Trattamento dei disturbi non motori delle distonie

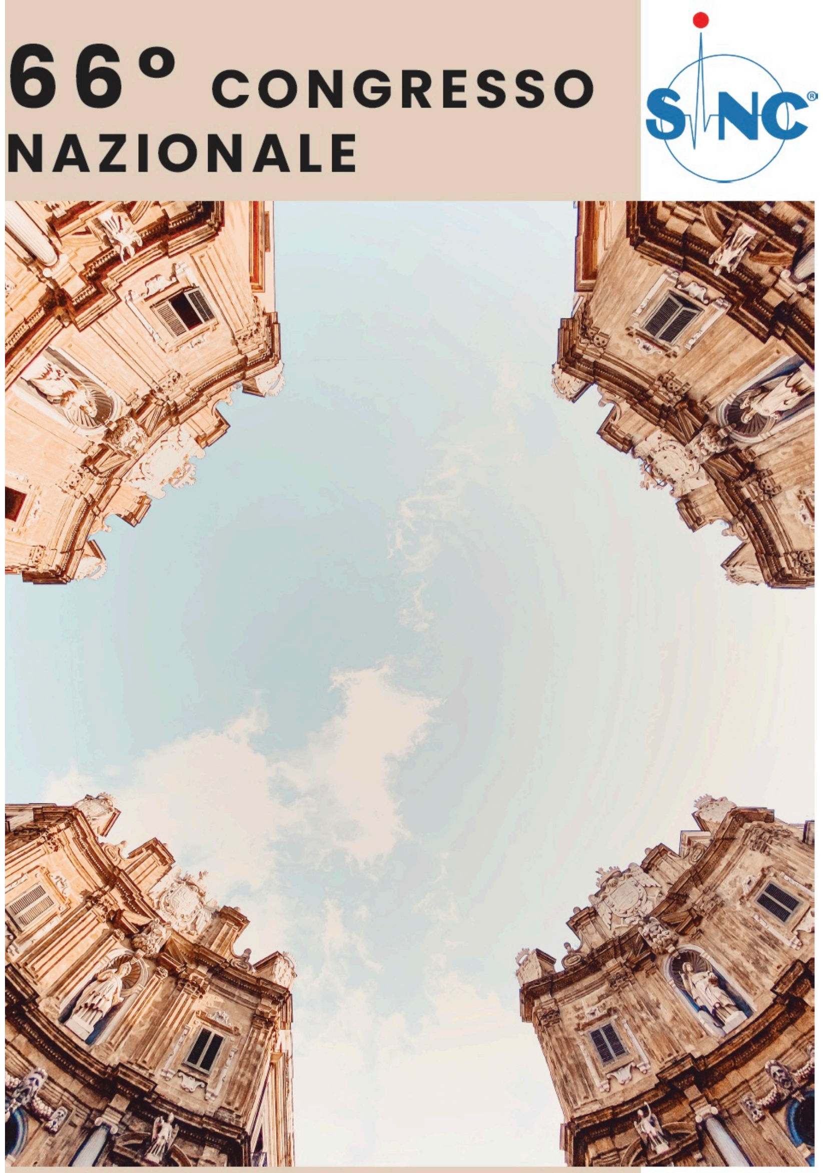
Palermo, 21 maggio 2022

66° CONGRESSO NAZIONALE

Sergio Bagnato

Servizio di Neurofisiologia e
UO Gravi Cerebrolesioni Acquisite
Fondazione G. Giglio
Cefalù (PA)

Trattamento dei disturbi non motori delle distonie

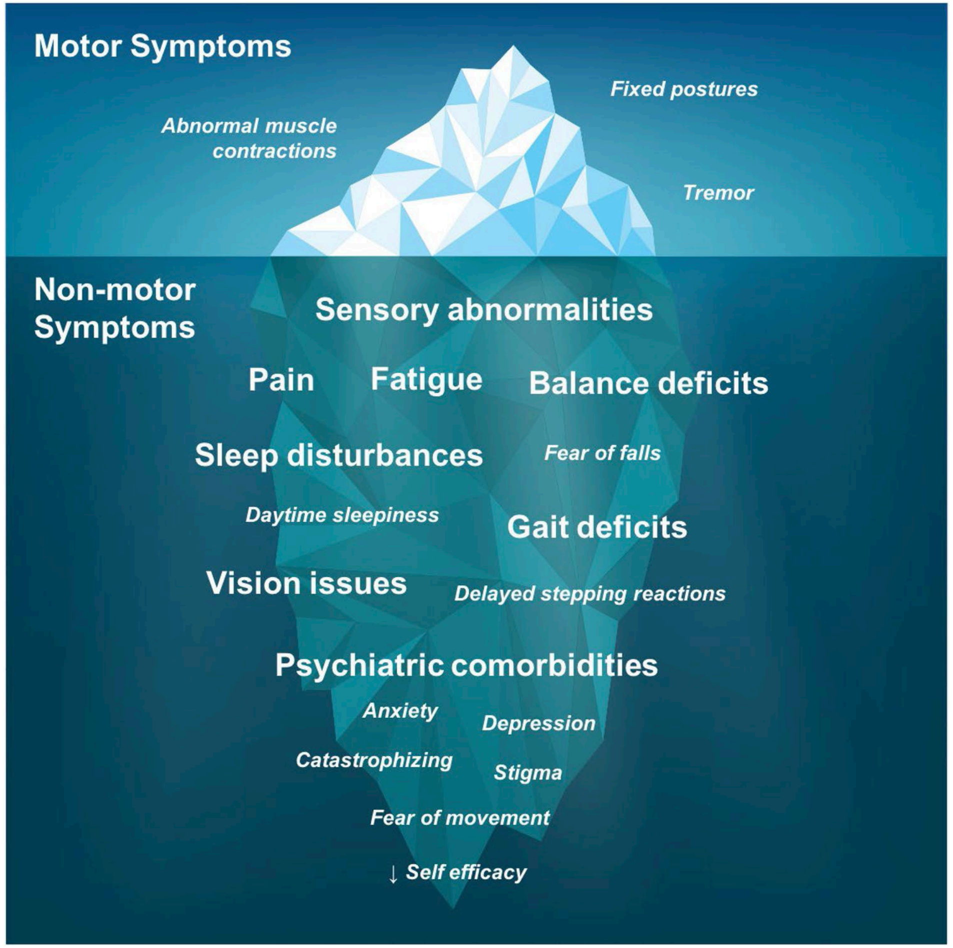

66° CONGRESSO NAZIONALE
SINC

Palermo, 21 maggio 2022

Dichiaro l'assenza di conflitti di interesse e l'assoluta autonomia dei contenuti scientifici e l'indipendenza da interessi economici commerciali.

Trattamento dei disturbi non motori delle distonie

Palermo, 21 maggio 2022


Motor Symptoms
Abnormal muscle contractions
Fixed postures
Tremor
Non-motor Symptoms
Sensory abnormalities
Pain
Fatigue
Balance deficits
Sleep disturbances
Fear of falls
Daytime sleepiness
Gait deficits
Vision issues
Delayed stepping reactions
Psychiatric comorbidities
Anxiety
Depression
Catastrophizing
Stigma
Fear of movement
↓ Self efficacy

Bradnam et al., 2021

Outline

- Inquadramento diagnostico dei disturbi non motori.
- Trattamenti disponibili (?).

Come valutare in maniera standardizzata i disturbi non motori nelle distonie?

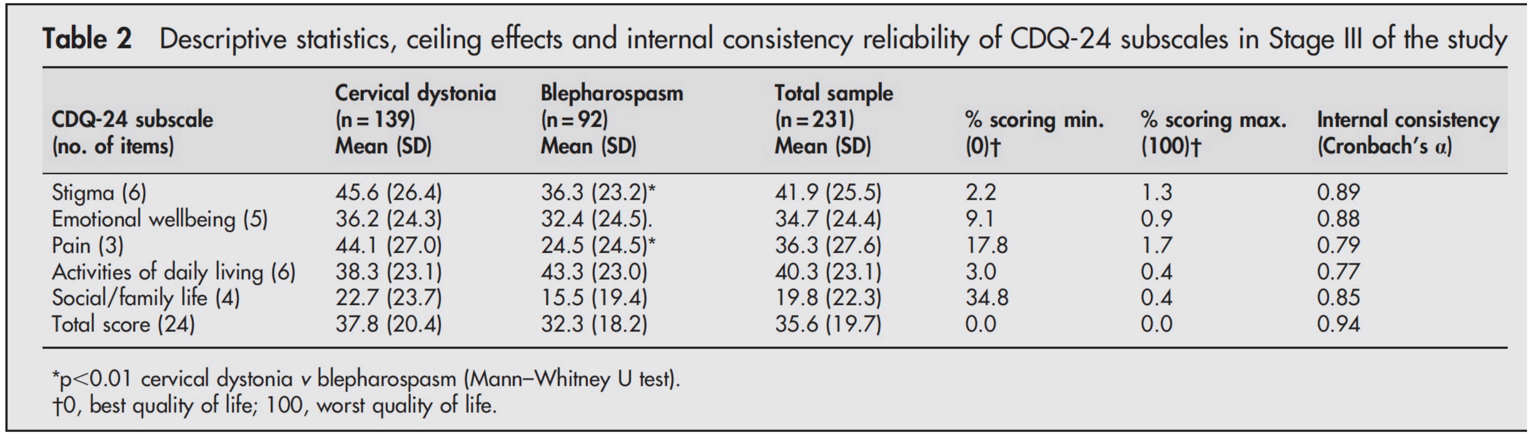
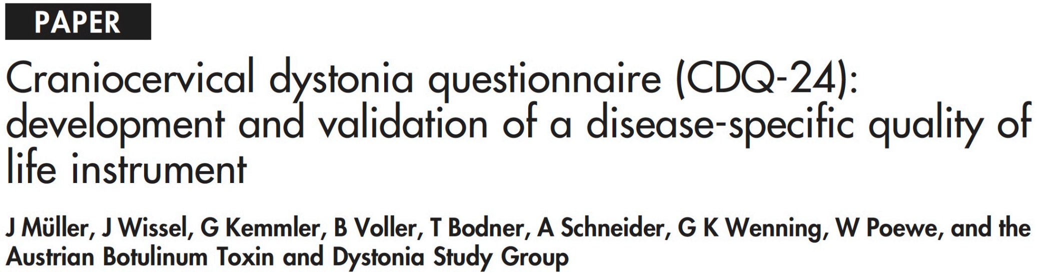


Table 2 Descriptive statistics, ceiling effects and internal consistency reliability of CDQ-24 subscales in Stage III of the study

CDQ-24 subscale (no. of items)	Cervical dystonia (n = 139) Mean (SD)	Blepharospasm (n = 92) Mean (SD)	Total sample (n = 231) Mean (SD)	% scoring min. (0)†	% scoring max. (100)†	Internal consistency (Cronbach's α)
Stigma (6)	45.6 (26.4)	36.3 (23.2)*	41.9 (25.5)	2.2	1.3	0.89
Emotional wellbeing (5)	36.2 (24.3)	32.4 (24.5).	34.7 (24.4)	9.1	0.9	0.88
Pain (3)	44.1 (27.0)	24.5 (24.5)*	36.3 (27.6)	17.8	1.7	0.79
Activities of daily living (6)	38.3 (23.1)	43.3 (23.0)	40.3 (23.1)	3.0	0.4	0.77
Social/family life (4)	22.7 (23.7)	15.5 (19.4)	19.8 (22.3)	34.8	0.4	0.85
Total score (24)	37.8 (20.4)	32.3 (18.2)	35.6 (19.7)	0.0	0.0	0.94

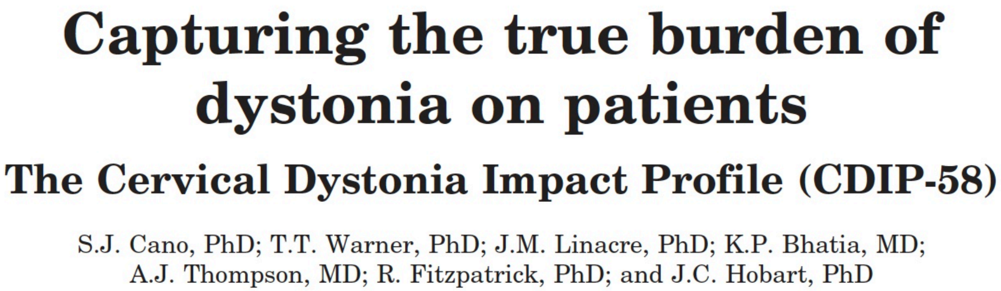
*$p<0.01$ cervical dystonia *v* blepharospasm (Mann–Whitney U test).
†0, best quality of life; 100, worst quality of life.



PAPER

Craniocervical dystonia questionnaire (CDQ-24): development and validation of a disease-specific quality of life instrument

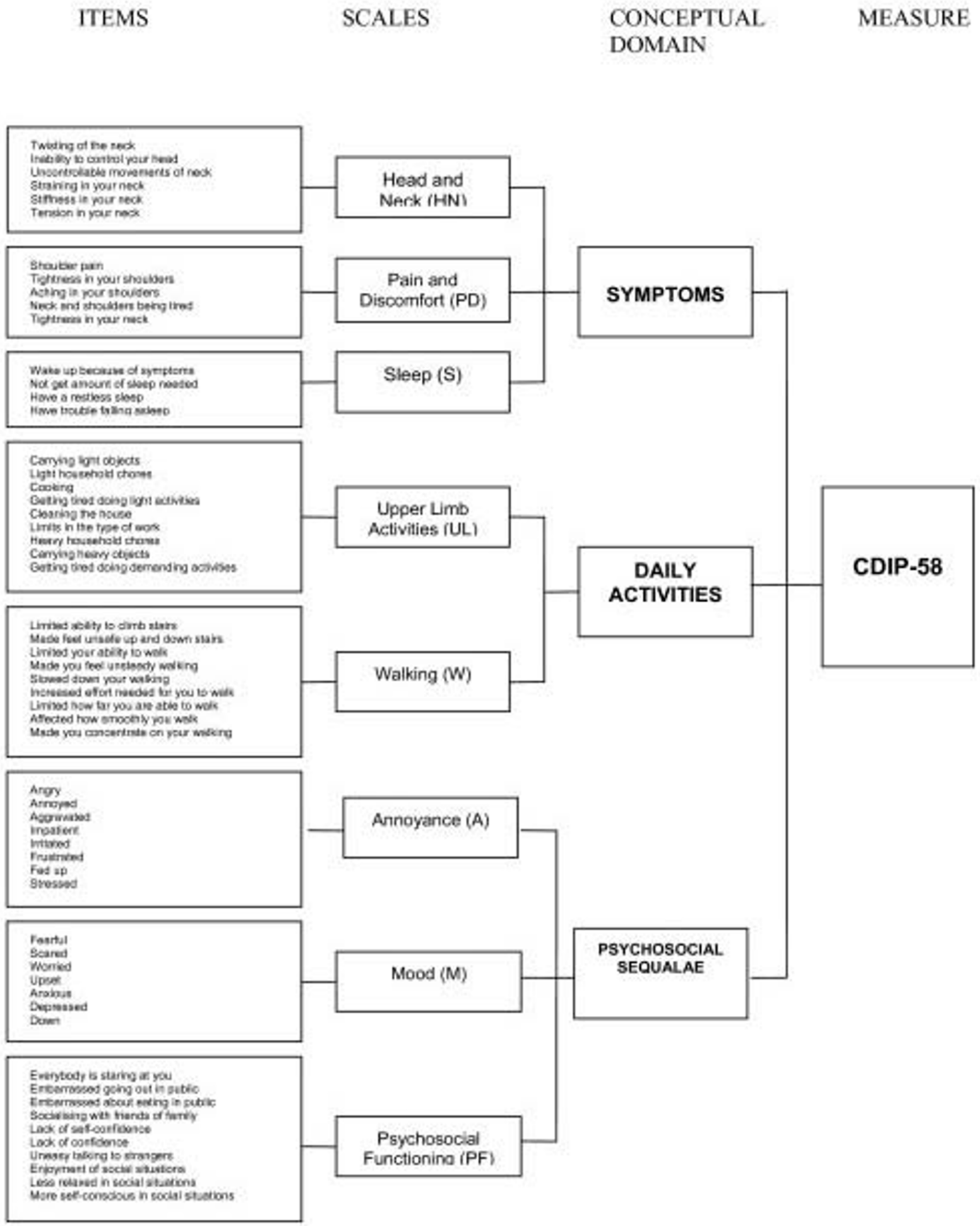
J Müller, J Wissel, G Kemmler, B Voller, T Bodner, A Schneider, G K Wenning, W Poewe, and the Austrian Botulinum Toxin and Dystonia Study Group



Capturing the true burden of dystonia on patients

The Cervical Dystonia Impact Profile (CDIP-58)

S.J. Cano, PhD; T.T. Warner, PhD; J.M. Linacre, PhD; K.P. Bhatia, MD;
A.J. Thompson, MD; R. Fitzpatrick, PhD; and J.C. Hobart, PhD



ITEMS

SCALES

CONCEPTUAL DOMAIN

MEASURE

Twisting of the neck
Inability to control your head
Uncontrollable movements of neck
Straining in your neck
Stiffness in your neck
Tension in your neck

Head and Neck (HN)

Shoulder pain
Tightness in your shoulders
Aching in your shoulders
Neck and shoulders being tired
Tightness in your neck

Pain and Discomfort (PD)

Wake up because of symptoms
Not get amount of sleep needed
Have a restless sleep
Have trouble falling asleep

Sleep (S)

SYMPTOMS

Carrying light objects
Light household chores
Cooking
Getting tired doing light activities
Cleaning the house
Limits in the type of work
Heavy household chores
Carrying heavy objects
Getting tired doing demanding activities

Upper Limb Activities (UL)

Limited ability to climb stairs
Made feel unsafe up and down stairs
Limited your ability to walk
Made you feel unsteady walking
Slowed down your walking
Increased effort needed for you to walk
Limited how far you are able to walk
Affected how smoothly you walk
Made you concentrate on your walking

Walking (W)

DAILY ACTIVITIES

CDIP-58

Angry
Annoyed
Aggravated
Impatient
Irritated
Frustrated
Fed up
Stressed

Annoyance (A)

Fearful
Scared
Worried
Upset
Anxious
Depressed
Down

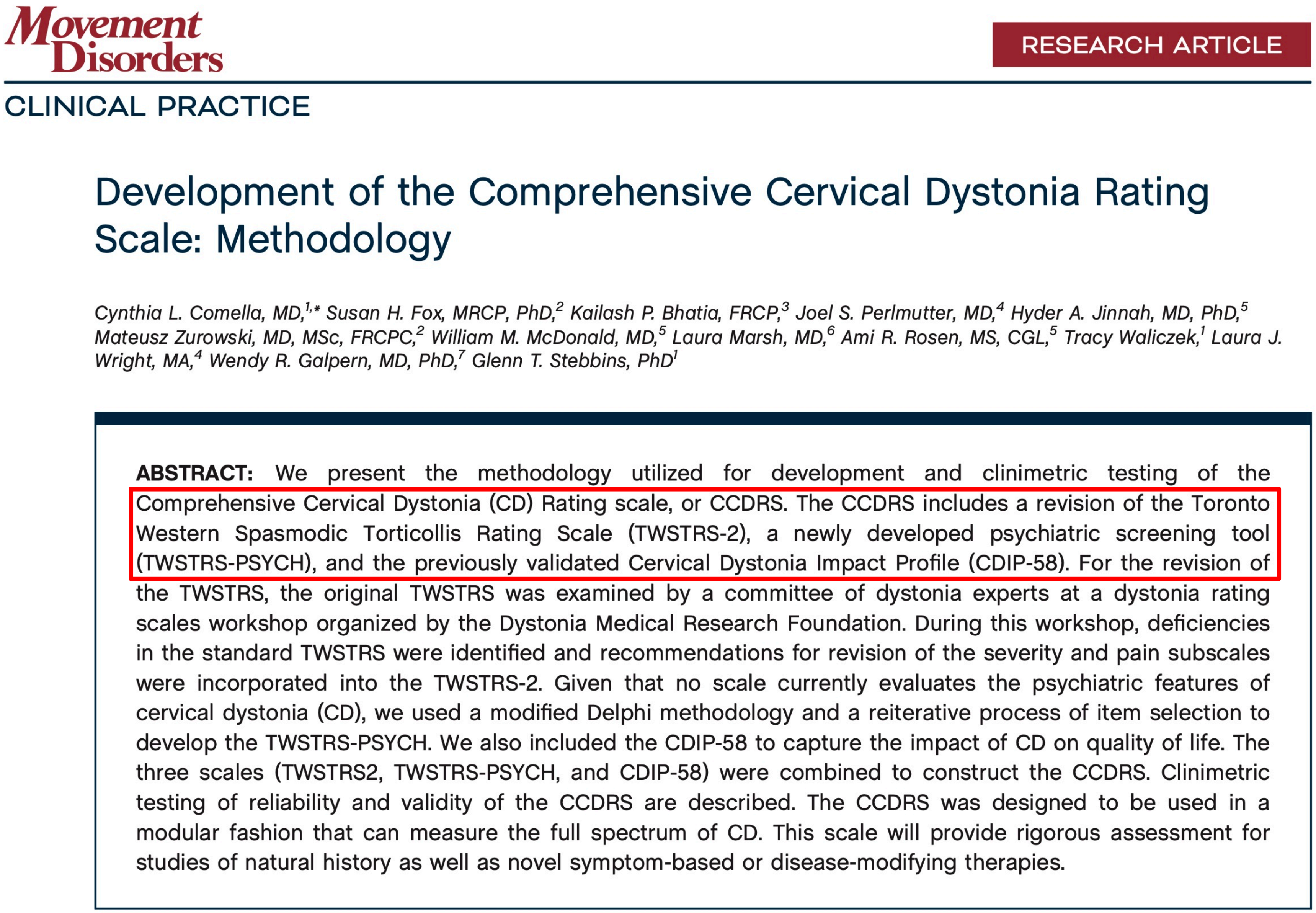
Mood (M)

Everybody is staring at you
Embarrassed going out in public
Embarrassed about eating in public
Socialising with friends of family
Lack of self-confidence
Lack of confidence
Uneasy talking to strangers
Enjoyment of social situations
Less relaxed in social situations
More self-conscious in social situations

Psychosocial Functioning (PF)

PSYCHOSOCIAL SEQUALAE

Come valutare in maniera standardizzata i disturbi non motori nelle distonie?



Movement Disorders
CLINICAL PRACTICE

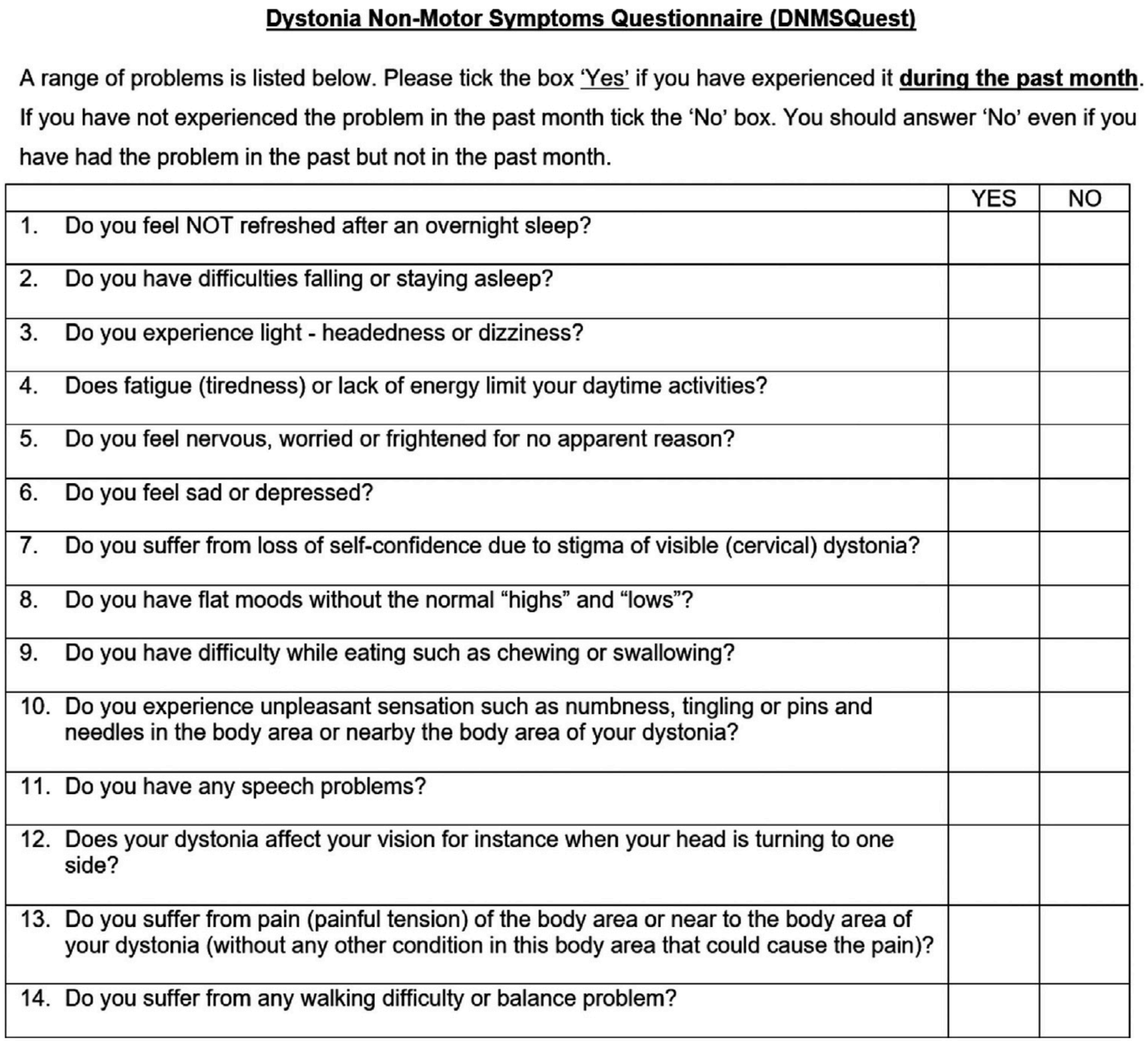
RESEARCH ARTICLE

Development of the Comprehensive Cervical Dystonia Rating Scale: Methodology

Cynthia L. Comella, MD,[1,] Susan H. Fox, MRCP, PhD,[2] Kailash P. Bhatia, FRCP,[3] Joel S. Perlmutter, MD,[4] Hyder A. Jinnah, MD, PhD,[5] Mateusz Zurowski, MD, MSc, FRCPC,[2] William M. McDonald, MD,[5] Laura Marsh, MD,[6] Ami R. Rosen, MS, CGL,[5] Tracy Waliczek,[1] Laura J. Wright, MA,[4] Wendy R. Galpern, MD, PhD,[7] Glenn T. Stebbins, PhD[1]*

ABSTRACT: We present the methodology utilized for development and clinimetric testing of the Comprehensive Cervical Dystonia (CD) Rating scale, or CCDRS. The CCDRS includes a revision of the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS-2), a newly developed psychiatric screening tool (TWSTRS-PSYCH), and the previously validated Cervical Dystonia Impact Profile (CDIP-58). For the revision of the TWSTRS, the original TWSTRS was examined by a committee of dystonia experts at a dystonia rating scales workshop organized by the Dystonia Medical Research Foundation. During this workshop, deficiencies in the standard TWSTRS were identified and recommendations for revision of the severity and pain subscales were incorporated into the TWSTRS-2. Given that no scale currently evaluates the psychiatric features of cervical dystonia (CD), we used a modified Delphi methodology and a reiterative process of item selection to develop the TWSTRS-PSYCH. We also included the CDIP-58 to capture the impact of CD on quality of life. The three scales (TWSTRS2, TWSTRS-PSYCH, and CDIP-58) were combined to construct the CCDRS. Clinimetric testing of reliability and validity of the CCDRS are described. The CCDRS was designed to be used in a modular fashion that can measure the full spectrum of CD. This scale will provide rigorous assessment for studies of natural history as well as novel symptom-based or disease-modifying therapies.

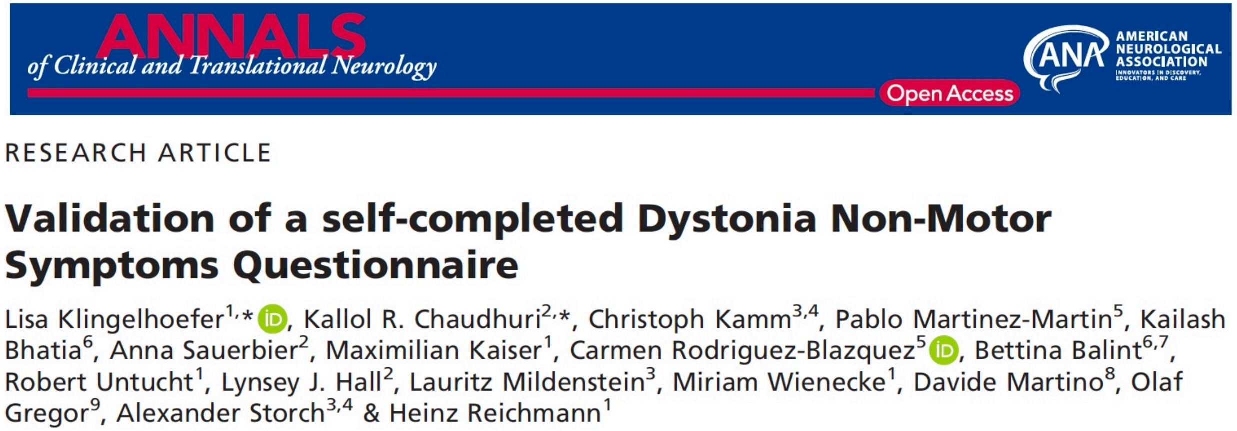
Come valutare in maniera standardizzata i disturbi non motori nelle distonie?



Dystonia Non-Motor Symptoms Questionnaire (DNMSQuest)

A range of problems is listed below. Please tick the box 'Yes' if you have experienced it **during the past month**. If you have not experienced the problem in the past month tick the 'No' box. You should answer 'No' even if you have had the problem in the past but not in the past month.

	YES	NO
1. Do you feel NOT refreshed after an overnight sleep?		
2. Do you have difficulties falling or staying asleep?		
3. Do you experience light - headedness or dizziness?		
4. Does fatigue (tiredness) or lack of energy limit your daytime activities?		
5. Do you feel nervous, worried or frightened for no apparent reason?		
6. Do you feel sad or depressed?		
7. Do you suffer from loss of self-confidence due to stigma of visible (cervical) dystonia?		
8. Do you have flat moods without the normal "highs" and "lows"?		
9. Do you have difficulty while eating such as chewing or swallowing?		
10. Do you experience unpleasant sensation such as numbness, tingling or pins and needles in the body area or nearby the body area of your dystonia?		
11. Do you have any speech problems?		
12. Does your dystonia affect your vision for instance when your head is turning to one side?		
13. Do you suffer from pain (painful tension) of the body area or near to the body area of your dystonia (without any other condition in this body area that could cause the pain)?		
14. Do you suffer from any walking difficulty or balance problem?		



ANNALS of Clinical and Translational Neurology

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RESEARCH ARTICLE

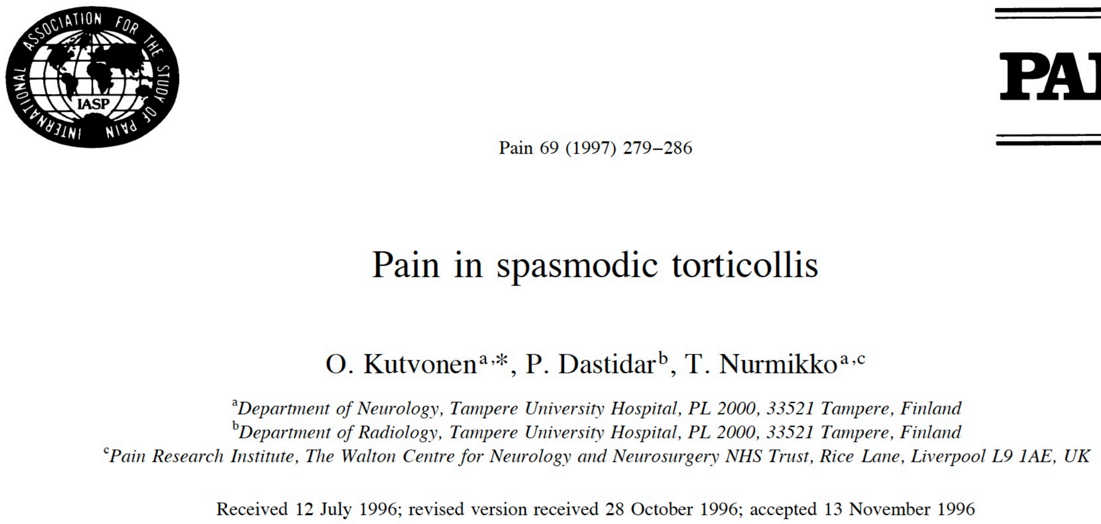
Validation of a self-completed Dystonia Non-Motor Symptoms Questionnaire

Lisa Klingelhoefer[1,*], Kallol R. Chaudhuri[2,*], Christoph Kamm[3,4], Pablo Martinez-Martin[5], Kailash Bhatia[6], Anna Sauerbier[2], Maximilian Kaiser[1], Carmen Rodriguez-Blazquez[5], Bettina Balint[6,7], Robert Untucht[1], Lynsey J. Hall[2], Lauritz Mildenstein[3], Miriam Wienecke[1], Davide Martino[8], Olaf Gregor[9], Alexander Storch[3,4] & Heinz Reichmann[1]

Annals of Clinical and Translational Neurology 2019; 6(10): 2054–2065

Il dolore nelle distonie

- Tra le varie forme di distonie, la più alta prevalenza di dolore si trova nella distonia cervicale, **interessando dal 55 al 90%** dei pazienti.
- Il dolore nella distonia cervicale è descritto come diffuso, trafittivo o talvolta urente a livello di collo e spalle che, spesso (ma non sempre), si irradia al lato della testa ed all’arto superiore omolaterali alla deviazione del capo.



PAIN

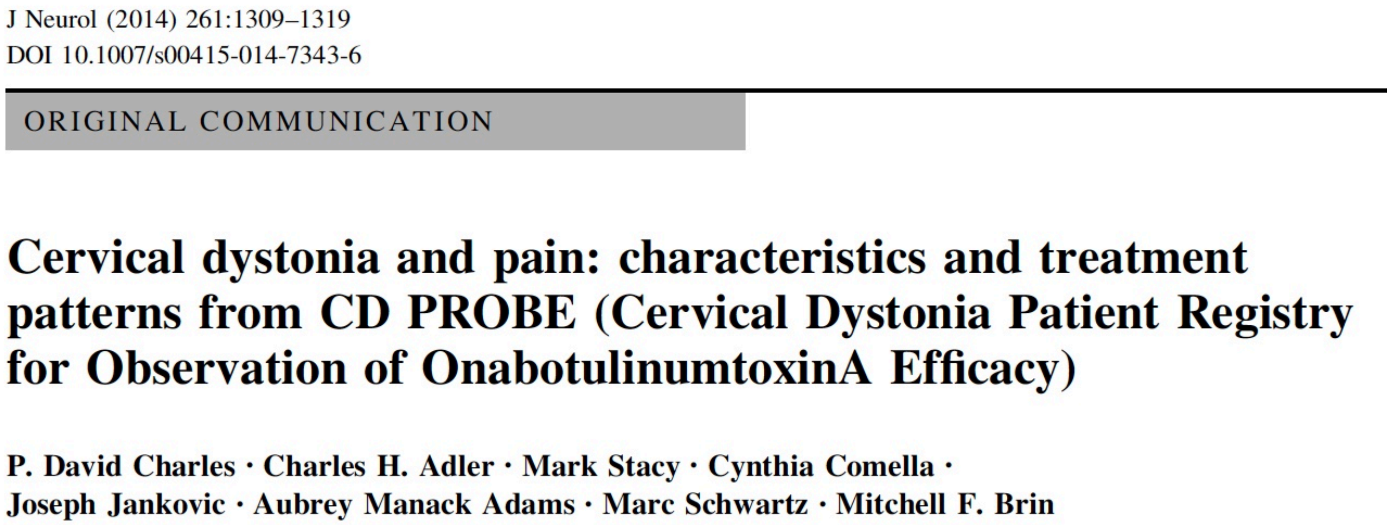
Pain 69 (1997) 279–286

Pain in spasmodic torticollis

O. Kutvonen[a,*], P. Dastidar[b], T. Nurmikko[a,c]

[a]*Department of Neurology, Tampere University Hospital, PL 2000, 33521 Tampere, Finland*
[b]*Department of Radiology, Tampere University Hospital, PL 2000, 33521 Tampere, Finland*
[c]*Pain Research Institute, The Walton Centre for Neurology and Neurosurgery NHS Trust, Rice Lane, Liverpool L9 1AE, UK*

Received 12 July 1996; revised version received 28 October 1996; accepted 13 November 1996



J Neurol (2014) 261:1309–1319
DOI 10.1007/s00415-014-7343-6

ORIGINAL COMMUNICATION

Cervical dystonia and pain: characteristics and treatment patterns from CD PROBE (Cervical Dystonia Patient Registry for Observation of OnabotulinumtoxinA Efficacy)

P. David Charles · Charles H. Adler · Mark Stacy · Cynthia Comella · Joseph Jankovic · Aubrey Manack Adams · Marc Schwartz · Mitchell F. Brin

Il dolore nella distonia cervicale

- Il dolore nella distonia cervicale non sempre correla con la severità della sintomatologia motoria o con l’entità dei cambiamenti della postura del capo.
- I meccanismi alla base del dolore nella distonia cervicale sono di tipo muscolare e non-muscolare. Diverse evidenze suggeriscono che, in aggiunta alla prolungata contrazione muscolare, possano contribuire al dolore altri meccanismi quali l’alterata trasmissione e processazione degli stimoli nocicettivi, la disfunzione dei sistemi discendenti di inibizione del dolore e la presenza di alterazioni funzionali a livello dei nuclei della base e della corteccia.

Parkinsonism and Related Disorders 65 (2019) 252–255

Contents lists available at ScienceDirect

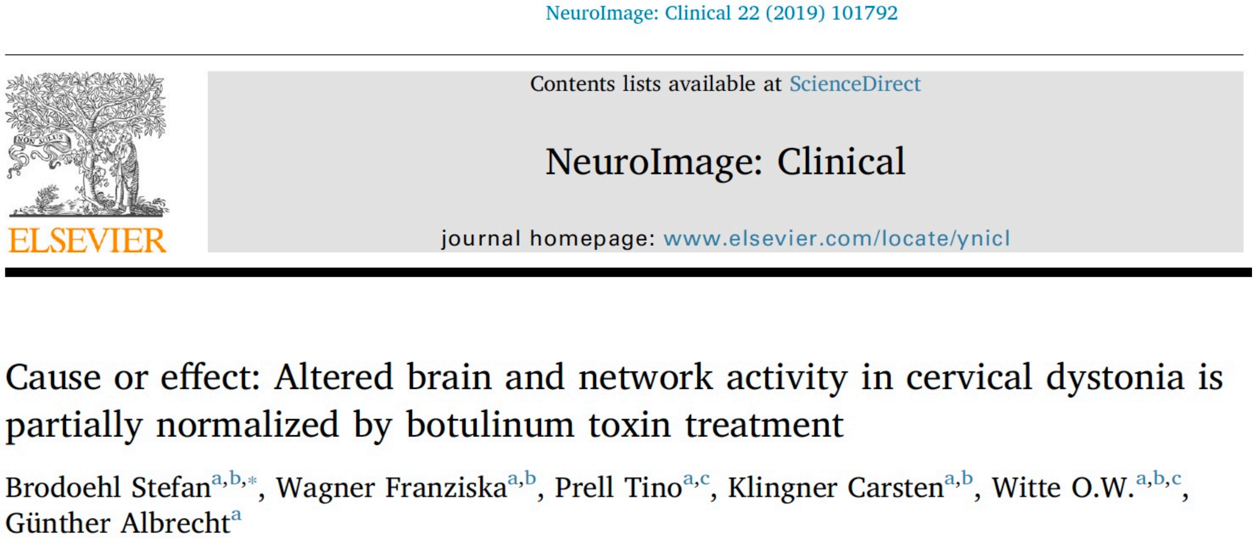
Parkinsonism and Related Disorders

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

Short communication

Pain in cervical dystonia: Evidence of abnormal inhibitory control

Michele Tinazzi[a,1], Giovanna Maddalena Squintani[b,1], Kailash P. Bhatia[c], Alessia Segatti[b], Francesco Donato[d], Massimiliano Valeriani[e], Roberto Erro[f,*]



NeuroImage: Clinical 22 (2019) 101792

Contents lists available at ScienceDirect

NeuroImage: Clinical

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

Cause or effect: Altered brain and network activity in cervical dystonia is partially normalized by botulinum toxin treatment

Brodoehl Stefan[a,b,*], Wagner Franziska[a,b], Prell Tino[a,c], Klingner Carsten[a,b], Witte O.W.[a,b,c], Günther Albrecht[a]

Come valutare il dolore nella distonia cervicale?

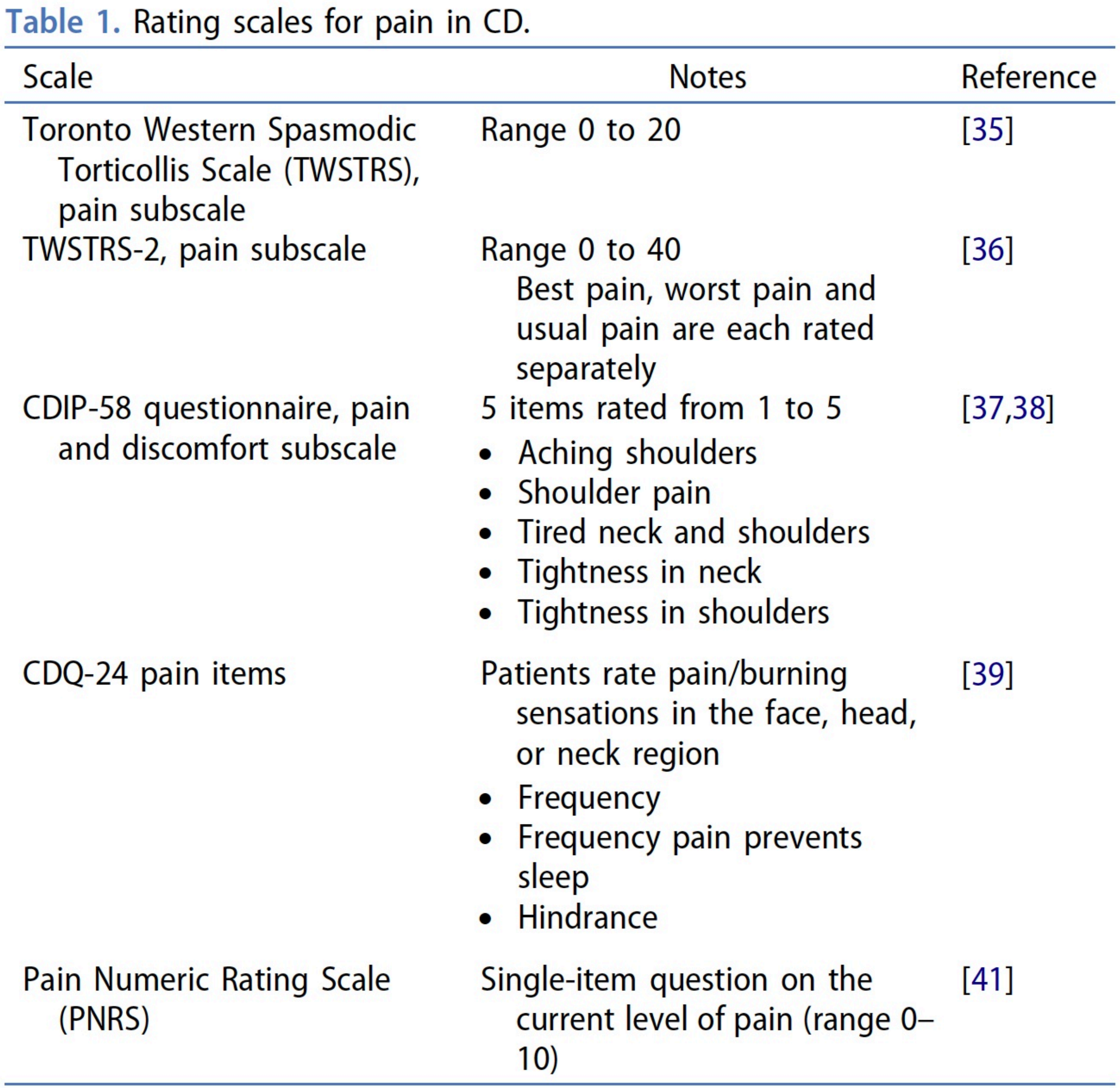
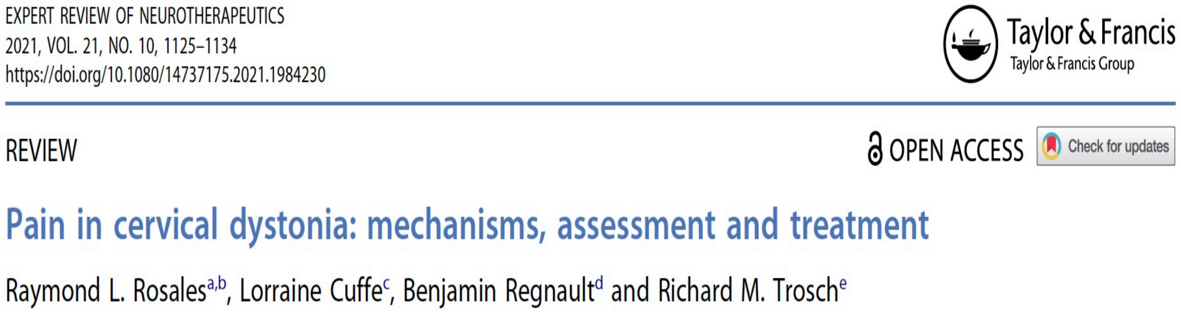


Table 1. Rating scales for pain in CD.

Scale	Notes	Reference
Toronto Western Spasmodic Torticollis Scale (TWSTRS), pain subscale	Range 0 to 20	[35]
TWSTRS-2, pain subscale	Range 0 to 40 Best pain, worst pain and usual pain are each rated separately	[36]
CDIP-58 questionnaire, pain and discomfort subscale	5 items rated from 1 to 5 • Aching shoulders • Shoulder pain • Tired neck and shoulders • Tightness in neck • Tightness in shoulders	[37,38]
CDQ-24 pain items	Patients rate pain/burning sensations in the face, head, or neck region • Frequency • Frequency pain prevents sleep • Hindrance	[39]
Pain Numeric Rating Scale (PNRS)	Single-item question on the current level of pain (range 0–10)	[41]



EXPERT REVIEW OF NEUROTHERAPEUTICS
2021, VOL. 21, NO. 10, 1125–1134
https://doi.org/10.1080/14737175.2021.1984230

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REVIEW

OPEN ACCESS Check for updates

Pain in cervical dystonia: mechanisms, assessment and treatment

Raymond L. Rosales[a,b], Lorraine Cuffe[c], Benjamin Regnault[d] and Richard M. Trosch[e]

Trattamento del dolore nella distonia cervicale

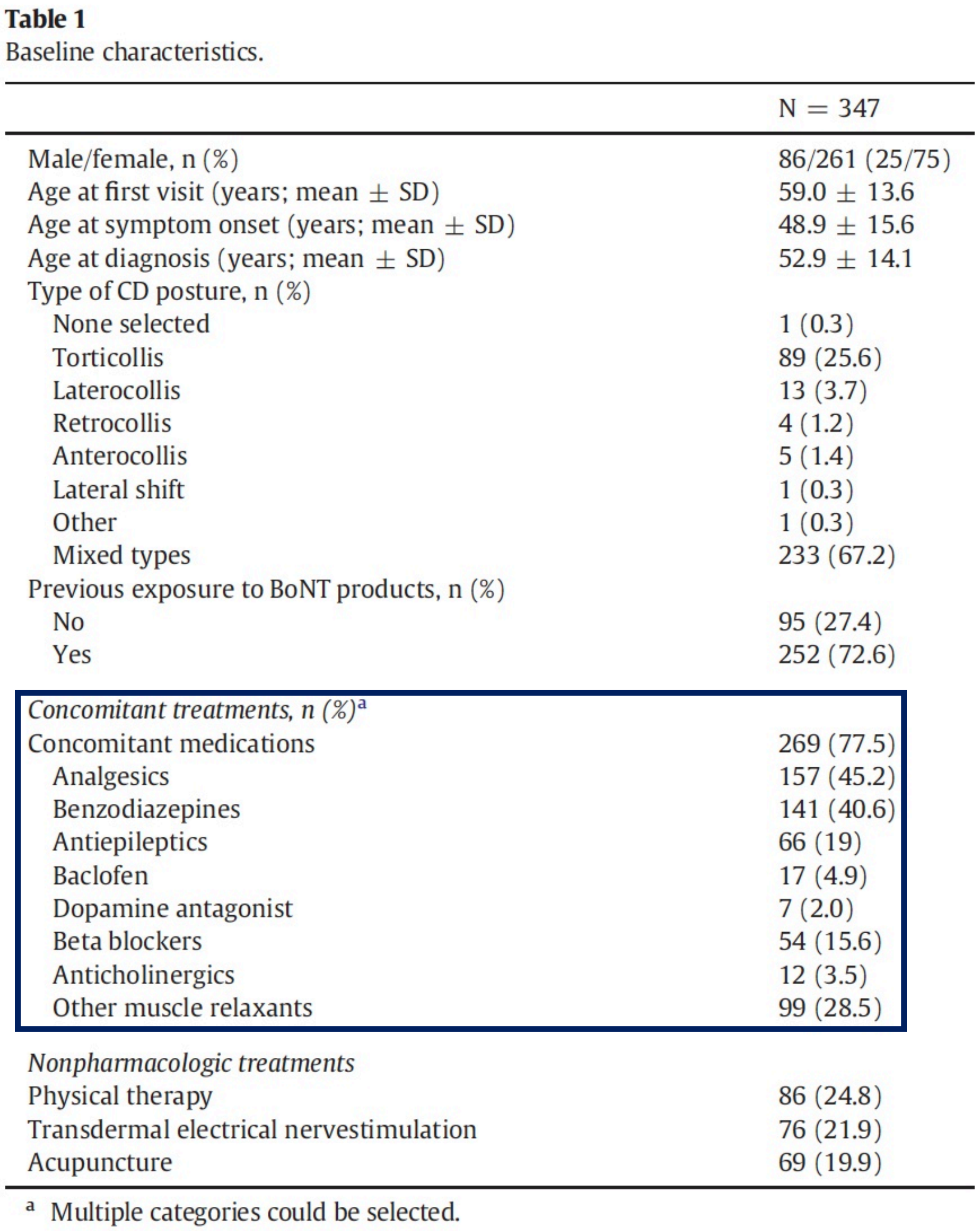
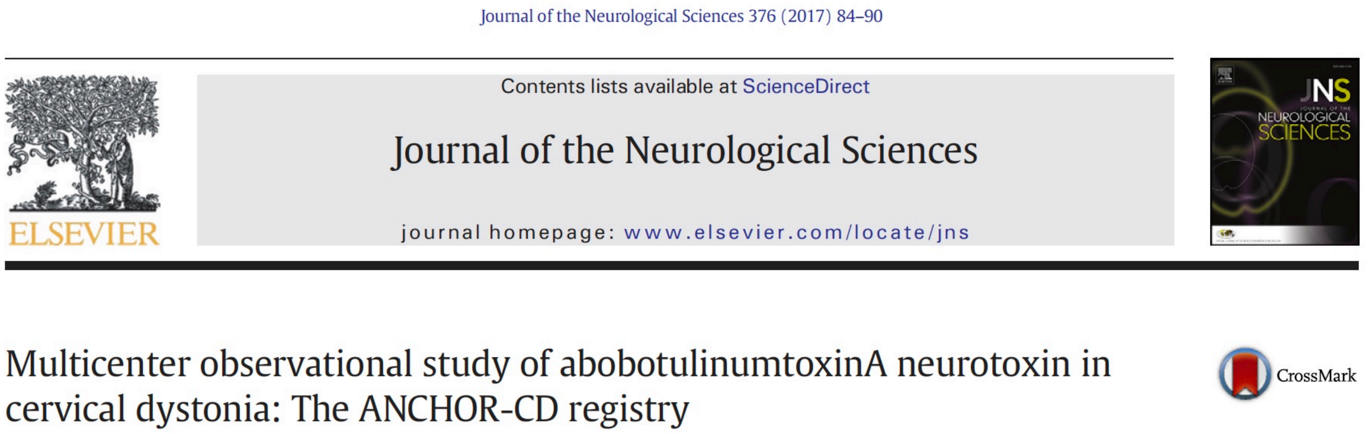


Table 1
Baseline characteristics.

	N = 347
Male/female, n (%)	86/261 (25/75)
Age at first visit (years; mean ± SD)	59.0 ± 13.6
Age at symptom onset (years; mean ± SD)	48.9 ± 15.6
Age at diagnosis (years; mean ± SD)	52.9 ± 14.1
Type of CD posture, n (%)	
None selected	1 (0.3)
Torticollis	89 (25.6)
Laterocollis	13 (3.7)
Retrocollis	4 (1.2)
Anterocollis	5 (1.4)
Lateral shift	1 (0.3)
Other	1 (0.3)
Mixed types	233 (67.2)
Previous exposure to BoNT products, n (%)	
No	95 (27.4)
Yes	252 (72.6)
Concomitant treatments, n (%)[a]	
Concomitant medications	269 (77.5)
Analgesics	157 (45.2)
Benzodiazepines	141 (40.6)
Antiepileptics	66 (19)
Baclofen	17 (4.9)
Dopamine antagonist	7 (2.0)
Beta blockers	54 (15.6)
Anticholinergics	12 (3.5)
Other muscle relaxants	99 (28.5)
Nonpharmacologic treatments	
Physical therapy	86 (24.8)
Transdermal electrical nervestimulation	76 (21.9)
Acupuncture	69 (19.9)

[a] Multiple categories could be selected.



Journal of the Neurological Sciences 376 (2017) 84–90

Contents lists available at ScienceDirect

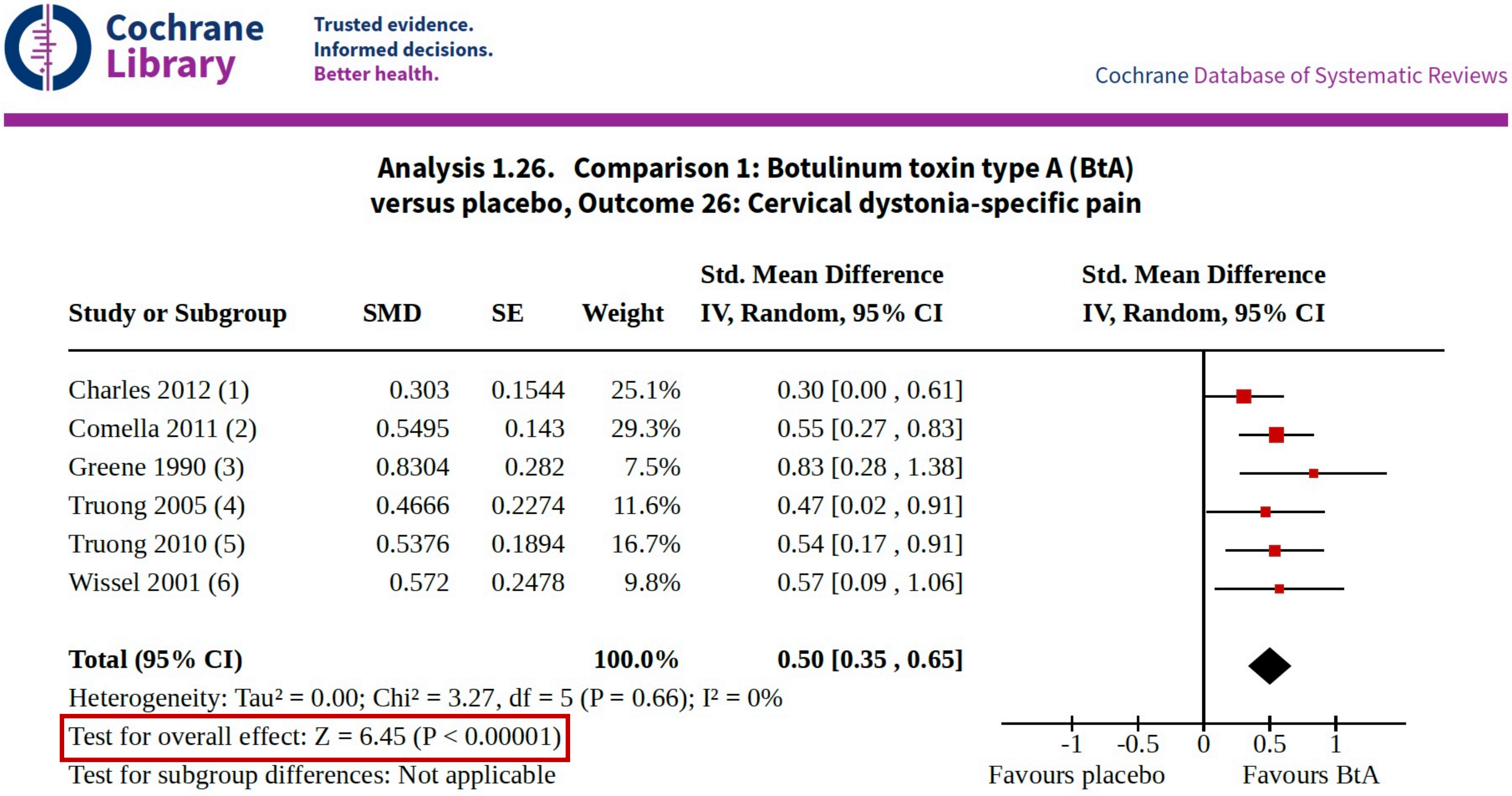
Journal of the Neurological Sciences

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

Multicenter observational study of abobotulinumtoxinA neurotoxin in cervical dystonia: The ANCHOR-CD registry

I farmaci analgesici (prevalentemente FANS) sono i farmaci più comunemente assunti dai pazienti con distonia cervicale.

Trattamento del dolore nella distonia cervicale: tossina botulinica



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Analysis 1.26. Comparison 1: Botulinum toxin type A (BtA) versus placebo, Outcome 26: Cervical dystonia-specific pain

Study or Subgroup	SMD	SE	Weight	Std. Mean Difference IV, Random, 95% CI
Charles 2012 (1)	0.303	0.1544	25.1%	0.30 [0.00 , 0.61]
Comella 2011 (2)	0.5495	0.143	29.3%	0.55 [0.27 , 0.83]
Greene 1990 (3)	0.8304	0.282	7.5%	0.83 [0.28 , 1.38]
Truong 2005 (4)	0.4666	0.2274	11.6%	0.47 [0.02 , 0.91]
Truong 2010 (5)	0.5376	0.1894	16.7%	0.54 [0.17 , 0.91]
Wissel 2001 (6)	0.572	0.2478	9.8%	0.57 [0.09 , 1.06]
Total (95% CI)			**100.0%**	**0.50 [0.35 , 0.65]**

Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.27, df = 5 ($P = 0.66$); I^2 = 0%

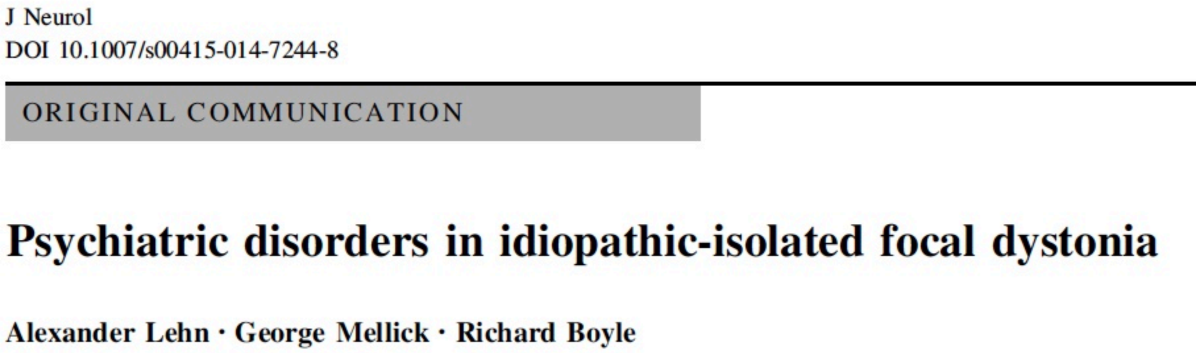
Test for overall effect: Z = 6.45 ($P < 0.00001$)

Test for subgroup differences: Not applicable

Riduzione di 2.11 punti vs. placebo del TWSTRS pain subscore a 4 settimane dal trattamento con BtA (qualunque brand).

Castelão et al. Cochrane Database Syst Rev. 2017

Disturbi psichiatrici nelle distonie


J Neurol
DOI 10.1007/s00415-014-7244-8

ORIGINAL COMMUNICATION

Psychiatric disorders in idiopathic-isolated focal dystonia

Alexander Lehn · George Mellick · Richard Boyle

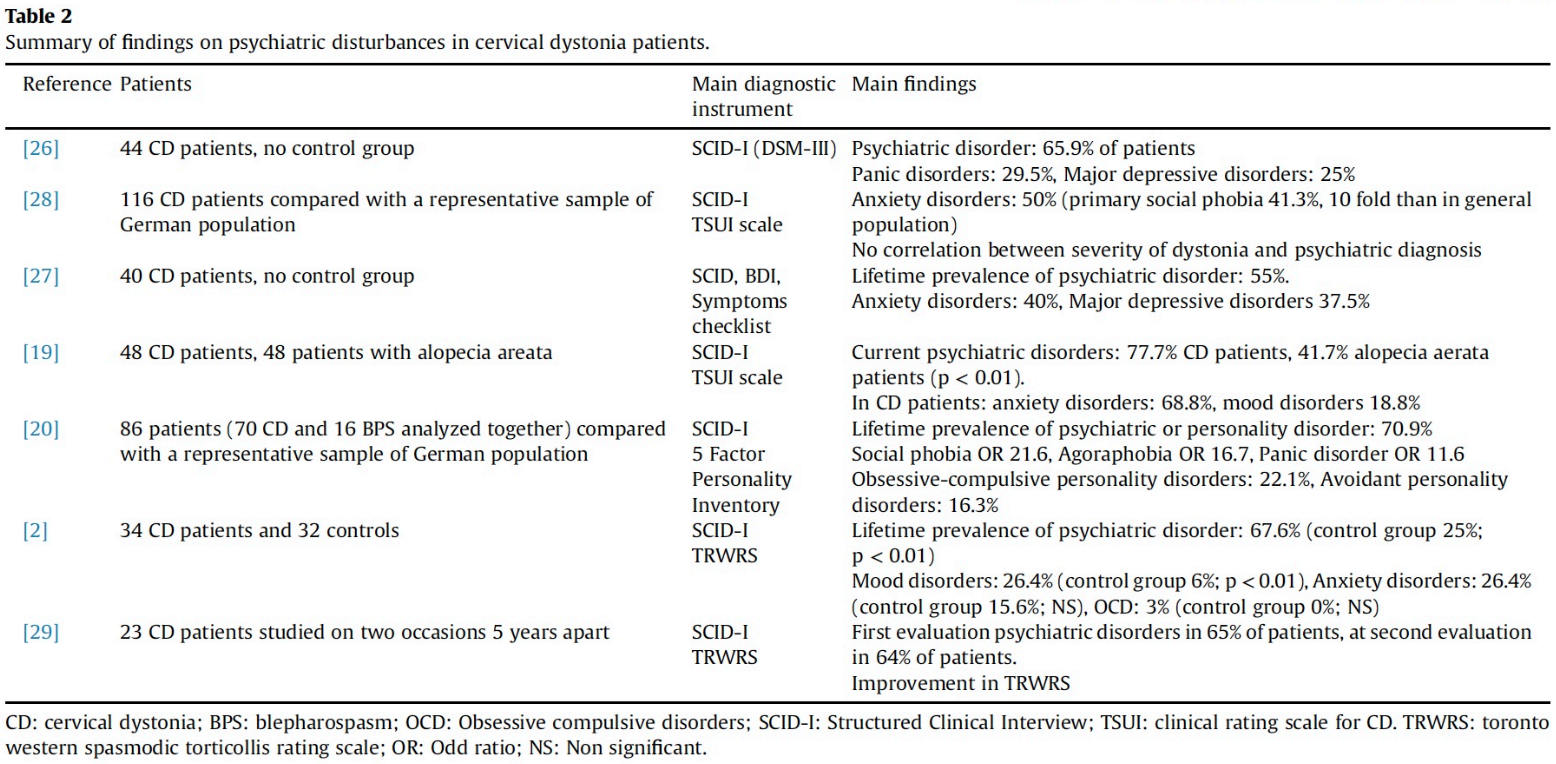
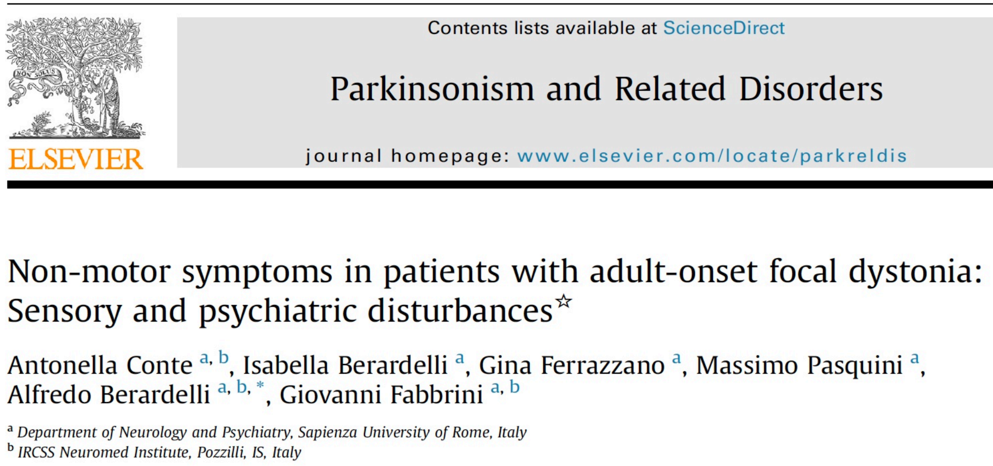


Table 2
Summary of findings on psychiatric disturbances in cervical dystonia patients.

Reference	Patients	Main diagnostic instrument	Main findings
[26]	44 CD patients, no control group	SCID-I (DSM-III)	Psychiatric disorder: 65.9% of patients Panic disorders: 29.5%, Major depressive disorders: 25%
[28]	116 CD patients compared with a representative sample of German population	SCID-I TSUI scale	Anxiety disorders: 50% (primary social phobia 41.3%, 10 fold than in general population) No correlation between severity of dystonia and psychiatric diagnosis
[27]	40 CD patients, no control group	SCID, BDI, Symptoms checklist	Lifetime prevalence of psychiatric disorder: 55%. Anxiety disorders: 40%, Major depressive disorders 37.5%
[19]	48 CD patients, 48 patients with alopecia areata	SCID-I TSUI scale	Current psychiatric disorders: 77.7% CD patients, 41.7% alopecia aerata patients ($p < 0.01$). In CD patients: anxiety disorders: 68.8%, mood disorders 18.8%
[20]	86 patients (70 CD and 16 BPS analyzed together) compared with a representative sample of German population	SCID-I 5 Factor Personality Inventory	Lifetime prevalence of psychiatric or personality disorder: 70.9% Social phobia OR 21.6, Agoraphobia OR 16.7, Panic disorder OR 11.6 Obsessive-compulsive personality disorders: 22.1%, Avoidant personality disorders: 16.3%
[2]	34 CD patients and 32 controls	SCID-I TRWRS	Lifetime prevalence of psychiatric disorder: 67.6% (control group 25%; $p < 0.01$) Mood disorders: 26.4% (control group 6%; $p < 0.01$), Anxiety disorders: 26.4% (control group 15.6%; NS), OCD: 3% (control group 0%; NS)
[29]	23 CD patients studied on two occasions 5 years apart	SCID-I TRWRS	First evaluation psychiatric disorders in 65% of patients, at second evaluation in 64% of patients. Improvement in TRWRS

CD: cervical dystonia; BPS: blepharospasm; OCD: Obsessive compulsive disorders; SCID-I: Structured Clinical Interview; TSUI: clinical rating scale for CD. TRWRS: toronto western spasmodic torticollis rating scale; OR: Odd ratio; NS: Non significant.


Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

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

ELSEVIER

Non-motor symptoms in patients with adult-onset focal dystonia: Sensory and psychiatric disturbances☆

Antonella Conte [a, b], Isabella Berardelli [a], Gina Ferrazzano [a], Massimo Pasquini [a], Alfredo Berardelli [a, b, *], Giovanni Fabbrini [a, b]

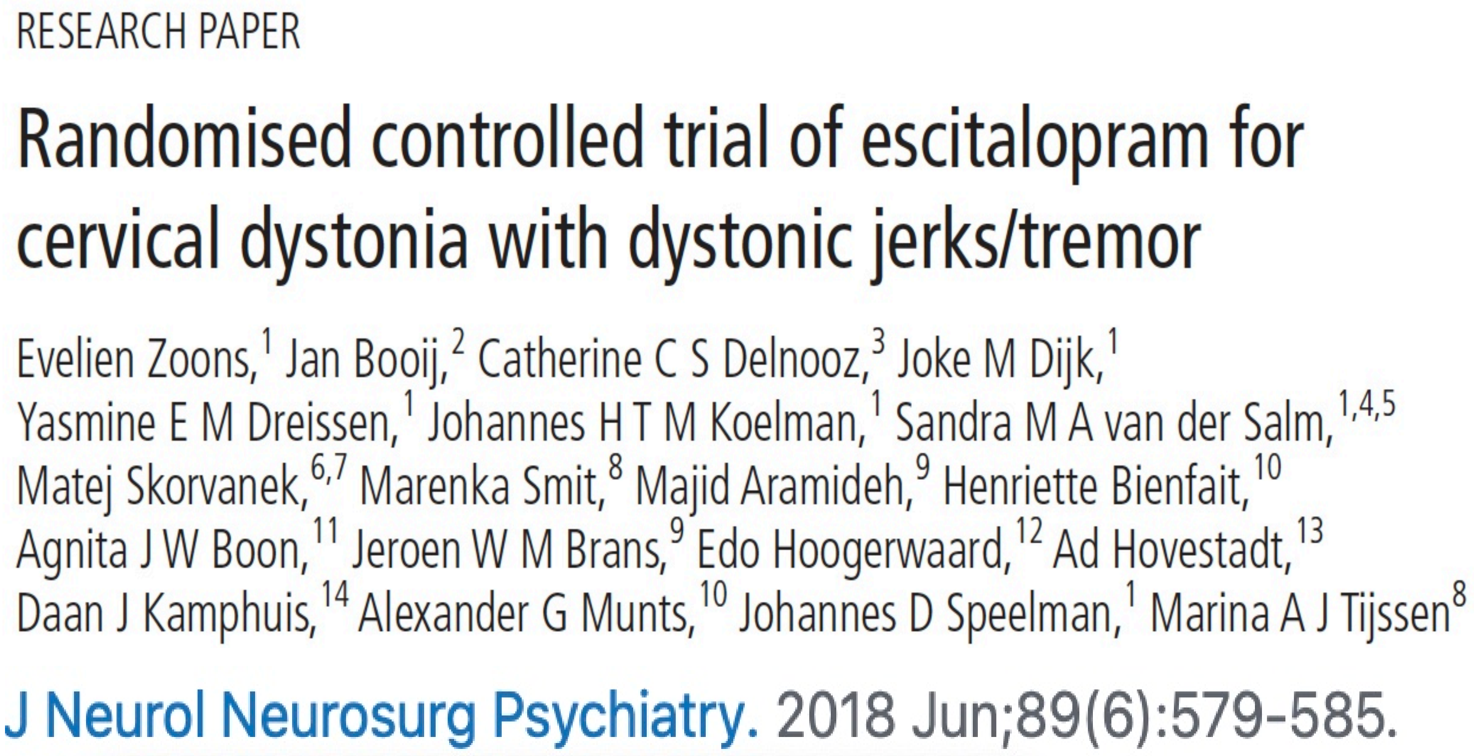
[a] *Department of Neurology and Psychiatry, Sapienza University of Rome, Italy*
[b] *IRCSS Neuromed Institute, Pozzilli, IS, Italy*

Tabella da Conte et al. 2016.

Trattamento dei disturbi psichiatrici nelle distonie: escitalopram

Studio randomizzato controllato con disegno crossover su 49 pazienti con distonia cervicale trattati per 6 settimane con escitalopram (10 mg) o placebo. L'endpoint primario era il miglioramento dei disturbi motori, il secondario il miglioramento dei disturbi psichiatrici e della qualità della vita.

Sia durante il trattamento con escitalopram che con placebo si è avuto un miglioramento dei disturbi motori e psichiatrici e della qualità della vita **senza differenze significative**.



RESEARCH PAPER

Randomised controlled trial of escitalopram for cervical dystonia with dystonic jerks/tremor

Evelien Zoons,[1] Jan Booij,[2] Catherine C S Delnooz,[3] Joke M Dijk,[1]
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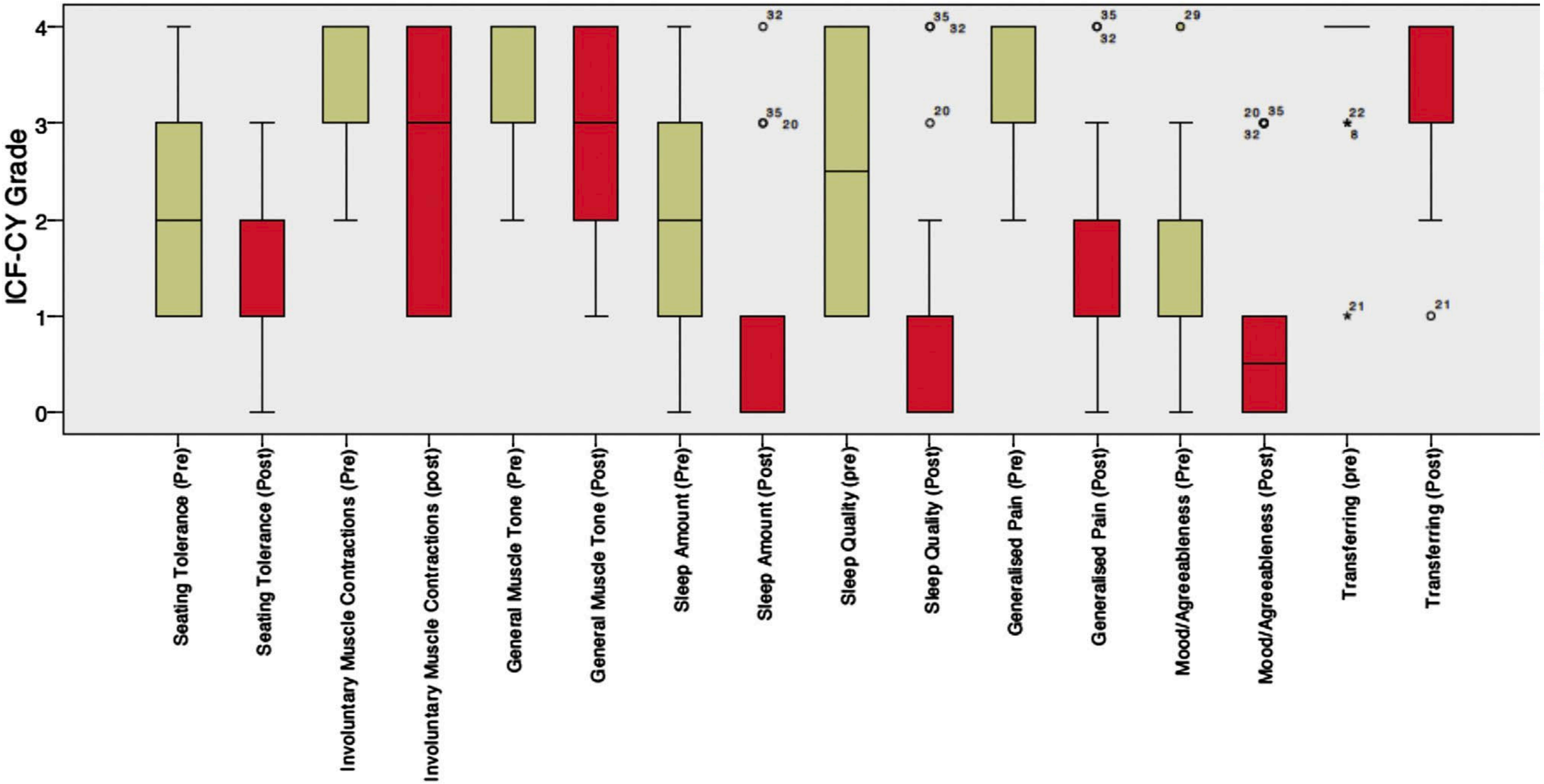
J Neurol Neurosurg Psychiatry. 2018 Jun;89(6):579-585.

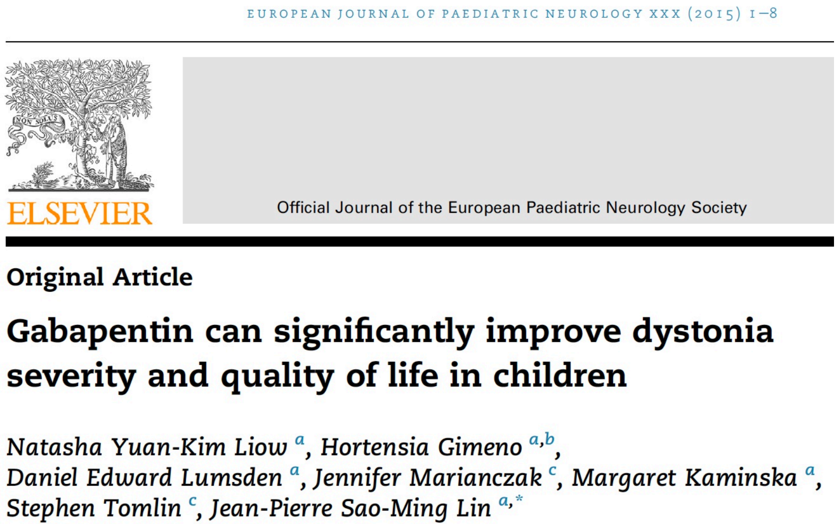
Trattamento dei disturbi psichiatrici nelle distonie: gabapentin

Studio retrospettivo su 69 bambini con distonia di diversa eziologia trattati con gabapentin a dosaggi molto variabili (anche oltre il dosaggio massimo raccomandato in età pediatrica di 70 mg/Kg/die).

Si è avuto un miglioramento sia dei sintomi motori che di umore, dolore, qualità del sonno e qualità della vita.

Limiti: disegno dello studio, eziologie differenti, non omogeneità nella gravità dei sintomi, assunzione di altri farmaci oltre il gabapentin in diversi bambini.

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Original Article

Gabapentin can significantly improve dystonia severity and quality of life in children

Natasha Yuan-Kim Liow [a], *Hortensia Gimeno* [a,b], *Daniel Edward Lumsden* [a], *Jennifer Marianczak* [c], *Margaret Kaminska* [a], *Stephen Tomlin* [c], *Jean-Pierre Sao-Ming Lin* [a,*]

Trattamento dei disturbi psichiatrici delle distonie: terapia cognitivo-comportamentale

Studio su 20 pazienti con distonia cervicale divisi in due gruppi (n = 10) trattati o non trattati per 8 settimane con terapia cognitivo-comportamentale somministrata su una specifica piattaforma internet.
Sebbene non siano state osservate differenze statisticamente significative tra i due gruppi a tre mesi (Beck's Depression Inventory p = 0.067), i pazienti trattati presentavano un trend verso un miglioramento dei livelli di ansia e depressione.

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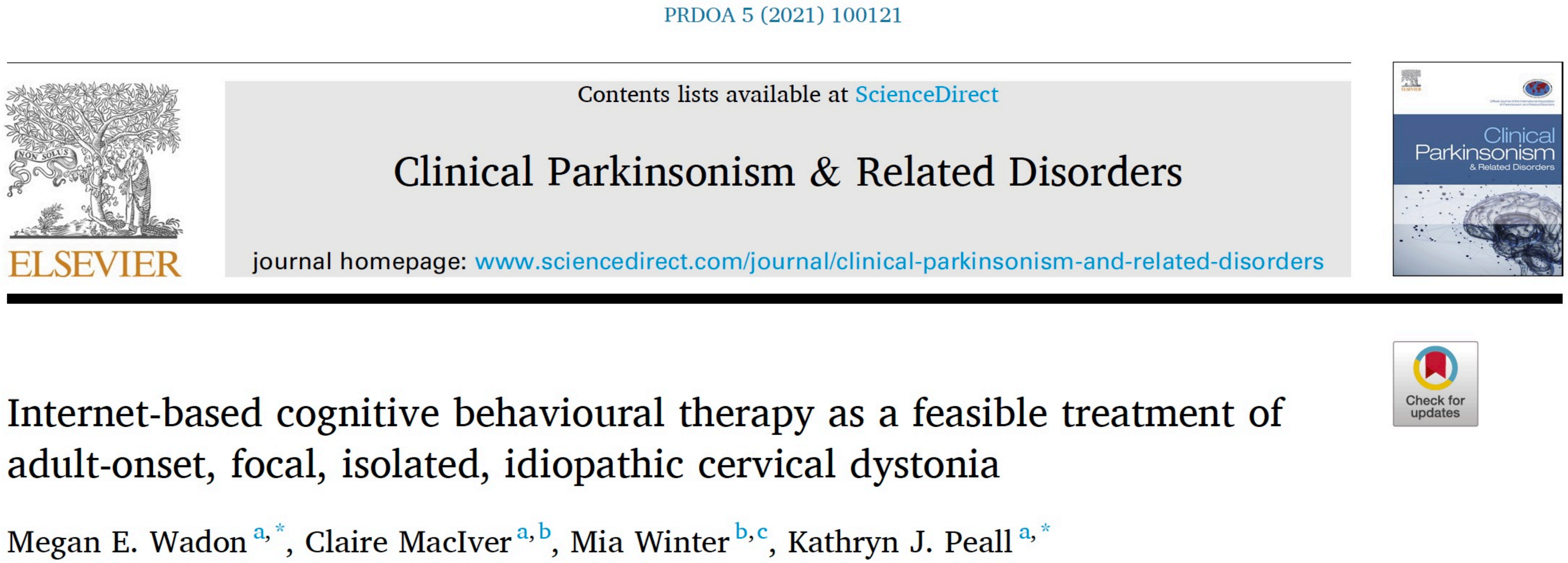

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Clinical Parkinsonism & Related Disorders

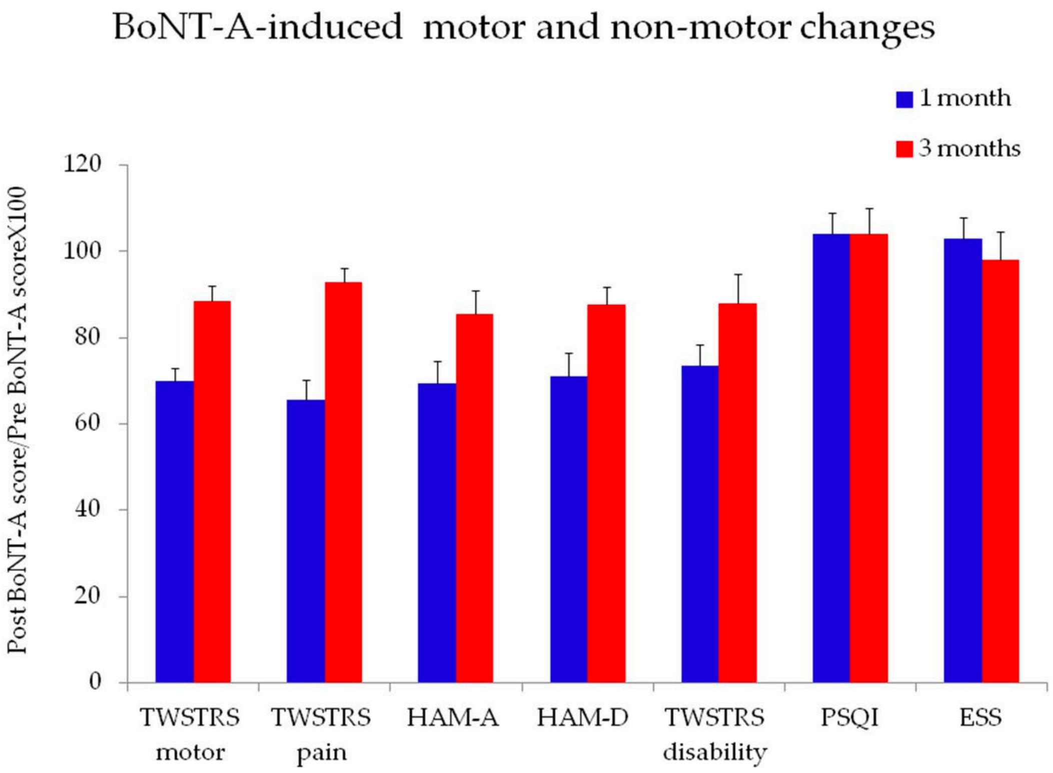
journal homepage: www.sciencedirect.com/journal/clinical-parkinsonism-and-related-disorders

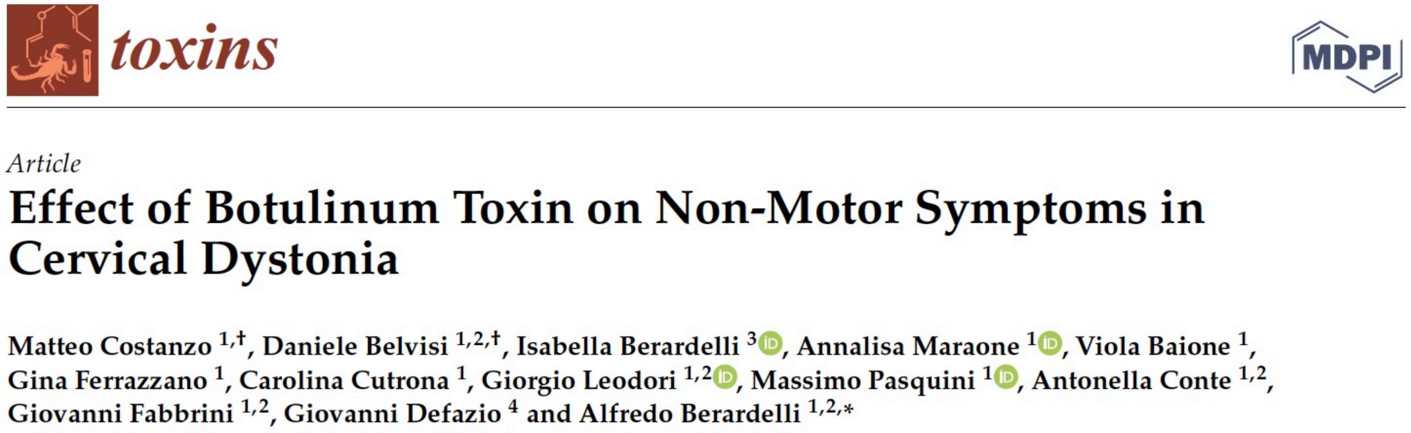
Internet-based cognitive behavioural therapy as a feasible treatment of adult-onset, focal, isolated, idiopathic cervical dystonia

Megan E. Wadon [a,*], Claire MacIver [a,b], Mia Winter [b,c], Kathryn J. Peall [a,*]

Trattamento dei disturbi non motori delle distonie: tossina botulinica

Studio prospettico su 45 pazienti con distonia cervicale (43 pazienti già trattati con tossina botulinica).
La tossina botulinica ha indotto un significativo miglioramento non solo nei disturbi motori ma anche dei disturbi psichiatrici, del dolore e della disabilità. Non si sono avuti effetti sulla qualità del sonno.



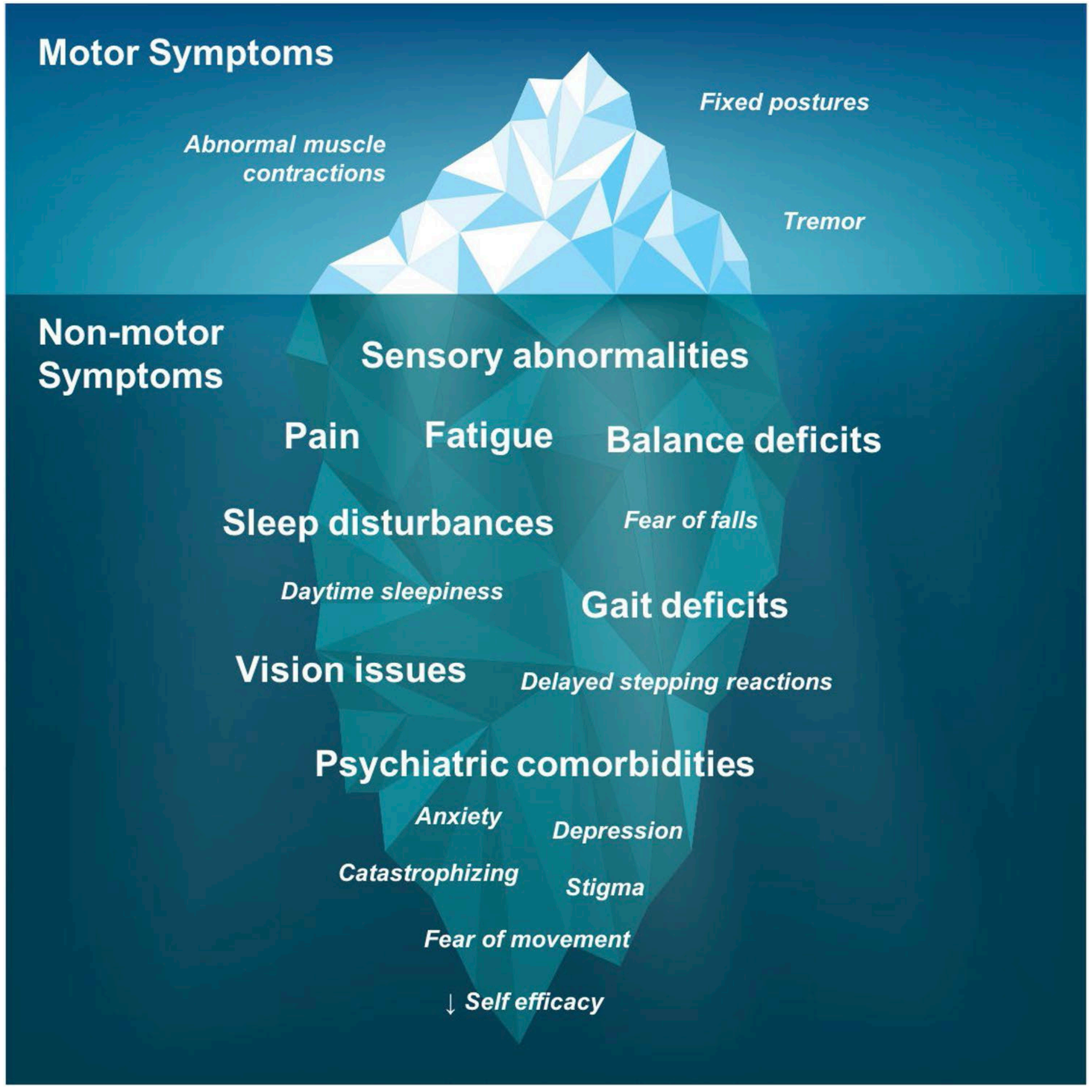

toxins

Article

Effect of Botulinum Toxin on Non-Motor Symptoms in Cervical Dystonia

Matteo Costanzo 1,†, Daniele Belvisi 1,2,†, Isabella Berardelli 3, Annalisa Maraone 1, Viola Baione 1, Gina Ferrazzano 1, Carolina Cutrona 1, Giorgio Leodori 1,2, Massimo Pasquini 1, Antonella Conte 1,2, Giovanni Fabbrini 1,2, Giovanni Defazio 4 and Alfredo Berardelli 1,2,*

Conclusioni


Motor Symptoms
Fixed postures
Abnormal muscle contractions
Tremor
Non-motor Symptoms
Sensory abnormalities
Pain
Fatigue
Balance deficits
Sleep disturbances
Fear of falls
Daytime sleepiness
Gait deficits
Vision issues
Delayed stepping reactions
Psychiatric comorbidities
Anxiety
Depression
Catastrophizing
Stigma
Fear of movement
↓ Self efficacy

Bradnam et al., Journal of Neural Transmission 2021;128:549–558

- Nella pratica clinica devono essere utilizzati degli strumenti di valutazione in grado di riconoscere la presenza di disturbi non motori.
- Le uniche evidenze solide sono per il trattamento del dolore con tossina botulinica (distonia cervicale).
- Per gli altri disturbi non motori i dati disponibili sono del tutto insufficienti.
- Sono necessarie evidenze basate su RCT per individuare trattamenti specifici per i disturbi non motori.

Grazie per l'attenzione!