Epidemiologologia e diagnosi delle distonie craniche

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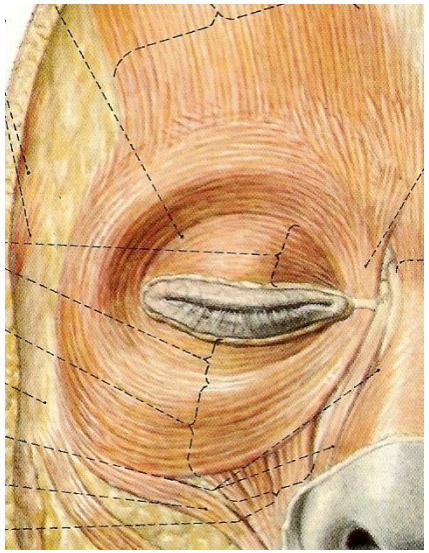
UNIVERSITÀ DEGLI STUDI DI BARI ALDO MORO

Blepharospasm

- involuntary spasms of the orbicularis oculi muscles
- frequent blinking, which may be either isolated or associated with spasms

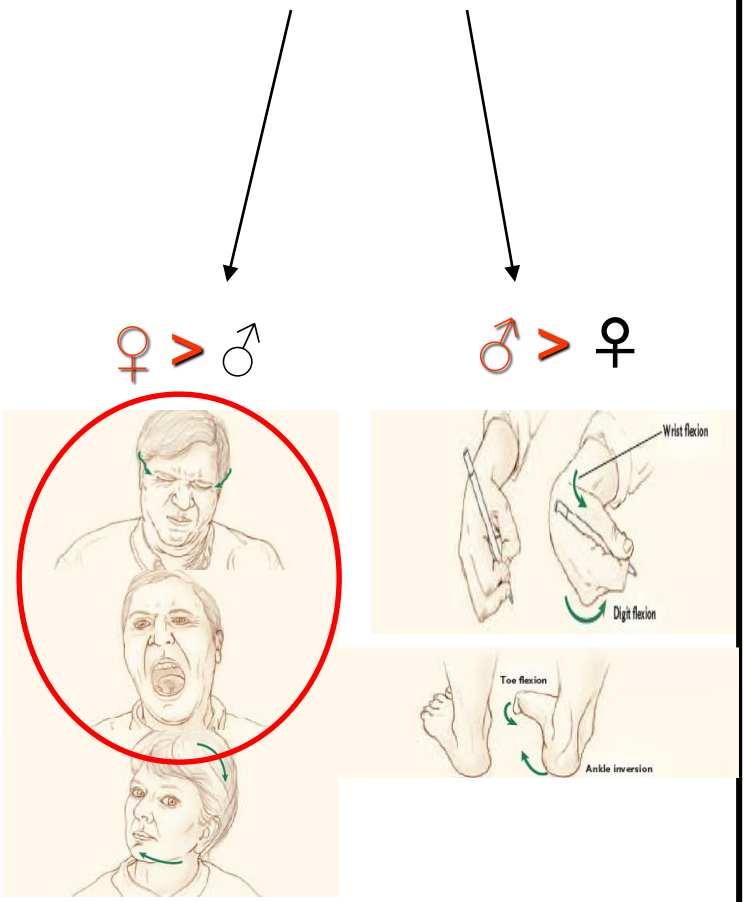


Oromandibular Dystonia

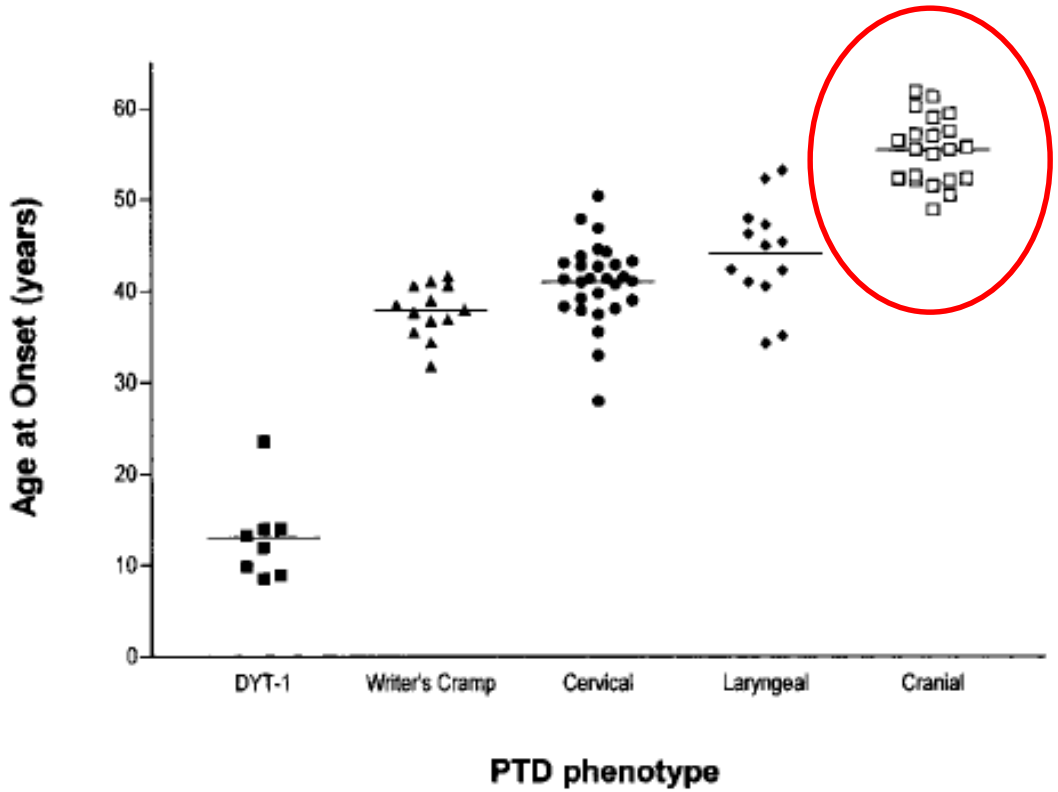
- movements of lower facial muscles, jaw, or tongue
- movements can be sustained, episodic, or action-induced

Primary late-onset dystonia: demographic features

Gender



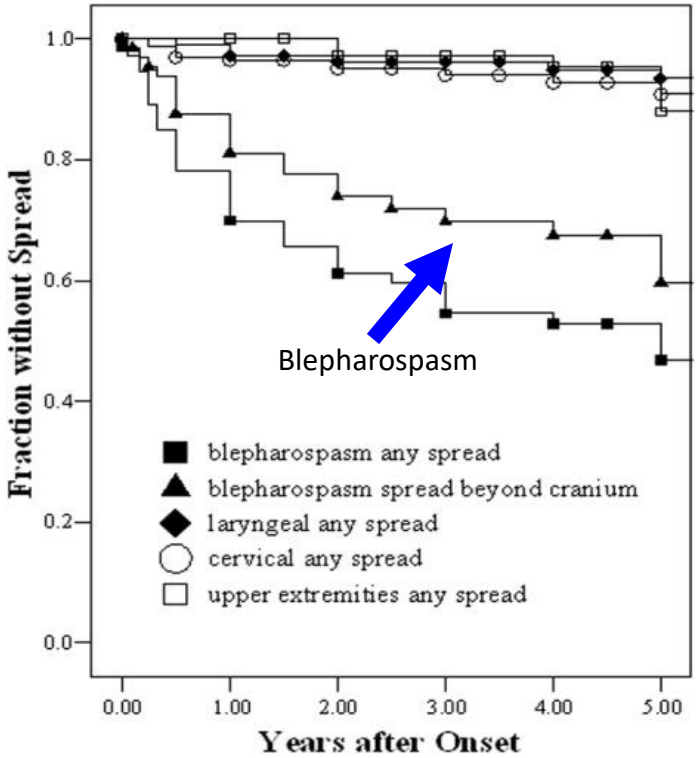
Age at onset



(O'Riordan S…Hutchinson M, *Neurology* 2004)

Spread of late-onset dystonia

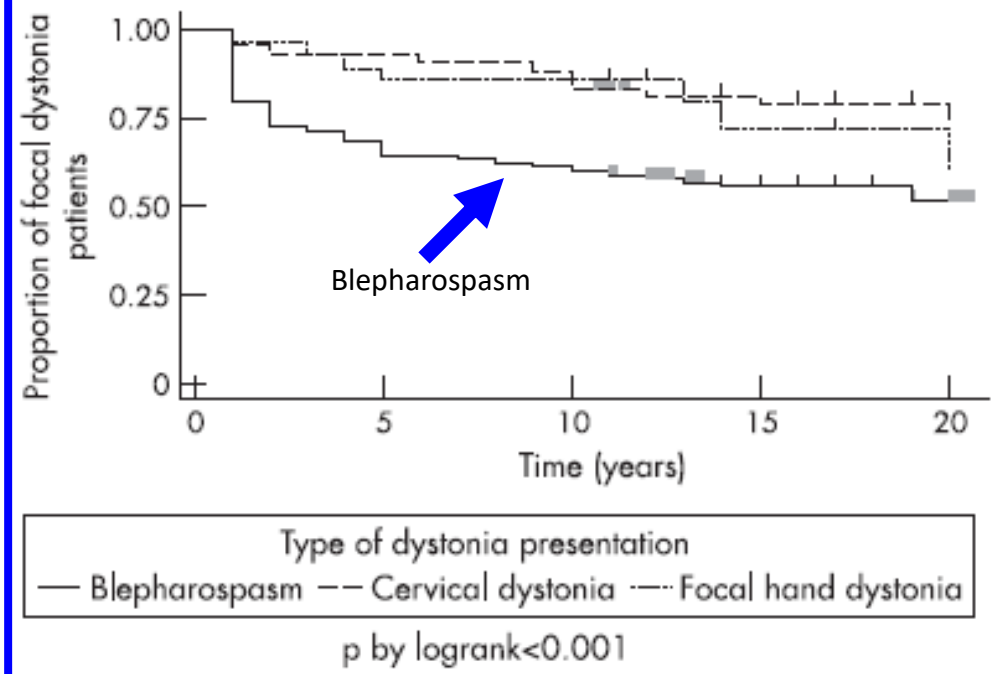
Weiss E…Perlmutter JL, *Mov Disord* 2006
Svetel M…Kostic VS, *J Neurol* 2007



Long-term assessment of the risk of spread in primary late-onset focal dystonia

G Abbruzzese,[1] A Berardelli,[2] P Girlanda,[3] R Marchese,[1] D Martino,[4] F Morgante,[3] L Avanzino,[1] C Colosimo,[2] G Defazio[4]

J Neurol Neurosurg Psychiatry 2008;



Lower limb involvement in adult-onset primary dystonia: frequency and clinical features

D. Martino[a], A. Macerollo[a], G. Abbruzzese[b], A. R. Bentivoglio[c], A. Berardelli[d], M. Esposito[e], G. Fabbrini[d], P. Girlanda[f], A. Guidubaldi[c], R. Liguori[g], D. Liuzzi[a], L. Marinelli[b], F. Morgante[f], A. Sabetta[g], L. Santoro[e] and G. Defazio[a,h]

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European Journal of Neurology 2010, **17:** 242–246

Table 1 Number (%) of patients, gender distribution, and age at onset of the various forms of adult-onset primary dystonia in our 579 patients

	Lower limb dystonia	Trunk dystonia	Upper limb dystonia	Cervical dystonia	Laryngeal dystonia	Oromandibular dystonia	Blepharospasm
Number (%)	11 (1.9%)	9 (1.5%)	64 (11%)	253 (43.6%)	32 (5.5%)	139 (24.1%)	329 (56.7%)
Women (%)	72.7	78	47	72	81	76	72
Men (%)	27.3	22	53	28	19	24	28
Age at onset, years (mean ± SD)	47.9 ± 17	40.3 ± 17.5	43.3 ± 15.7	47.8 ± 15.5	58.1 ± 14.4	58.9 ± 11.8	57.9 ± 10.7

One-way analysis of variance for age at onset between the different forms of dystonia: $F = 27.54$, $P < 0.00001$ (Bonferroni *post hoc* tests: lower limb dystonia vs. trunk dystonia, upper limb dystonia, cervical dystonia, laryngeal dystonia: $P > 0.05$; lower limb dystonia vs. blepharospasm, oromandibular dystonia: $P < 0.05$).

ACCADEMIA LIMPE-DISMOV

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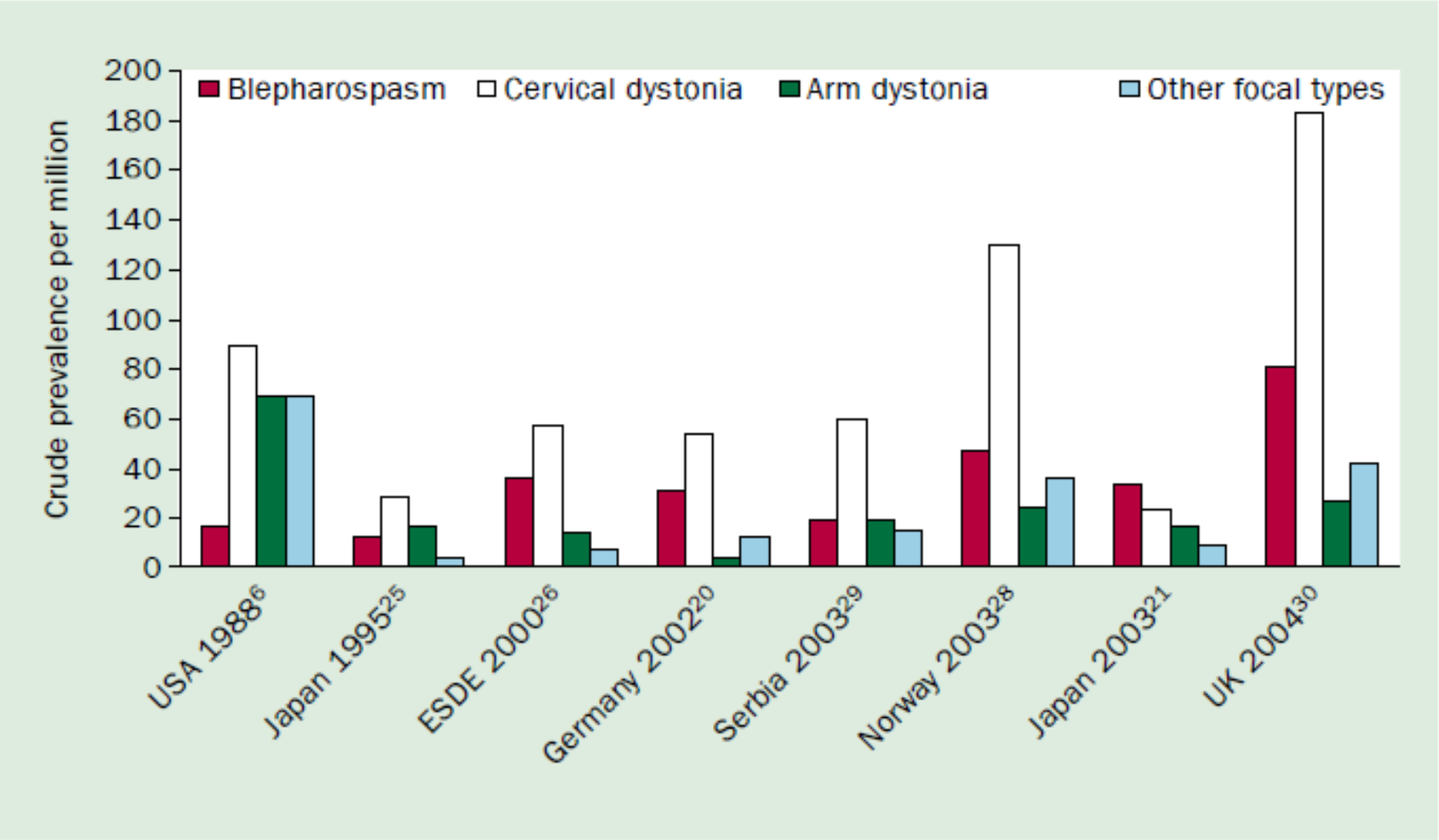
Giornata Nazionale Parkinson

Registro Italiano Distonie Adulto

Informazioni al baseline (664 records)

Distonia	n. Pazienti (%)
Blefarospasmo	296 (45%)
D cervicale	315 (47%)
D laringea	27 (4%)
D oromandibolare	96 (15%)
D arti superiori	75 (11%)
D tronco	12 (1.8%)
D arti inferiori	24 (3.6%)



G. Defazio et al., Lancet Neurology, 2004

Time elapsing from dystonia onset to diagnosis according to the year of dystonia onset.

Year of dystonia onset	All patients (171)	**Cranial Dystonia (100)**	Extracranial dystonia (71)
Before 1973	39 ± 5,1 (5)	**36,6 ± 5,5 (3)**	42,5 ± 2,1 (2)
1973 to1982	20,5 ± 3,5 (2)	**-**	20,5 ± 3,5 (2)
1983 to 1992	13, 8 ± 8,5 (25)	**9,6 ± 7,1 (15)**	16 ± 6,5 (10)
1993 to 2002	5,5 ± 4,1 (54)	**4,6 ± 3,4 (28)**	6,5 ± 4,6 (26)
2003 to 2012	2,2 ± 2,3 (85)	**1,9 ± 1,4(54)**	2,6 ±3,4 (31)

Values are mean years ± SD. Total number of patients is in parenthesis

Focal dystonias – factors contributing to misdiagnosis

- Phenomenological variability of dystonia in different body sites
- Neurological and non neurological conditions mimicking the abnormal movements or postures induced by dystonia (pseudodystonia)

Development of guidelines for the clinical diagnosis of focal dystonias

PROCEDURE

1. Identification of the phenomenological aspects of each focal dystonia possibly contributing to diagnosis (Positive signs)
2. Identification of features that are usually absent in dystonia but are part of the clinical spectrum of pseudo- dystonia (negative signs).
3. Content validity analysis

Content validity ratio (CVR) = (ne-N/2)/(N/2)

ne=number of raters indicating the item as relevant for diagnosis

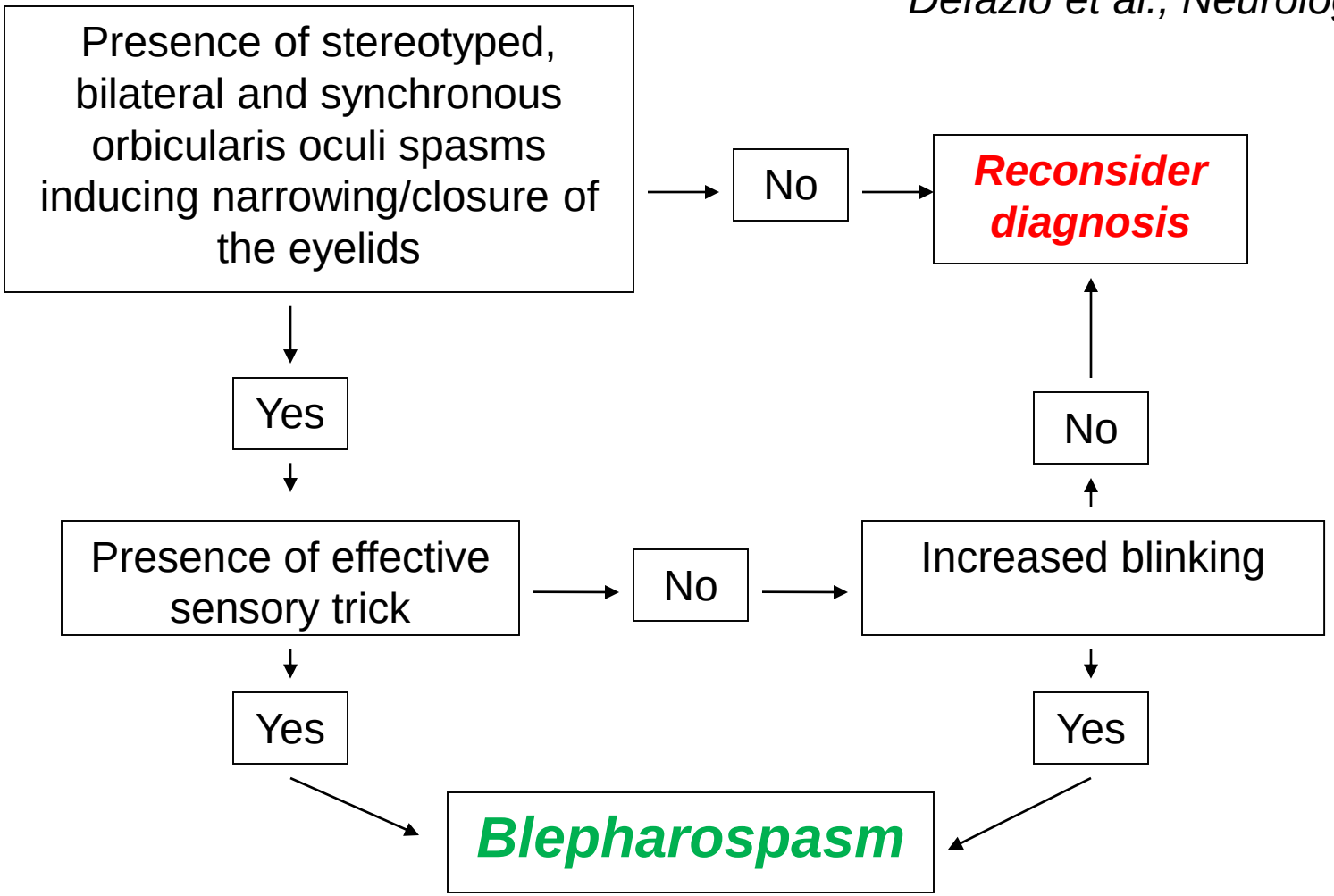
N=total number of raters.

CVR ranges between -1 and +1 (all raters judge the item as essential).

Phenomenological aspects of blepharospasm possibly contributing to diagnosis	Content validity ratio
1) **Involuntary narrowing/closure of the eyelids due to orbicularis oculi spasms**	**1**
2) Presence of the Charcot's sign	0
3) **Increased blinking rate**	**0.6**
4) **Bilateral spasms**	**1**
5) Symmetrical symptoms	0
6) Apraxia of eyelid opening	0.3
7) Frontal hyperactivity	0
8) Spasms in the lower face	0.2
9) Dystonia in other body sites	0
10) **Sensory trick**	**0.6**
11) Presence of ocular symptoms	0.2
12) Photophobia/photo-oculodynia	0.4
13) **Inability to voluntarily suppress the spasms**	**0.8**
14) Absence of premonitory sensations	0.4
15) Absence of paresis of the orbicularis oculi muscles	0
16) Absence of eyelid ptosis	
17) Absence of double vision	0.2
	0

Blepharospasm diagnostic guideline

Defazio et al., Neurology 2013



93 % sensitivity and 90 % specificity

Raccomandazioni per la diagnosi di distonia focale

- Distonia cervicale
- Distonia oromandibolare
- Distonia dell’arto superiore
- Distonia laringea
- Distonia arto inferiore

Registro Italiano Distonie Adulto

Oromandibular dystonia

Positive Clinical signs	Content Validity ratio (CVR)
Oromandibular movements / postures - either spontaneous or triggered by motor tasks	1
Mobile involuntary posture	0.6
Stereotyped or patterned movements	0.6
Jaw tremor	0.4
Difficult voluntary jaw movements	0.6
Sensory trick	-0.8
Dystonia in other body parts	-0.8

Alternative Diagnoses	Negative Clinical signs	Content validity ratio
Bruxism	- Prolonged/forceful jaw closing and marked dental attrition during sleep or emotional situations - teeth/periodontium lesions	**0.4** **-0.8**
Hemimasticatory spasm	Unilateral masseter and temporal muscle ipertrophy	**0**
Geniospasm	Autosomal dominant inheritance and high penetrance	**0.2**
lower motor neuron disease/miopathy	Jaw drop associated with masticatory muscle weakness	**0.8**
Temporomandibular joint disorders	- Fixed jaw posture - Temporo-mandibular joint pain	**0.6** **-0.6**
Edentulous diskinesia	Edentoulism	**0**
Non-dystonic jaw tremor	jaw tremor without any jaw dystonic posturing or limitation in jaw movements	**0.6**
Jaw chorea	Non-stereotyped movements	**0.6**
Jaw tics	Ability in voluntarily suppress movements / postures	**0.8**

Raccomandazioni diagnostiche

Positive/negative Clinical signs	OROMANDIBOLAR DYSTONIA	ALTERNATIVE DIAGNOSIS
Oromandibular movements / postures - either spontaneous or triggered by motor tasks	YES	
Mobile involuntary posture	YES	NO [TMJ disorders]
Stereotyped or patterned movements	YES	NO [chorea]
Jaw tremor without dystonic posturing and no limitation in jaw movements	NO	YES [non-dystonic tremor]
Ability in voluntarily suppressing movements/postures	NO	YES [jaw tics]
Masticatory muscle weakness	NO	YES [lower motorneuron disease/miopathy

Raccomandazioni diagnostiche

Positive/negative Clinical signs	**OROMANDIBOLAR DYSTONIA,** BRUXISM, HEMIMASTICATORY SPASM, GENIOSPASM	**ALTERNATIVE DIAGNOSIS**
Oromandibular movements / postures - either spontaneous or triggered by motor tasks	**YES**	
Mobile involuntary posture	**YES**	**NO [TMJ disorders]**
Stereotyped or patterned movements	**YES**	**NO [chorea]**
Jaw tremor without dystonic posturing and no limitation in jaw movements	**NO**	**YES [non-dystonic tremor]**
Ability in voluntarily suppressing movements/postures	**NO**	**YES [jaw tics]**
Masticatory muscle weakness	**NO**	**YES [lower motorneuron disease/miopathy**

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GRAZIE PER L'ATTENZIONE

P.C. 65 anni

Esordio BSP con fotofobia e GA **- EON: quando parla si manifestano spasmi prolungati, quando tace gli occhi si aprono; parziale controllo volontario degli spasmi**	**2008**

P.C. 65 anni

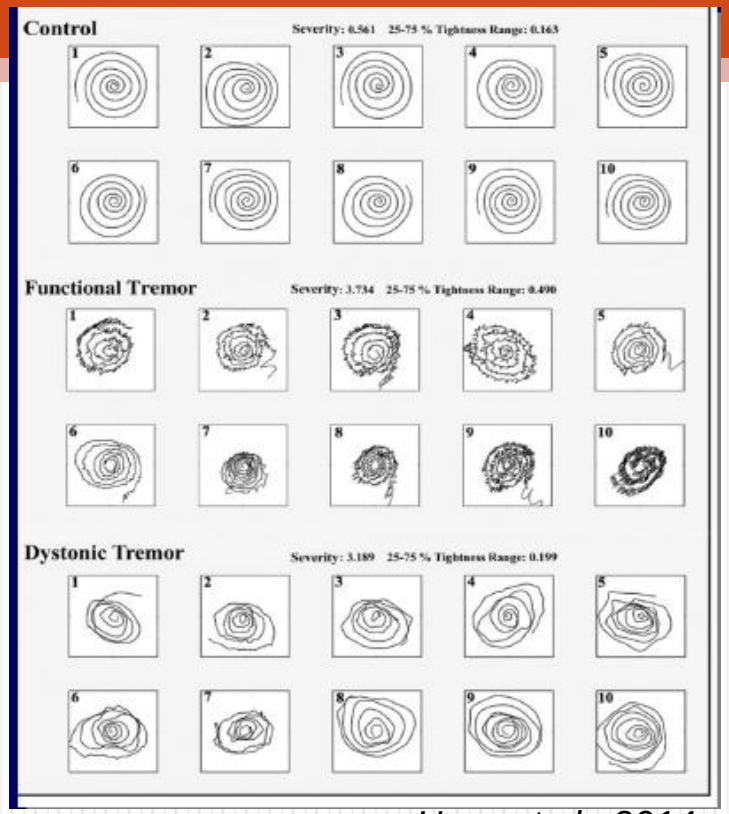
Esordio BSP con fotofobia e GA **- EON: quando parla si manifestano spasmi prolungati, quando tace gli occhi si aprono; parziale controllo volontario degli spasmi**	**2008**
Infiltrazione BTX e sol fisiologica senza effetto	**2012 -2013**
Remissione completa BSP in seguito all'uso di 3 colliri	**2014 – 2016**
Ripresa BSP con efficacia transitoria di diversi colliri	**2016**

Incongruenza

- **Il disturbo psicogeno non è congruente con il corrispondente organico**
- **I segni clinici psicogeni si modellano su credenze personali circa l'anatomia e la fisiologia, non sulla realtà clinica**

Inconsistenza

- **La tipologia del disturbo psicogeno si modifica nel tempo**
- **La severità del disturbo psicogeno fluttua da una situazione all'altra (periodi di remissione spontanea, effetto di distraibilità, risposta atipica ad agenti farmacologici…)**



Hess et al., 2014

The blink reflex recovery cycle differs between essential and presumed psychogenic blepharospasm

Neurology 76 February 15, 2011

P. Schwingenschuh, MD
P. Katschnig, MD
M.J. Edwards, MD, PhD
J.T.H. Teo, MD, PhD
L.V.P. Korlipara, MD, PhD
J.C. Rothwell, PhD
K.P. Bhatia, MD

Table 2 Blink reflex results[a]

	BEB	AB	Controls	pValue
Sensory threshold, mA	1.6 (0.4)	2.0 (0.8)	1.7 (0.4)	0.248
Stimulation intensity, mA	9.6 (2.1)	11.7 (4.9)	10.8 (5.5)	0.568
R1 area, mV.s	0.00020 (0.00018)	0.00037 (0.00019)	0.00049 (0.00026)	0.024[b]
R1 latency, ms	10.03 (0.78)	10.48 (0.75)	10.43 (0.68)	0.367
R1 duration, ms	9.64 (3.42)	9.56 (0.99)	11.45 (2.99)	0.254
R2 area, mV.s	0.0014 (0.0012)	0.0038 (0.0018)	0.0033 (0.0016)	0.006[b]
R2 latency, ms	35.8 (3.3)	34.3 (2.1)	34.6 (2.5)	0.440
R2 duration, ms	47.3 (5.7)	49.6 (9.3)	49.1 (6.6)	0.854

Abbreviations: AB = atypical (presumed psychogenic) blepharospasm; BEB = benign essential blepharospasm.
[a] All values are given as mean (SD).
[b] Indicates significance at a 5% level.

Normal excitability of brainstem blink reflex circuit
as measured by R2 area in the blink reflex recovery cycle

P.C. 65 anni

Esordio BSP con fotofobia e GA **- EON: quando parla si manifestano spasmi prolungati, quando tace gli occhi si aprono; parziale controllo volontario degli spasmi**	**2008**
Infiltrazione BTX e sol fisiologica senza effetto	**2012 -2013**
Remissione completa BSP in seguito all'uso di 3 colliri	**2014 – 2016**
Ripresa BSP con efficacia transitoria di diversi colliri	**2016**
Blink reflex recovery cycle normale	**2016**

P.C. 65 anni

Esordio BSP con fotofobia e GA **- EON: quando parla si manifestano spasmi prolungati, quando tace gli occhi si aprono**	**2008**
Infiltrazione BTX e sol fisiologica senza effetto	**2012 -2013**
Remissione completa BSP in seguito all'uso di 3 colliri	**2014 – 2016**
Ripresa BSP con efficacia transitoria di diversi colliri	**2016**
Normal blink reflex habituation cycle	**2016**
Valutazione psichiatrica **DDSI: lamentele somatiche** **SCID I: Disturbo depressivo maggiore ricorrente in remissione** **SCIDII: Disturbo dipendente di personalità**	**2016**

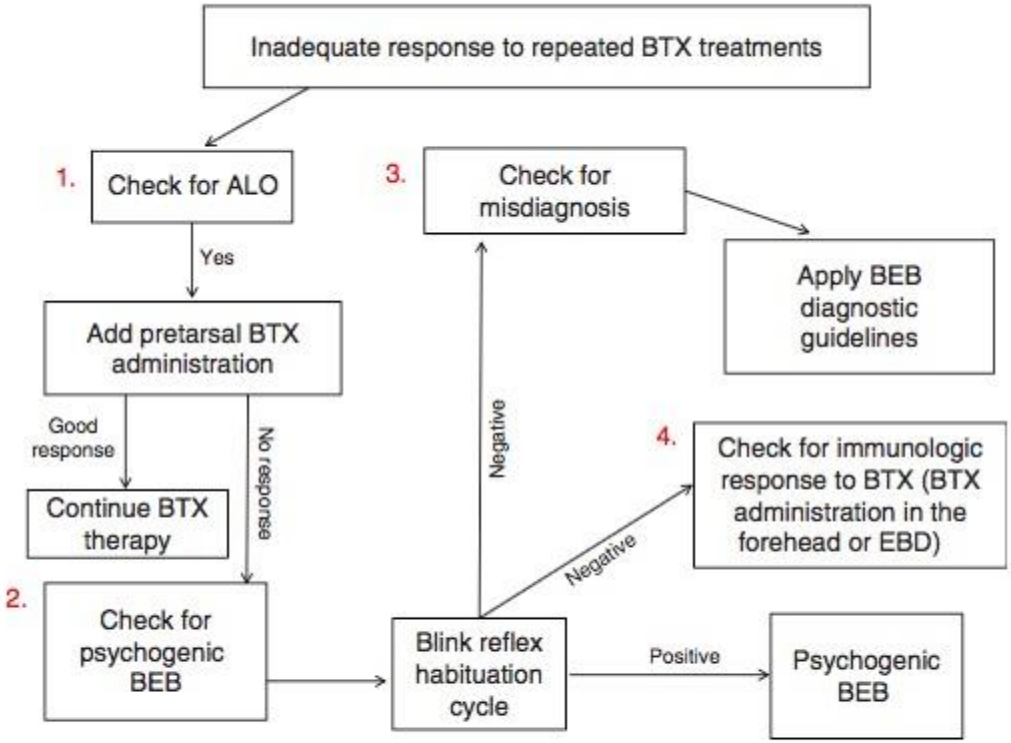


Figure 1. Guideline to check for reasons of botulinum toxin failure in patients with blepharospasm. The various possibilities are considered from the more frequent to the less frequent.

ALO: Apraxia of lid opening; BEB: Benign essential blepharospasm; BTX: Botulinum A toxin; EBD: Extensor brevis digitorum.

Pellicciari R and Defazio G, 2015