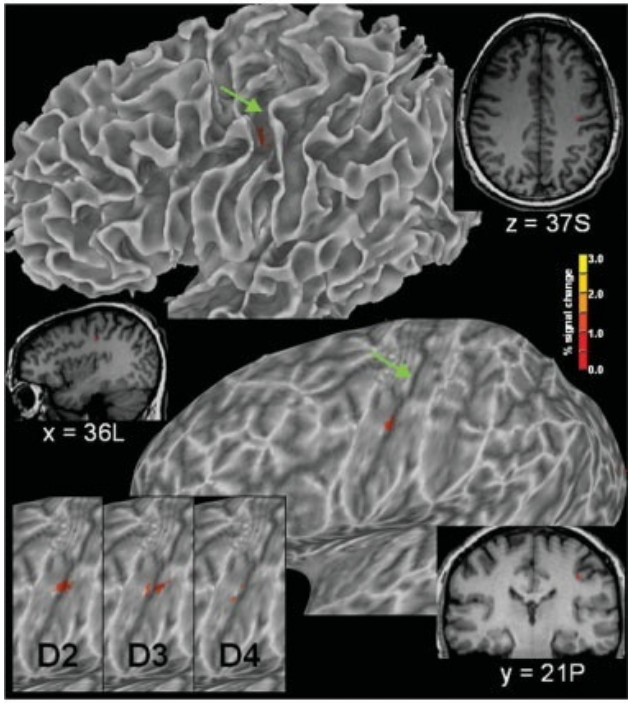
Digit-Specific Aberrations in the Primary Somatosensory Cortex in Writer's Cramp

Aimee J. Nelson, PhD,[1,2] David T. Blake, PhD,[3] and Robert Chen, MBBChir, MSc, FRCPC[1]

Ann Neurol 2009;66:146–154

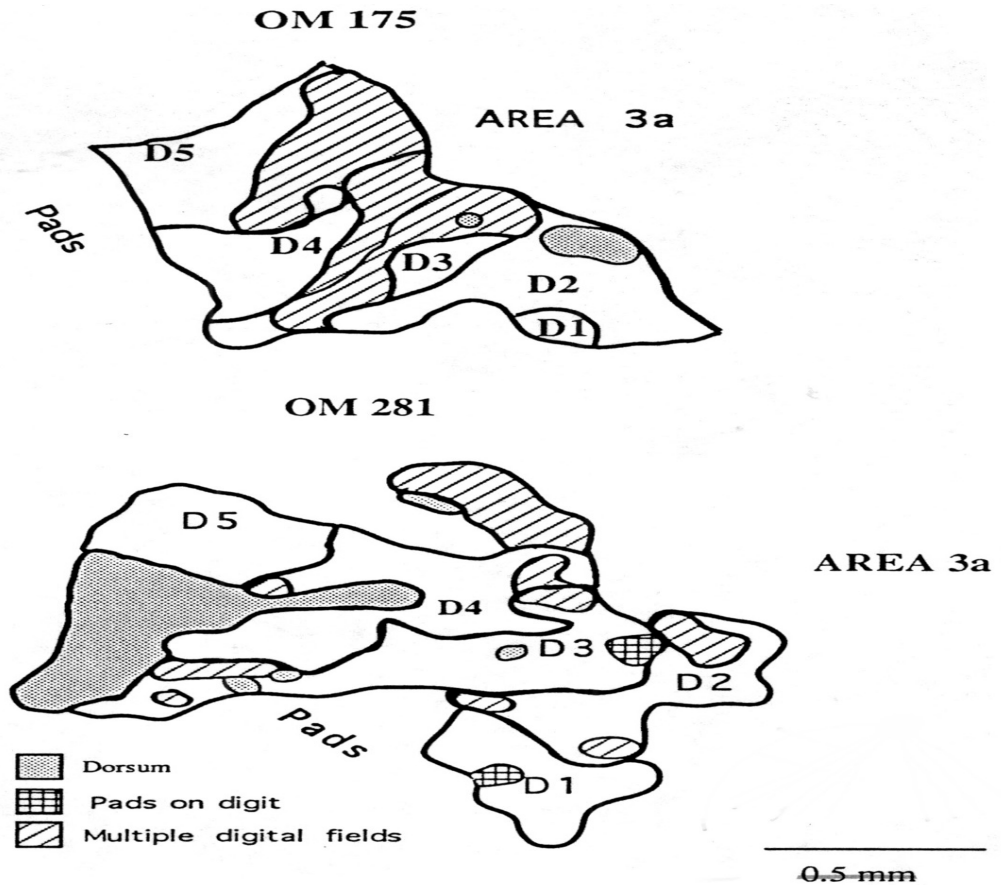
Decreased activation to vibrotactile stimulation in S1 for 2, 3 and 4 fingers but not for the 1 and 5 fingers was observed.

Hence, the reduced percentage of illusion in 4-5 condition we observed, might be due to a different level of activation of these two fingers in S1.



Experimental animal model of dystonia

The search for abnormalities of sensation was stimulated by the observation in a **primate model of dystonia** (monkeys) that showed enlarged and overlapped receptive fields of the hand in area 3b of S1 after stereotypic movements of the hand.

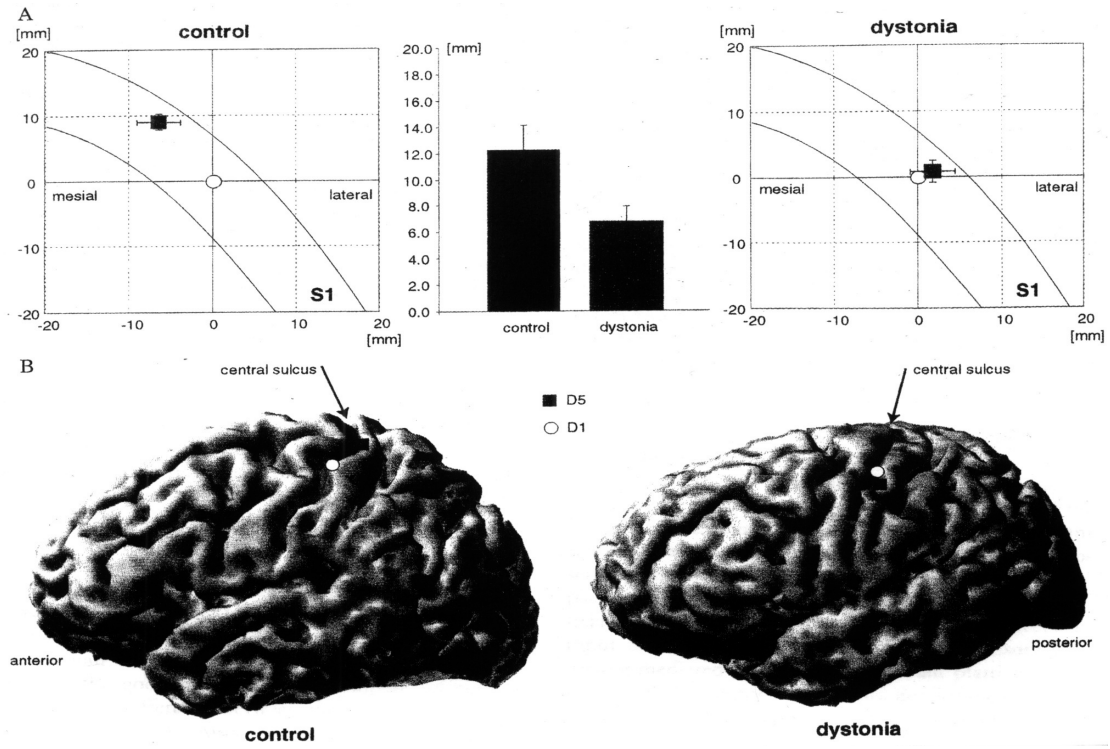


Byl et al. Neurology 1996

Neuroimaging studies (MEG and fMRI)

Abnormal somatotopy in S1

Abnormal representation in S1 of the fingers involved in dystonia: smaller distance (fusion) between the S1 representations of the digits of the affected hand in focal-hand dystonia *(Bara-Jimenez et al. 1998; Meunier et al. 2001; (Butterworth et al. 2003; Nelson et al., 2009)* and in dystonic musicians *(Elbert et al 1998).*



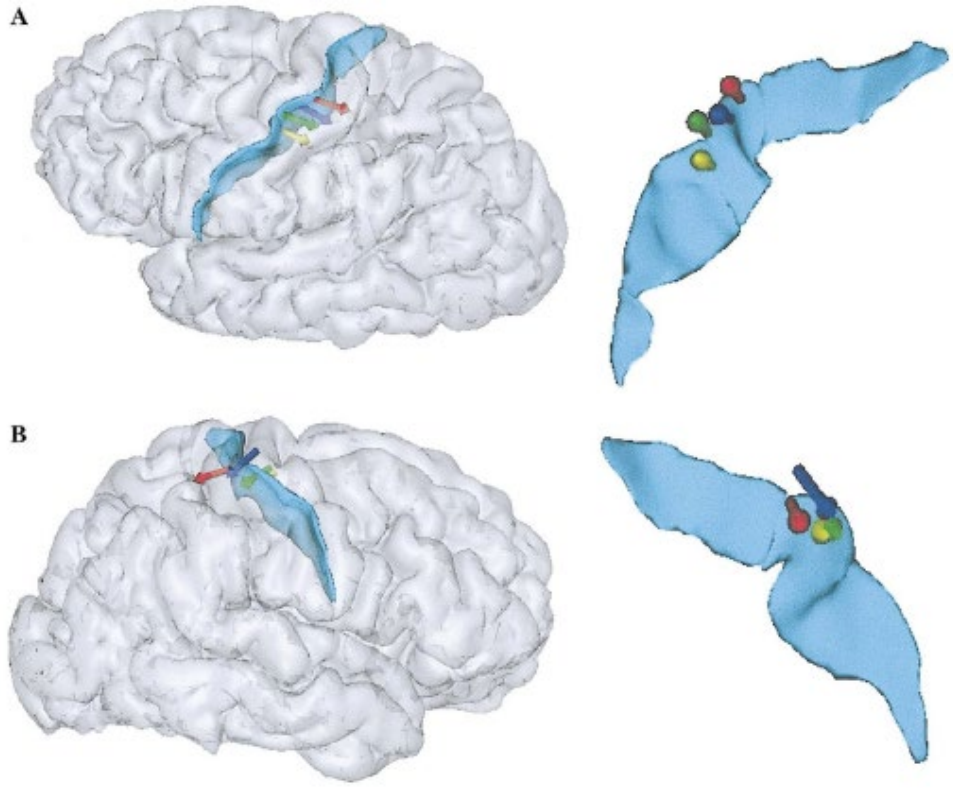
Bara-Jimenez et al. Ann Neur 1998

Human Brain Mapping in Dystonia Reveals Both Endophenotypic Traits and Adaptive Reorganization

Sabine Meunier, MD, PhD,[1] Line Garnero, PhD,[4,6] Antoine Ducorps, BSc,[6] Leonor Mazières, MD, PhD,[1] Stéphane Lehéricy, MD, PhD,[2] Sophie Tézenas du Montcel, MD,[3] Bernard Renault, PhD,[4,6] and Marie Vidailhet, MD, PhD[5,7]

Ann Neurol 2001;50:521–527

Abnormal representations of the hand are present on both the affected and unaffected side of patients with unilateral hand dystonia, suggesting that **sensory abnormalities may pre-exist overt manifestation of dystonia.**

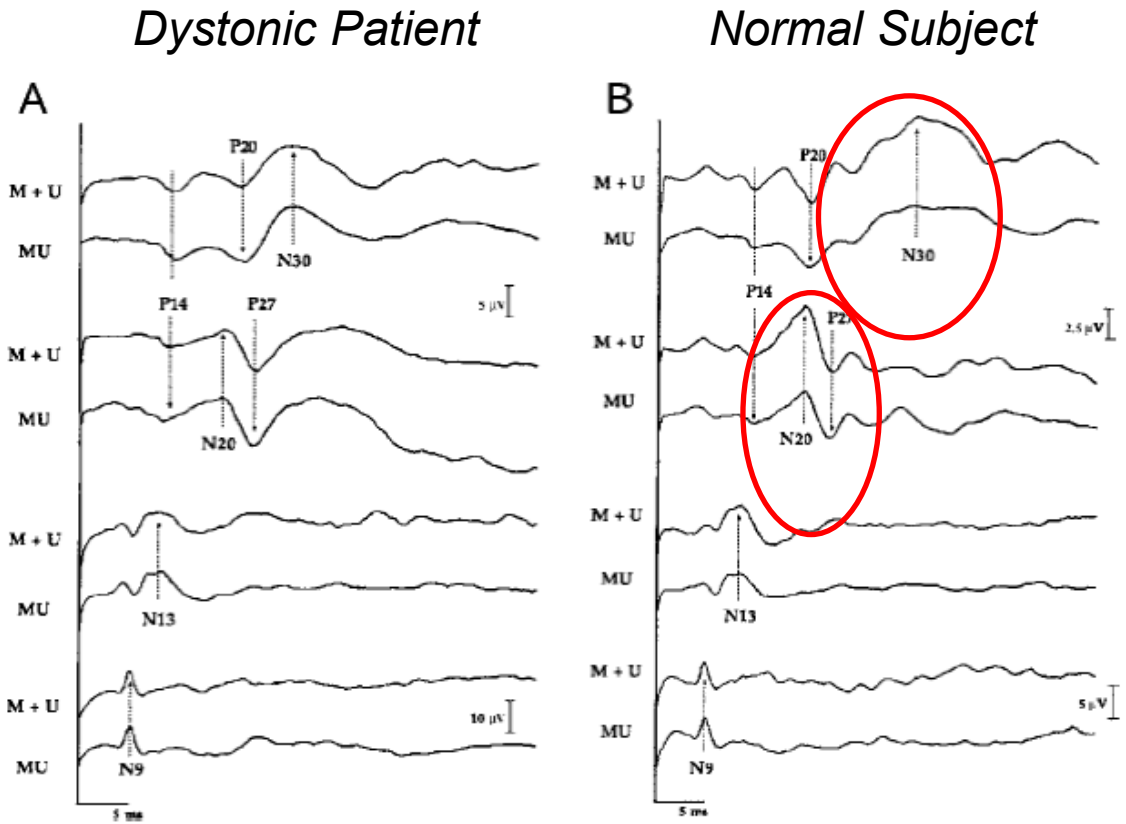


Neurophysiological (SEPs) Studies

Abnormal surrounding inhibition

One possible pathophysiological mechanism for these abnormalities could be a loss of surrounding inhibition.

In normal subjects when the median and ulnar central SEPs are produced together the combined SEPs amplitude is less than the sum of the two individual ones because of mutual inhibition. This does not happen in dystonia suggesting a **defect on inhibition at multiple levels of the somatosensory system**.



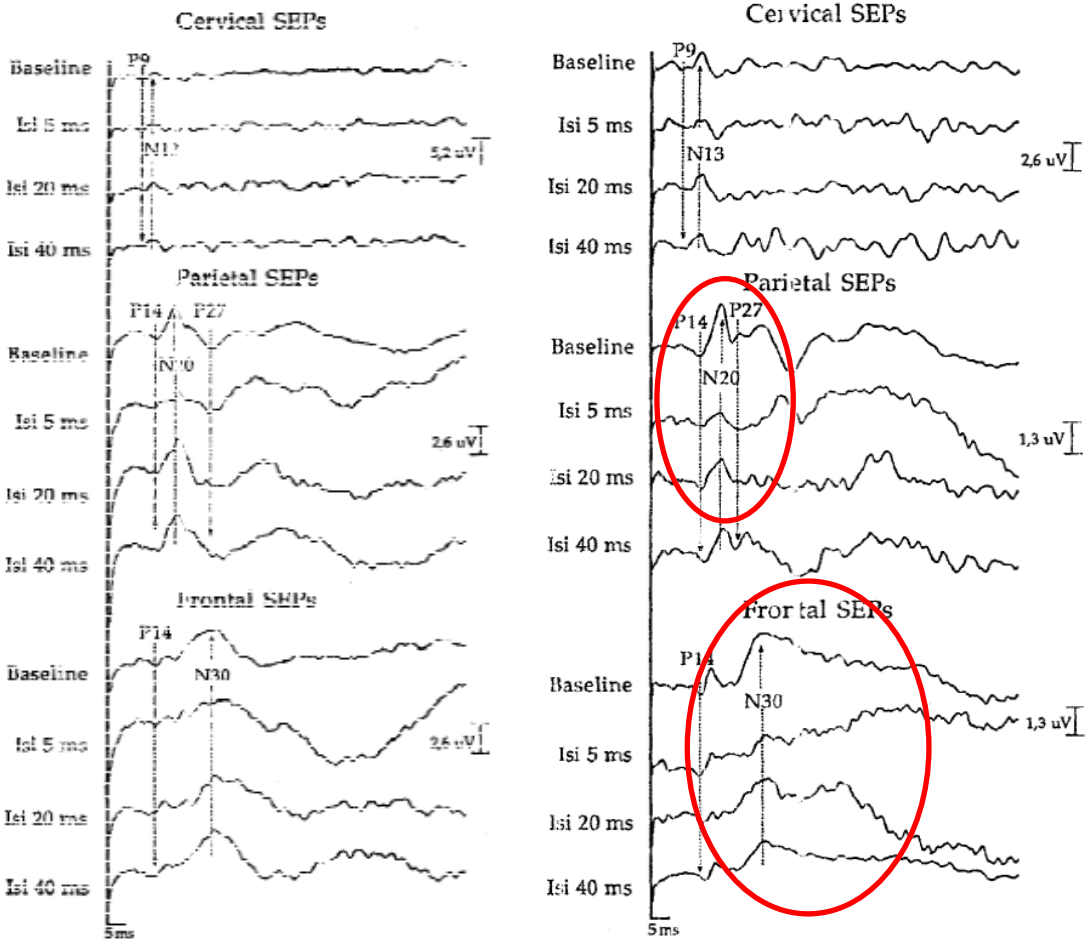
Tinazzi et al. Brain 2000

Neurophysiological (SEPs) Studies

Abnormal in-field inhibition

The pathophysiology of the temporal discrimination abnormality has been explored using SEP recovery cycles. If two SEPs are produced at short interval, components of the second SEP are inhibited by the first one. We also showed loss of in-field inhibition in several SEP components at several intervals in dystonia after paired stimuli.

Dystonic Patient *Normal Subject*



Tinazzi et al. Mov Disord 2001

RESEARCH ARTICLE

2017

Neurophysiological Correlates of Abnormal Somatosensory Temporal Discrimination in Dystonia

Elena Antelmi, MD,[1,2,3*] Roberto Erro, MD,[1,4] Lorenzo Rocchi, MD,[1,5] Rocco Liguori, MD,[2,3] Michele Tinazzi, MD,[4] Flavio Di Stasio, MD,[6] Alfredo Berardelli, MD,[5,6] John C. Rothwell, PhD,[1] and Kailash P. Bhatia, MD[1]

We recently reported that these neurophysiological abnormalities **(surrounding and in-field inhibition)** correlated with increased TDT.

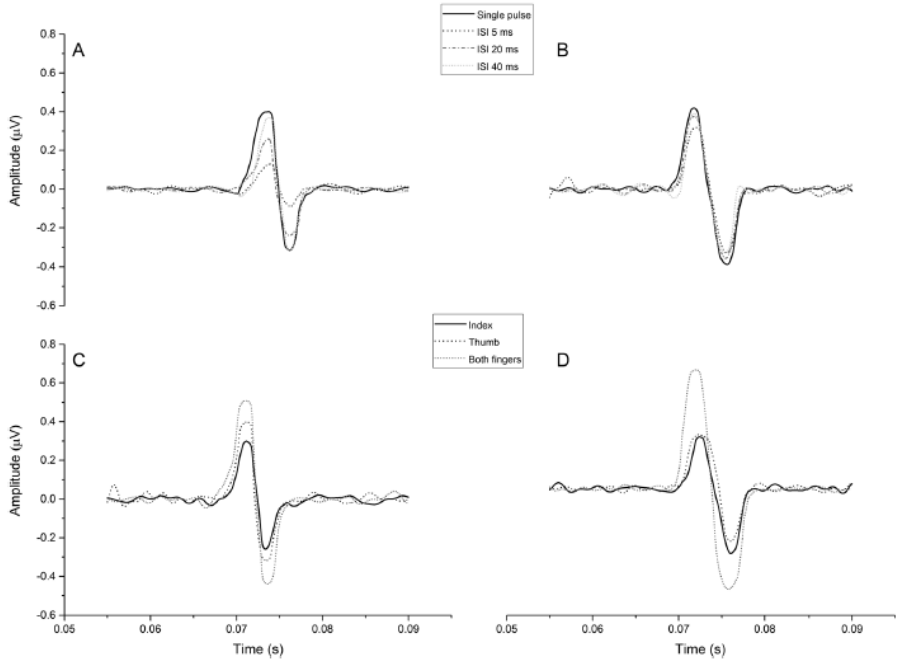


FIG. 1. Example of paired-pulse somatosensory evoked potentials (SSEPs; upper row) and surround inhibition ratio (lower row) measured on the N20 wave in one healthy participant (panels A and C) and in a patient with dystonia (panels B and D). SSEPs recorded from the dystonic patient show less paired-pulse inhibition at all ISI and less suppression when the thumb and index finger were stimulated at the same time when compared with the healthy participant. The signals were bandpassed between 20 and 500 Hz for visualization purposes. ISI, interstimulus interval; μV, microvolts; ms, milliseconds.

Abnormal Plasticity in PTD

Abnormal inhibition

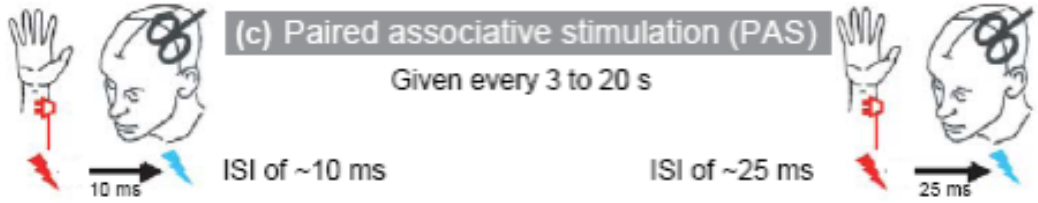
Handbook of Clinical Neurology, Vol. 116 (3rd series)
Brain Stimulation
A.M. Lozano and M. Hallett, Editors

Chapter 43

Transcranial magnetic stimulation in dystonia

ANGELO QUARTARONE[1,2,3,4]*

An abnormality of plasticity (as assessed by the PAS protocol) could be secondary to the abnormality of inhibition because plasticity depends on the amount of inhibition.



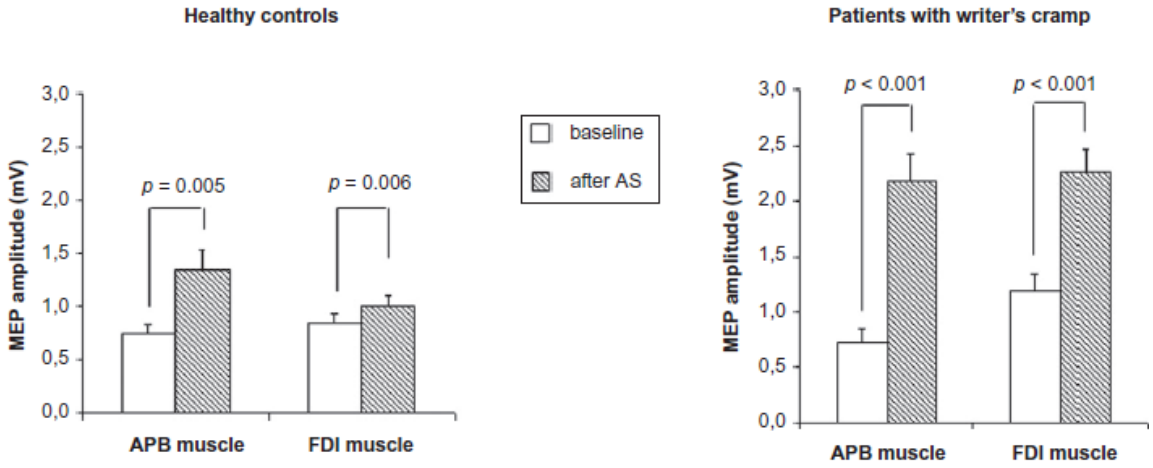
A well-established approach to test plasticity in the sensori-motor system in humans in a noninvasive way **is paired associative stimulation (PAS).**

Abnormal Plasticity in writer's cramp

Using PAS, TMS evoked potential recorded from the target muscle**, is enhanced in controls**

In patients with writer's cramp MEP is more enhanced and PAS tends to also change cortical excitability of nearby muscle representations.

This abnormal plasticity is not confined to the neural circuits affected by **dystonia but is generalized across the entire sensorimotor system,** representing an endophenotypic trait of dystonia.



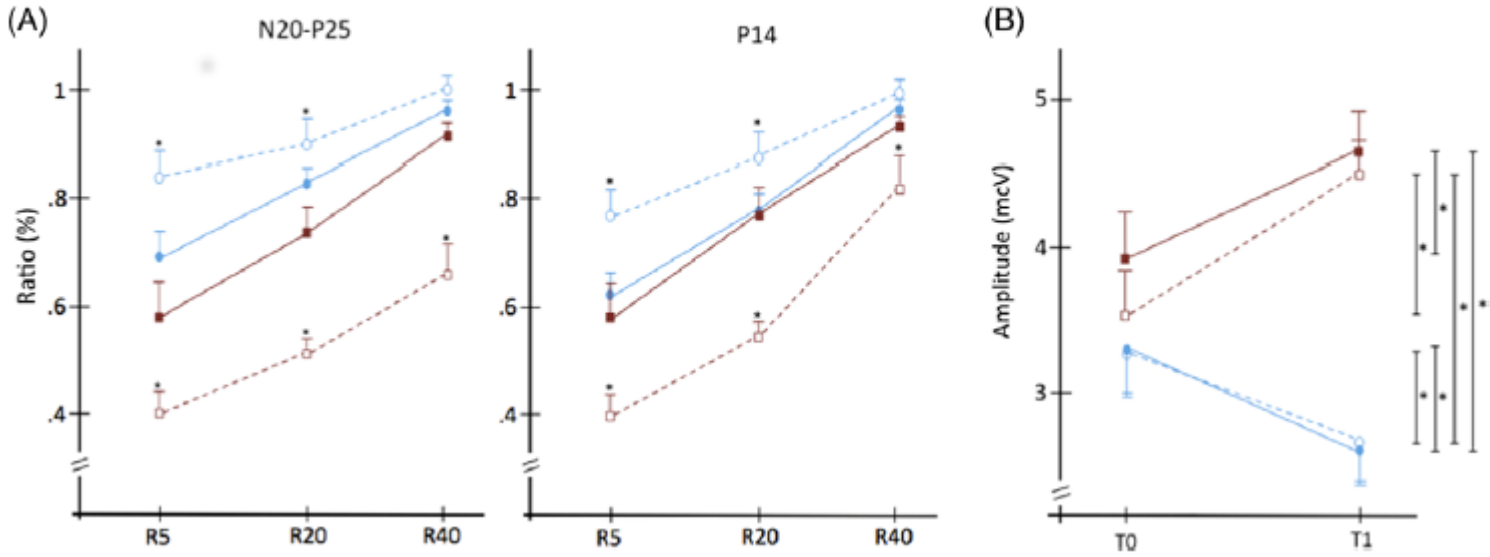
Quartarone et al. Brain 2003

Received: 27 February 2018; **Revised:** 20 April 2018; **Accepted:** 22 May 2018

RESEARCH ARTICLE

High Frequency Somatosensory Stimulation in Dystonia: Evidence for Defective Inhibitory Plasticity

Roberto Erro, MD, PhD [1,2*] Lorenzo Rocchi, MD, [1,3] Elena Antelmi, MD, PhD, [1,4,5] Rocco Liguori, MD, PhD, [4,5] Michele Tinazzi, MD, PhD, [6] Alfredo Berardelli, MD, PhD, [3,7] John Rothwell, MA, PhD [1] and Kailash P. Bhatia, MD, FRCP [1]



Neuropsychologia 79 (2015) 288–300

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,*]

- Vibration of the affected arm can induce dystonia in patients with focal hand dystonia *(Kaji et al. 1995b)* and it can be blocked with lidocaine indicating that it is mediated by spindle afferents.

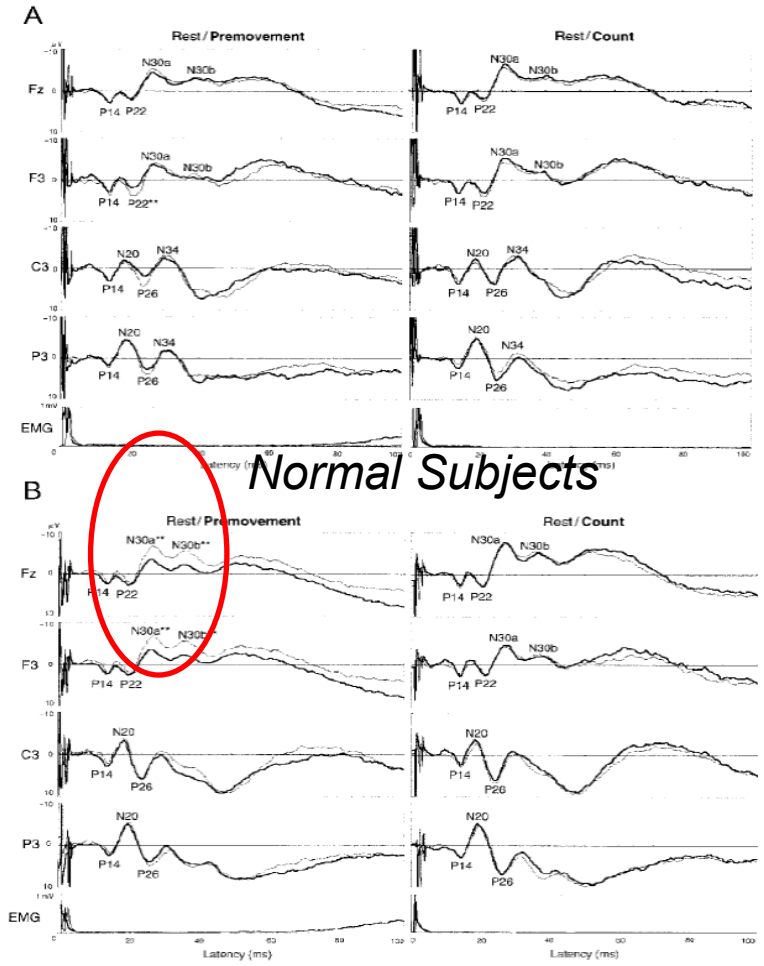
- Vibration of a muscle leads to an augmentation of its MEP and a reduction of its SICI; these effects are lacking in patients with writer's cramp *(Rosenkranz et al. 2000, 2005).*

- Patients with primary dystonia have normal SAI *(Kessler et al. 2005)* and those with writer's cramp have abnormal LAI when TMS is conditioned by median-nerve stimulation *(Abbruzzese et al. 2001).*

Abnormal sensorimotor integration

Recording SEPs before and during movement, Murase et al. (2000) showed that in normal subjects but not in writer's cramp the N30 was gated before movement indicating a defect of motor area inhibition on incoming sensory inputs. This is in line with the finding that pre-movement EEG potentials (CNV and BP), are abnormal in dystonia *(Deuschl et al. 1992; Hamano et al.1999; Ikeda et al. 1996; Zeuner et al. 2009).*

Dystonic Patients



Normal Subjects

Murase et al. Brain 2000

Role of Sensory System

Are sensory abnormalities specific to particular types of dystonia?

The observation that SD and TDT abnormalities shared by the various forms of dystonia and that the degree of TDT increase does not differ between patients with different forms of dystonia suggests that age-related effects become negligible when a dystonic trait is present.

Are sensory abnormalities responsible for or secondary to dystonic motor features?

Three different levels of pathophysiological relevance:

1) a **background level** that predisposes individuals to dystonia: **TDT**
2) a **disease-related level** that is present when dystonia becomes manifest: **SD**
3) a **causative level** that triggers dystonia: **TVR**

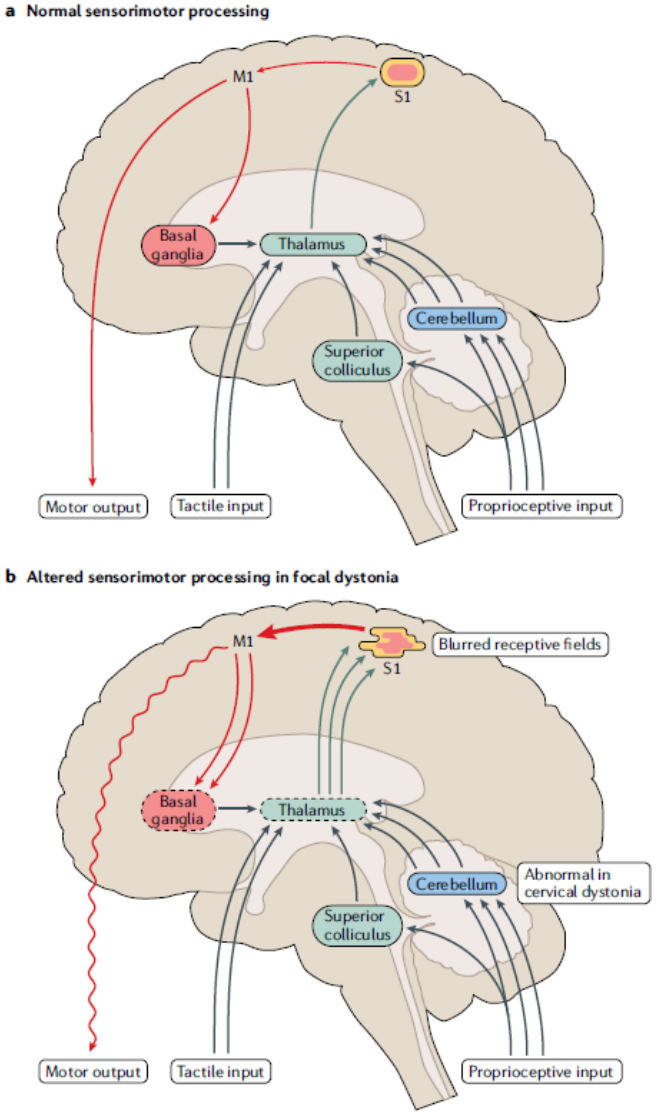


Fig. 2 | **Tactile and sensorimotor processing. a** | Normal sensorimotor processing in healthy individuals. **b** | Altered sensorimotor processing in patients with focal dystonias. In focal dystonias, altered subcortical gating of sensory information in the thalamus leads to an overflow of sensory input to the cortex, which in turn alters the intrinsic mechanisms of temporal shaping of sensory input with widened and blurred sensory receptive fields at the cortical level. In predisposed individuals, behavioural and environmental conditions that impinge on proprioceptive information might worsen the defective connectivity and drive further abnormal representations in the motor system, giving rise to more overt dystonic movements. M1, primary motor cortex; S1, primary somatosensory cortex.

Conte et al. Nature Rev Neurol 2019

Sensory Dysfunction

Neuroanatomical Correlates

The network model entails derangements in communication among **cortical areas**, **the basal ganglia and the cerebellum**, and we believe that this model can be used to interpret the **sensory-motor abnormalities** that are present in dystonia.

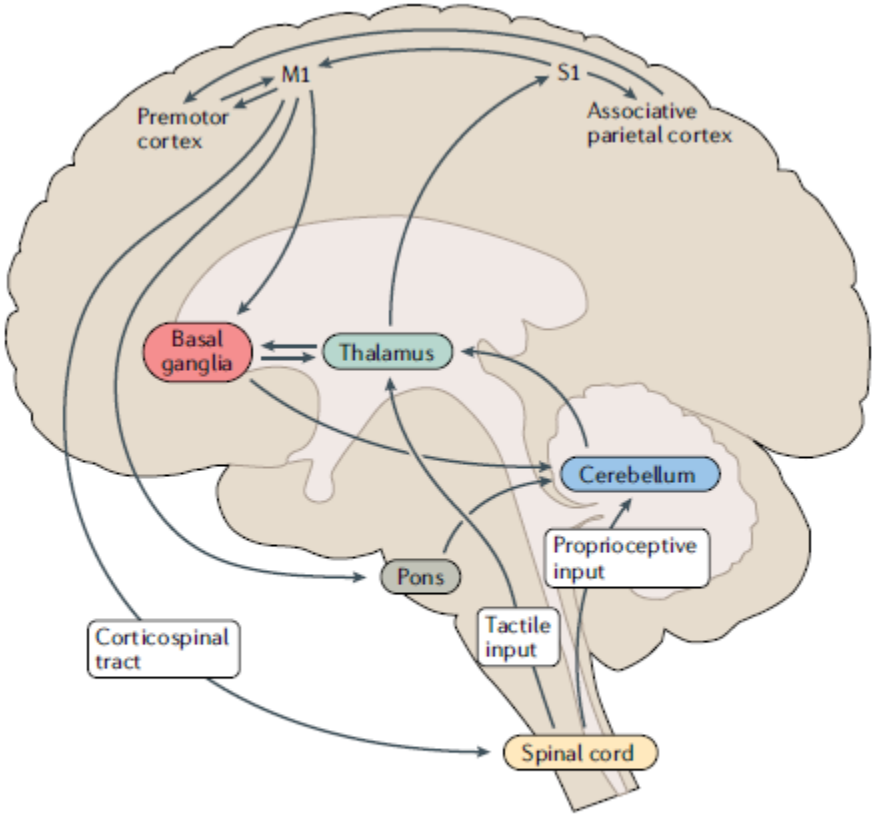


Fig. 1 | **The network model of dystonia.** The figure shows the normal pathways of communication between the basal ganglia, thalamus, cortical areas and cerebellum. According to the network model, dystonia might arise from interference with any node or connection in the network and not only from dysfunction of the basal ganglia. M1, primary motor cortex; S1, primary somatosensory cortex.

Conte et al. Nature Rev Neurol 2019

OPEN ACCESS Freely available online

Tremor and Other Hyperkinetic Movements 2017

Reviews

The Anatomical Basis for Dystonia: The Motor Network Model

H. A. Jinnah[1*], Vladimir Neychev[2] & Ellen J. Hess[3]

Concepts regarding the neuroanatomical basis for dystonia have **evolved from a narrow focus on dysfunction of the basal ganglia** to **a broader motor network model** in which the basal ganglia, cerebellum, cerebral cortex, and other brain regions play a key role.

In keeping with this idea, **dystonia may result from** a single-node dysfunction, from an involvement of multiple nodes, or from aberrant communication among the nodes.

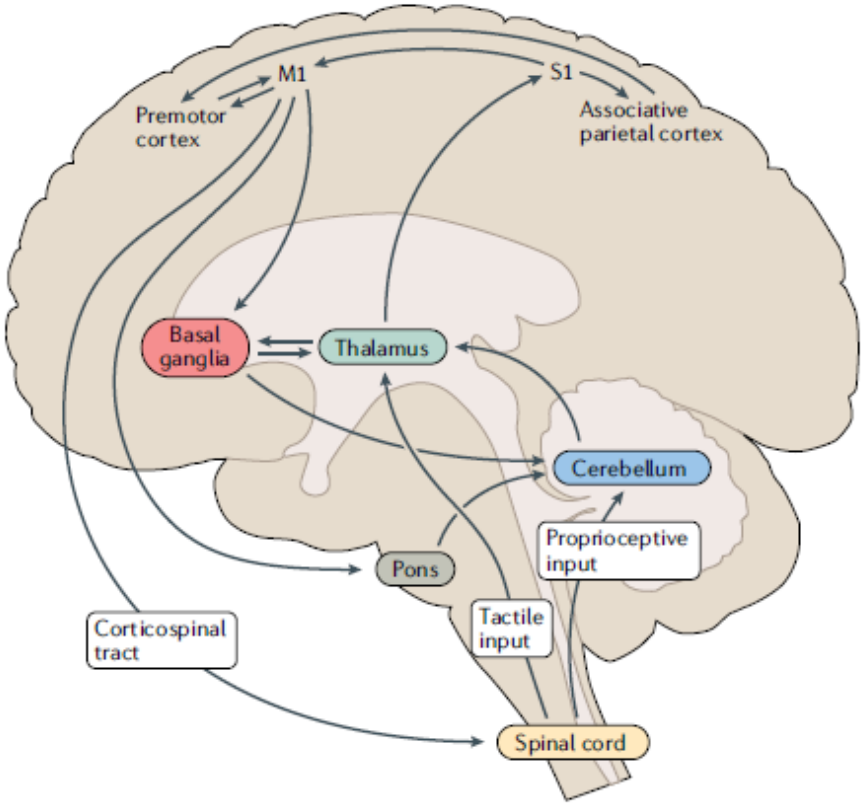


Fig. 1 | **The network model of dystonia.** The figure shows the normal pathways of communication between the basal ganglia, thalamus, cortical areas and cerebellum. According to the network model, dystonia might arise from interference with any node or connection in the network and not only from dysfunction of the basal ganglia. M1, primary motor cortex; S1, primary somatosensory cortex.

Conte et al. Nature Rev Neurol 2019

Evolving Concepts in the Pathogenesis of Dystonia

Parkinsonism Relat Disord. 2018 .

H. A. Jinnah, MD, PhD[1] and **Ellen J. Hess**[2]

Received: 3 June 2019; **Revised:** 20 August 2019; **Accepted:** 23 August 2019

ONE DECADE AGO, ONE DECADE AHEAD

Ten-Year Reflections on the Neurophysiological Abnormalities of Focal Dystonias in Humans

Antonella Conte, MD, PhD,[1,2] Lorenzo Rocchi, MD,[3] Anna Latorre, MD,[1,3] Daniele Belvisi, MD, PhD,[2] John C. Rothwell, PhD,[3] and Alfredo Berardelli, MD[1,2*]

Combinations of dysfunction and compensation could occur at one or many levels of the extended sensory-motor network.

For example, it could be that various forms of focal dystonias emerge at different levels of the network: the **sensorimotor cortex** for task-specific dystonia involving the upper limb, the **cerebellum and the brainstem** for cervical dystonia, and the **brainstem** for blepharospasm.

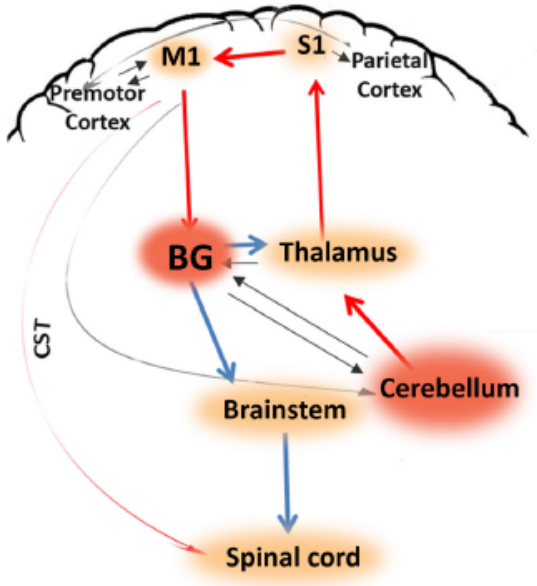


FIG. 1. Pathophysiology of focal dystonias modeled as a network disorder. Basal ganglia (BG) and cerebellum may be the central contributors in the network (red shading), which integrate unbalanced information from different nodes of the network. The different nodes (primary motor cortex [M1], primary somatosensory cortex [S1], thalamus, brain stem, and spinal cord [orange shading]) may differently intervene in the pathophysiology of the various forms of focal dystonia. Red arrows represent excessive distorted neurotransmission, blue arrows reduced neurotransmission. CST, corticospinal tract. [Color figure can be viewed at wileyonlinelibrary.com]

Clinical Neurophysiology 120 (2009) 1424–1432

Contents lists available at ScienceDirect

Clinical Neurophysiology

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

Invited review

Does neurophysiological testing provide the information we need to improve the clinical management of primary dystonia?

Michele Tinazzi [a,b], Giovanna Squintani [a,b,*], Alfredo Berardelli [c]

To improve the current neurophysiological approach to the clinical diagnosis of primary dystonia, **future studies should aim to**:

-use standardized study designs and methods
-enroll homogeneous and clinically well-defined populations
-investigate the diagnostic sensitivity and specificity of the available neurophysiological tests.

RATHER than to be addressed for pathophysiological purposes

Acknowledgements

Prof. S. Aglioti

Prof. M. Fiorio

Prof. EM. Valente

Prof. K Bhatia

Prof. A. Berardelli

Prof. G. Defazio

Prof. F. Morgante

Prof. G. Abbruzzese

Dr. R. Erro

Dr. E. Antelmi