SOCIETÀ ITALIANA G.U.I.D.A.
PER LA GESTIONE UNIFICATA E INTERDISCIPLINARE DEL DOLORE MUSCOLO-SCHELETRICO E DELL'ALGODISTROFIA

IV CONGRESSO NAZIONALE

IL PATIENT-JOURNEY DELLA PERSONA CON DOLORE MUSCOLO-SCHELETRICO O CON ALGODISTROFIA

Dolore e spasticità

Alessio Baricich MD PhD

Dipartimento di Scienze della Salute
Università del Piemonte Orientale

SCDU Medicina Fisica e Riabilitativa
Az. Ospedaliero Universitaria Maggiore della Carità

Novara

HOSPITALIS MAIORIS CHARITATIS NOVARIÆ CIVITATIS

UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Disclosures

- Honoraria/Expenses from AbbVie, Ipsen, Nordic Pharma
- Consulting/Advisory Board from Amgen, AbbVie, Ipsen, Merz, Sandoz
- Funded Research from AbbVie, Ipsen, Merz, Fidia, IBSA

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Journal of Neurology
https://doi.org/10.1007/s00415-018-8759-1

ORIGINAL COMMUNICATION

Defining spasticity: a new approach considering current movement disorders terminology and botulinum toxin therapy

Dirk Dressler[1] · Roongroj Bhidayasiri[2] · Saeed Bohlega[3] · Pedro Chana[4] · Hsin Fen Chien[5] · Tae Mo Chung[6] · Carlo Colosimo[7] · Markus Ebke[8] · Klemens Fedoroff[9] · Bernd Frank[10] · Ryuji Kaji[11] · Petr Kanovsky[12] · Serdar Koçer[13] · Federico Micheli[14] · Olga Orlova[15] · Sebastian Paus[16] · Zvezdan Pirtosek[17] · Maja Relja[18] · Raymond L. Rosales[19] · José Alberto Sagástegui-Rodríguez[20] · Paul W. Schoenle[21] · Gholam Ali Shahidi[22] · Sofia Timerbaeva[23] · Uwe Walter[24] · Fereshte Adib Saberi[25]

Involuntary muscle hyperactivity
in the presence of central paresis

Received: 23 October 2017 / Revised: 17 January 2018 / Accepted: 18 January 2018

Spasticity: causes

Supraspinal
Stroke
Multiple sclerosis
Cerebral palsy
Hypoxic brain damage
Traumatic brain injury
Mass lesions: tumours, vascular malformations
Inflammation
Spinal
Cervical myelopathy
Mass lesions: tumours, vascular malformations
Inflammation
Stroke
Traumatic spinal cord lesion
Hereditary spastic paraplegia
Spina bifida
Myelomeningocele
Tethered cord
Mixed
Multiple sclerosis
Motoneuron disease, primary lateral sclerosis
Inflammation

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticity: definition

The involuntary muscle hyperactivity can consist of various forms of muscle hyperactivity:

- spasticity sensu strictu: involuntary muscle hyperactivity triggered by rapid passive joint movements
- rigidity: involuntary muscle hyperactivity triggered by slow passive joint movements
- dystonia: spontaneous involuntary muscle hyperactivity
- spasms: complex involuntary movements usually triggered by sensory or acoustic stimuli.
- complications: contractures, pain

Dressler et al, J Neurol 2018

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticity: definition

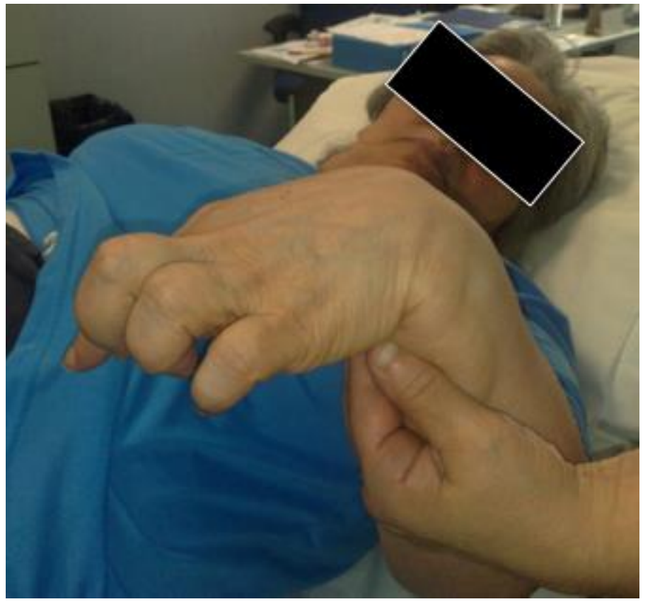
The involuntary muscle hyperactivity can consist of various forms of muscle hyperactivity:

- spasticity sensu strictu: involuntary muscle hyperactivity triggered by rapid passive joint movements
- rigidity: involuntary muscle hyperactivity triggered by slow passive joint movements
- dystonia: spontaneous involuntary muscle hyperactivity
- spasms: complex involuntary movements usually triggered by sensory or acoustic stimuli.
- complications: contractures, pain

Dressler et al, J Neurol 2018

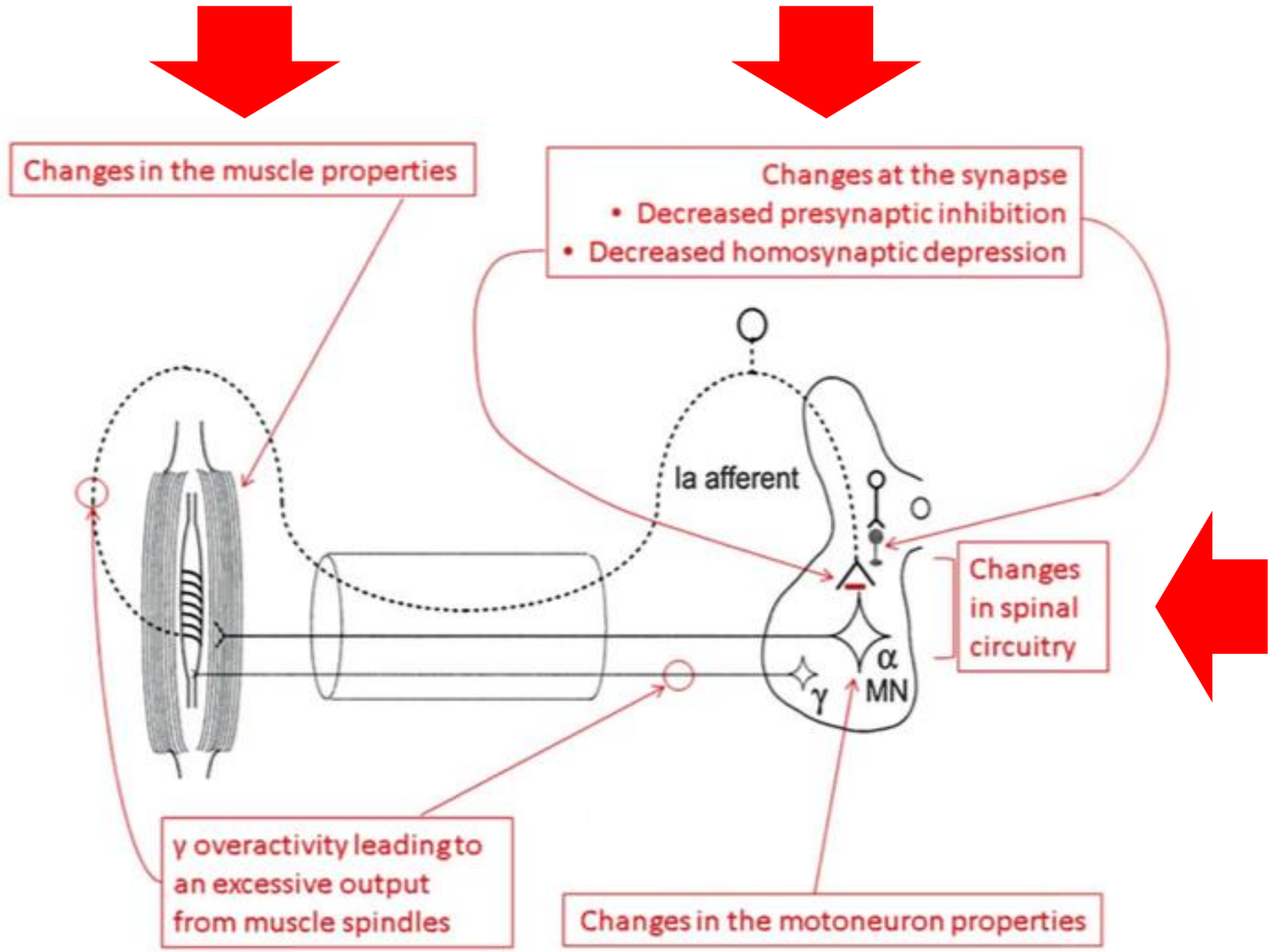
UNIVERSITÀ DEL PIEMONTE ORIENTALE

UNIVERSITÀ DEL PIEMONTE ORIENTALE

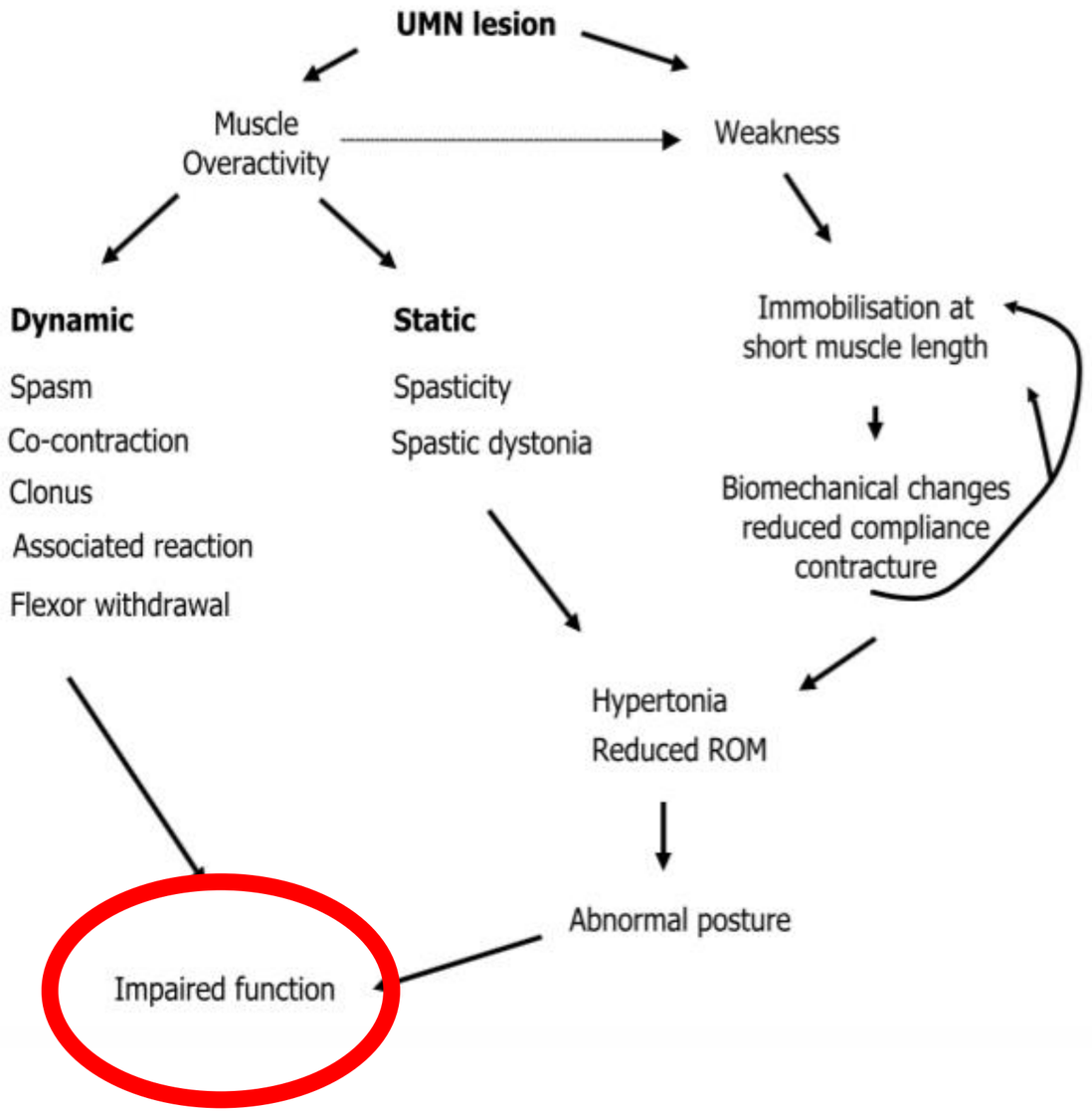


UNIVERSITÀ DEL PIEMONTE ORIENTALE

Pathophysiology of spasticity



Burke et al, Neurology 2013



Spasticità e dolore

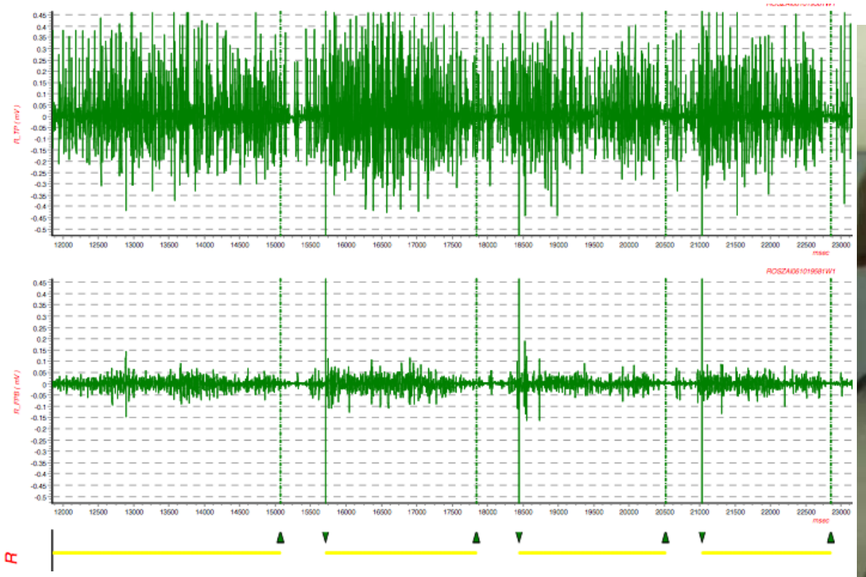
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticità e dolore

- Meccanismo fisiopatologico non del tutto chiarito
- “Mixed pain syndrome”
  - Dolore neuropatico (possibile)
  - Dolore nocicettivo (overuse, danno tissutale, possibile presenza di ischemia muscolare)

Paolucci et al, EJPRM 2016

UNIVERSITÀ DEL PIEMONTE ORIENTALE

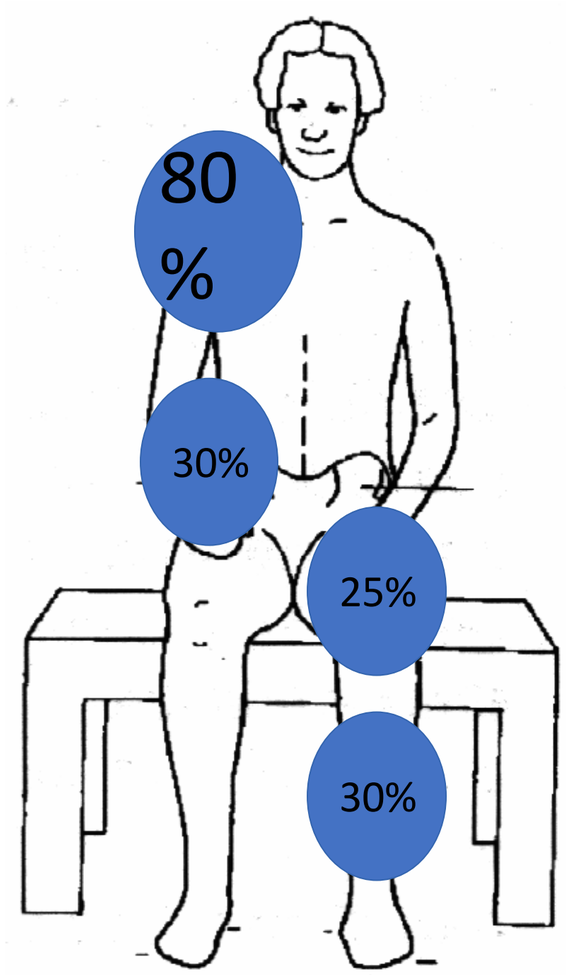


UNIVERSITÀ DEL PIEMONTE ORIENTALE


Sn

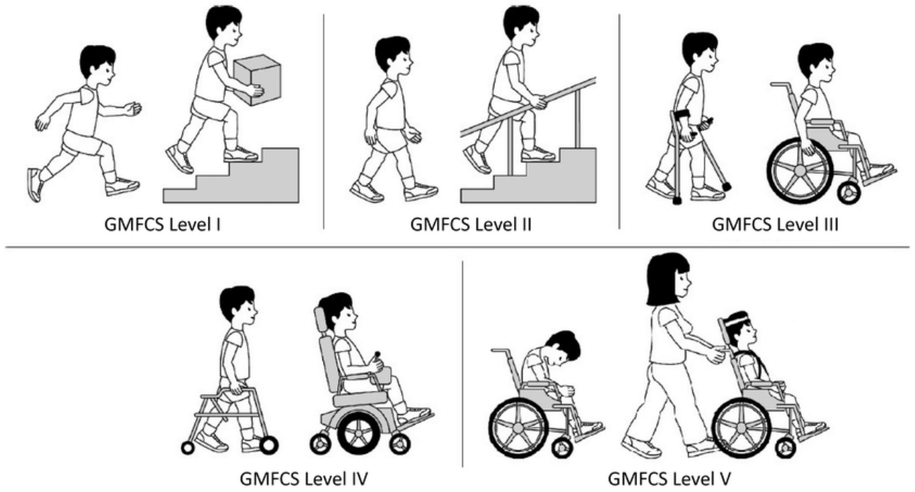
UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticità e dolore nell'ictus



UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticità e dolore nelle PCI



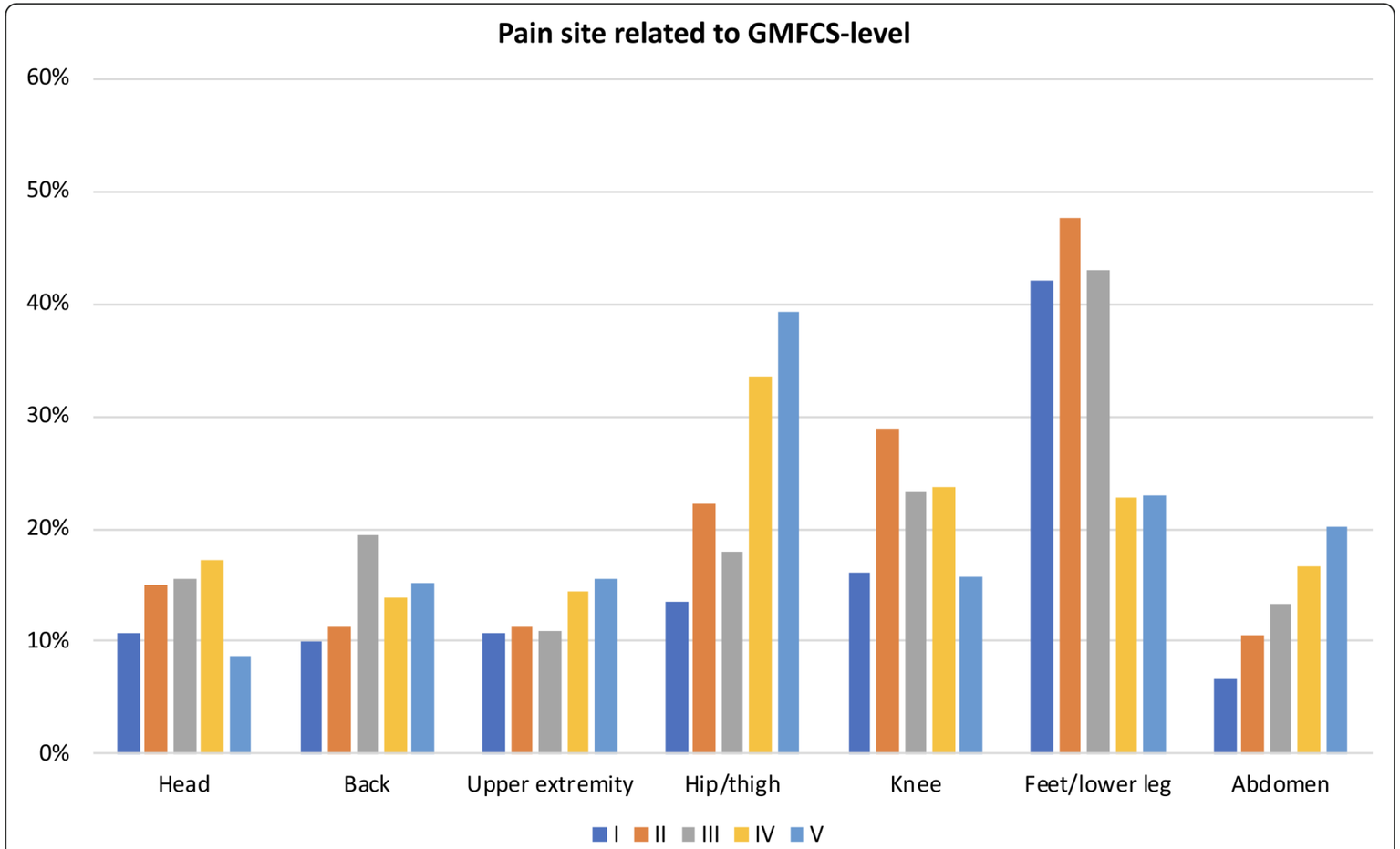
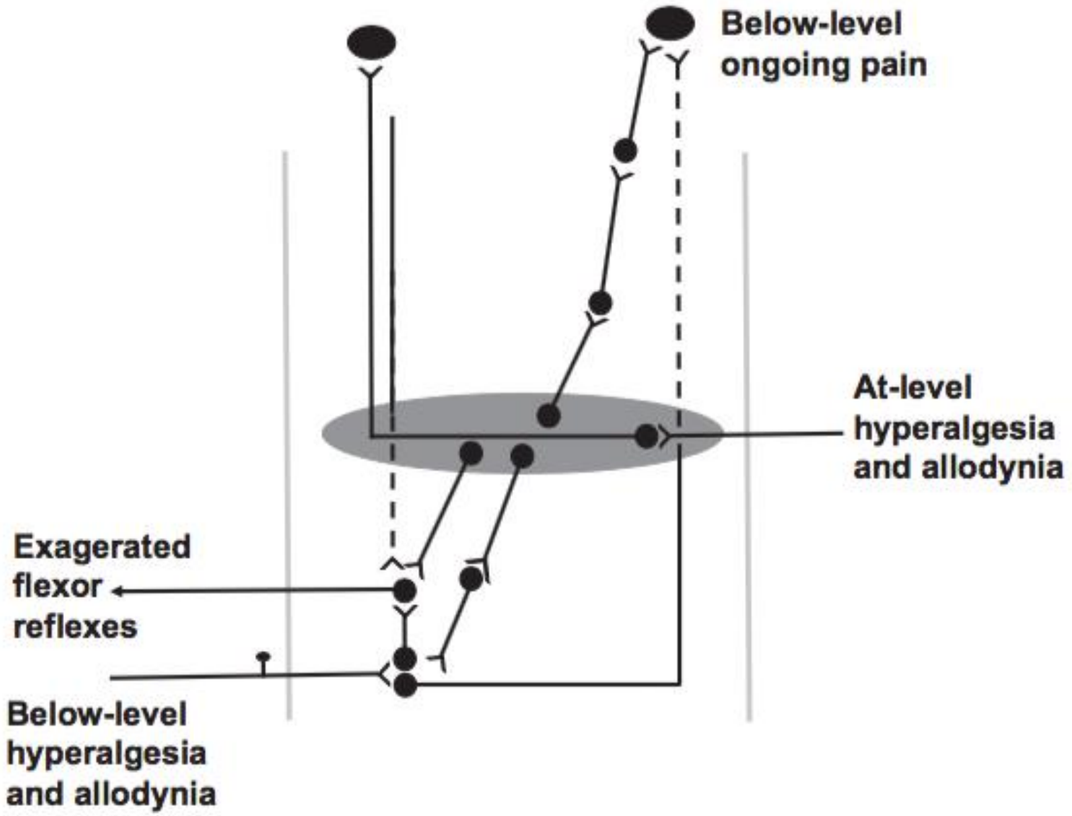


Fig. 3 Pain prevalence at different pain sites related to GMFCS-level. Each bar represents the percentage of children with pain related to the total number of children in the same GMFCS-level with pain. GMFCS = Gross Motor Function Classification System

Eriksson *et al. BMC Neurology* (2020) 20:15

Neuropathic pain and spasticity: intricate consequences of spinal cord injury

NB Finnerup

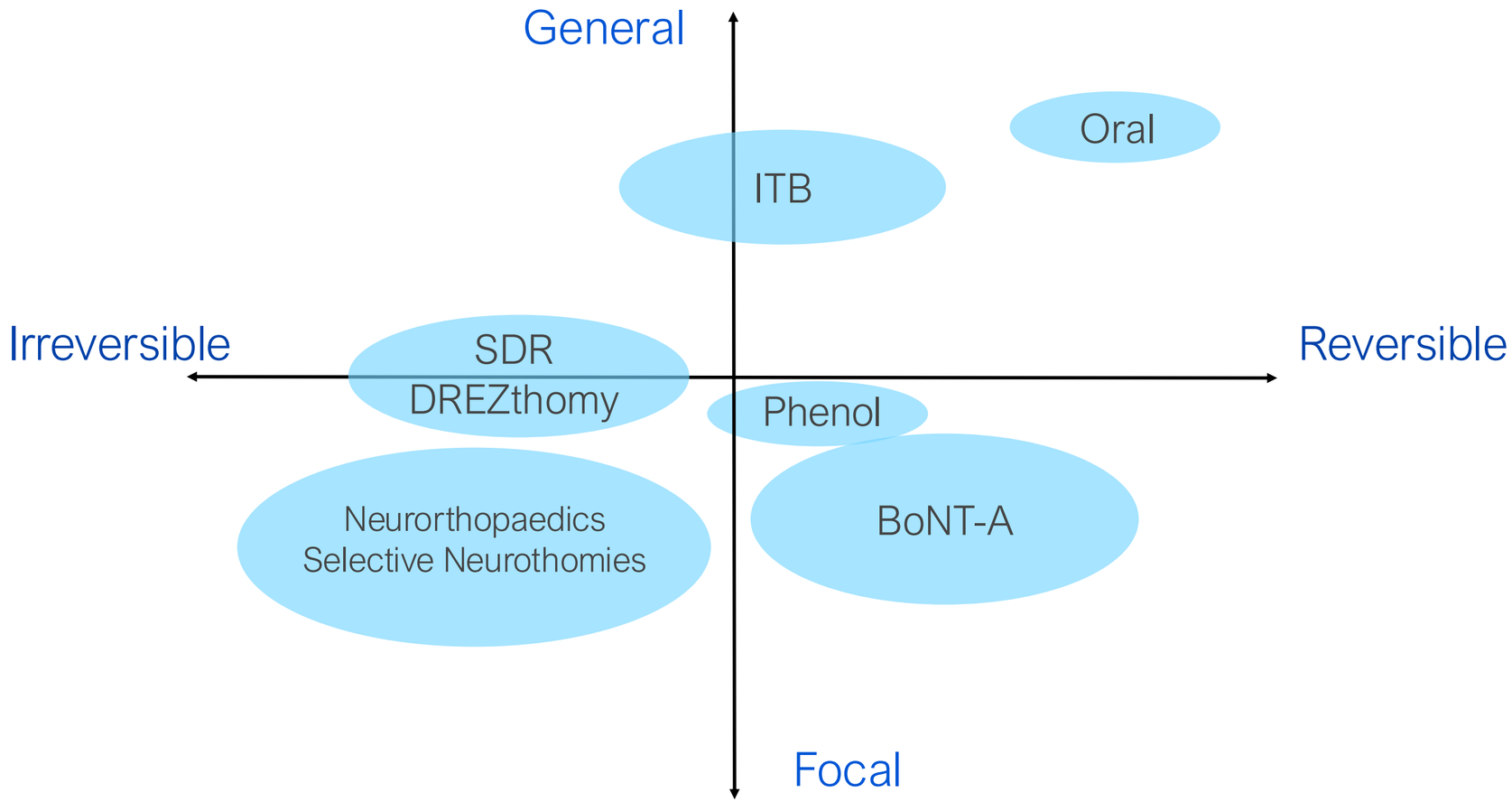


Spinal Cord (2017) 55, 1046–1050

www.nature.com/sc

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Spasticity Treatment Compass



UNIVERSITÀ DEL PIEMONTE ORIENTALE

Original Article

Management of Spasticity Associated Pain with Botulinum Toxin A

Jörg Wissel, MD, Jörg Müller, MD, Jürgen Dressnandt, MD, Florian Heinen, MD, Markus Naumann, MD, Helge Topka, MD, and Werner Poewe, MD

Department of Neurology (J.W., J.M., W.P.), University of Innsbruck, Innsbruck, Austria; Hospital for Neurology (J.D.), Bad Aibling; Department of Neuropediatrics (F.H.), University of Freiburg, Freiburg; Department of Neurology (M.N.), University of Würzburg, Würzburg; and Department of Neurology (H.T.), University of Tübingen, Tübingen, Germany

- Mean total dose of 165.7 +/- 108.2 [30-400] units (Botox) per treatment session in a mean 3.4 +/- 1.5 muscles.

- 55/60 experienced improvement in pain after 6 week-follow up period
- The effects were comparable in acute (n = 17) and chronic (n = 43) spasticity

UNIVERSITÀ DEL PIEMONTE ORIENTALE

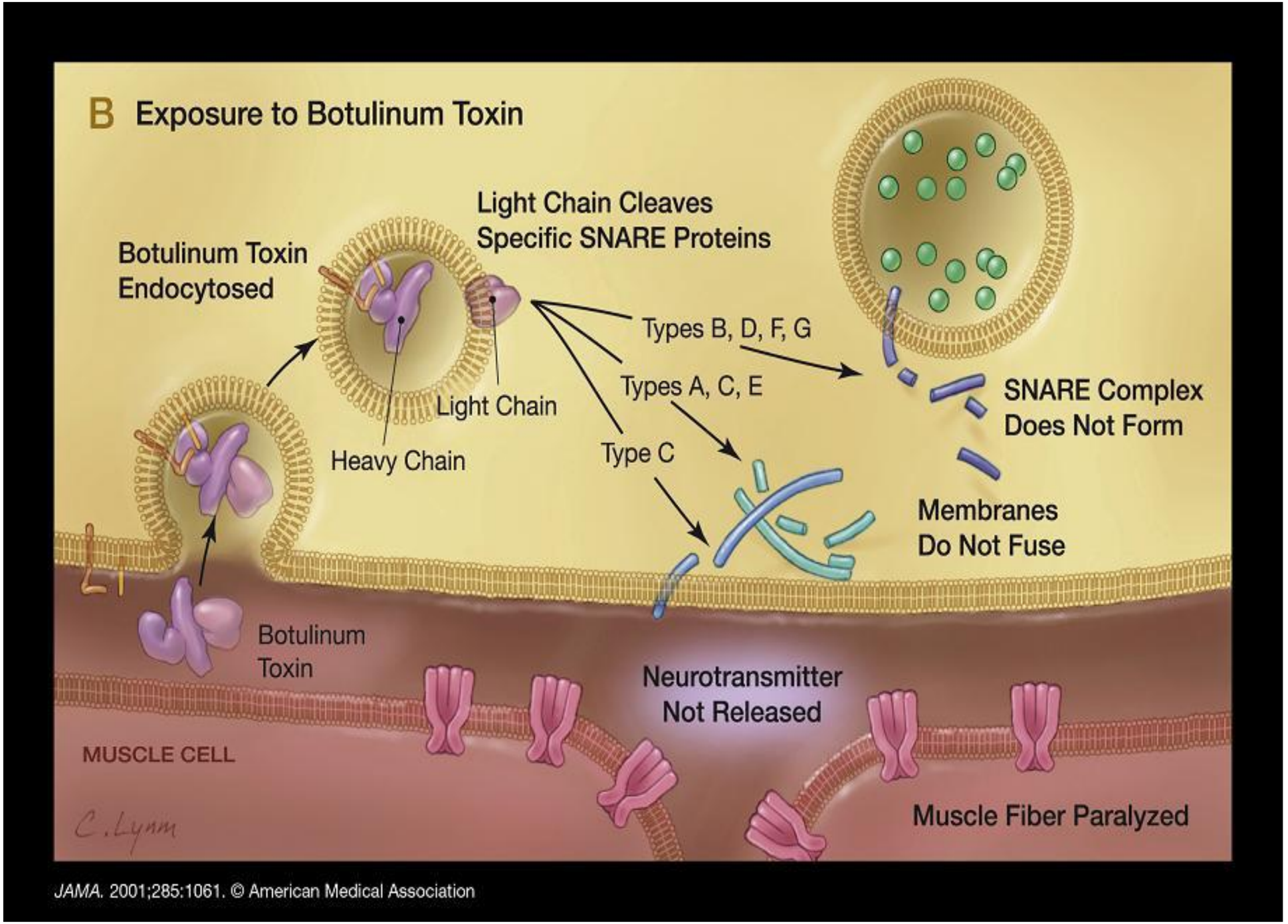

B Exposure to Botulinum Toxin
Botulinum Toxin Endocytosed
Light Chain Cleaves Specific SNARE Proteins
Light Chain
Heavy Chain
Types B, D, F, G
Types A, C, E
Type C
SNARE Complex Does Not Form
Membranes Do Not Fuse
Botulinum Toxin
Neurotransmitter Not Released
MUSCLE CELL
Muscle Fiber Paralyzed
C. Lynn
JAMA. 2001;285:1061. © American Medical Association

Table 1 BoNT preparations and FDA-approved indications

BoNT preparation	Brand name (manufacturer)	FDA-approved indications[a]
OnabotulinumtoxinA	Botox (Allergan, Inc., Irvine, CA)	Blepharospasm, CD, upper extremity spasticity, lower extremity spasticity, CM
AbobotulinumtoxinA	Dysport (Ipsen Ltd., Paris, France)	CD, upper extremity spasticity
IncobotulinumtoxinA	Xeomin (Merz Pharmaceuticals, Frankfurt, Germany)	Blepharospasm, CD, upper extremity spasticity
RimabotulinumtoxinB	Myobloc Neurobloc (US WorldMeds/Solstice Neurosciences, Louisville, KY)	CD

Abbreviations: BoNT = botulinum neurotoxin; CD = cervical dystonia; CM = chronic migraine; FDA = Food and Drug Administration.
[a] FDA approvals relevant to this review.

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Simpson et al, Neurology 2016

Table 2 Evidence-based conclusions and recommendations for the efficacy of various botulinum neurotoxin formulations by indication

Indication	Level A[a] effective	Level B[b] probably effective	Level C[c] possibly effective	Level U[d] insufficient evidence	Level A[e] ineffective	Level B[f] ineffective
Blepharospasm		OnabotulinumtoxinA, incobotulinumtoxinA	AbobotulinumtoxinA	RimabotulinumtoxinB		
Cervical dystonia	AbobotulinumtoxinA, rimabotulinumtoxinB	OnabotulinumtoxinA, incobotulinumtoxinA				
Upper limb spasticity[g]	AbobotulinumtoxinA, onabotulinumtoxinA,[h] incobotulinumtoxinA	RimabotulinumtoxinB				
Lower limb spasticity	OnabotulinumtoxinA, abobotulinumtoxinA			IncobotulinumtoxinA, rimabotulinumtoxinB		
Chronic migraine	OnabotulinumtoxinA[i]					
Episodic migraine					OnabotulinumtoxinA	
Tension-type headache						OnabotulinumtoxinA

Abbreviations: aboBoNT-A = abobotulinumtoxinA; incoBoNT-A = incobotulinumtoxinA; onaBoNT-A = onabotulinumtoxinA; rimaBoNT-B = rimabotulinumtoxinB.

[a] Level A recommendation for effectiveness signifies intervention should be offered.
[b] Level B recommendation for effectiveness signifies intervention should be considered.
[c] Level C recommendation for effectiveness signifies intervention may be considered.
[d] Level U recommendation signifies insufficient evidence to support or refute effectiveness of intervention.
[e] Level A recommendation for ineffectiveness signifies intervention should not be offered.
[f] Level B recommendation for ineffectiveness signifies intervention should not be considered.
[g] Evidence demonstrates efficacy in reducing spasticity but is inadequate to determine improvement in active function associated with limb spasticity.
[h] Probably superior to tizanidine and exercise alone for reducing spasticity.
[i] Established as effective for decreasing the number and severity of headaches; probably effective in improvement of health-related quality of life.

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Simpson et al, Neurology 2016

BoNT-A e analgesia

- Inizialmente effetto analgesico correlato alla riduzione della contrazione muscolare (effetto presinaptico)
- Successive osservazioni di una significativa riduzione del dolore in CD indipendente dalla riduzione dei fenomeni distonici

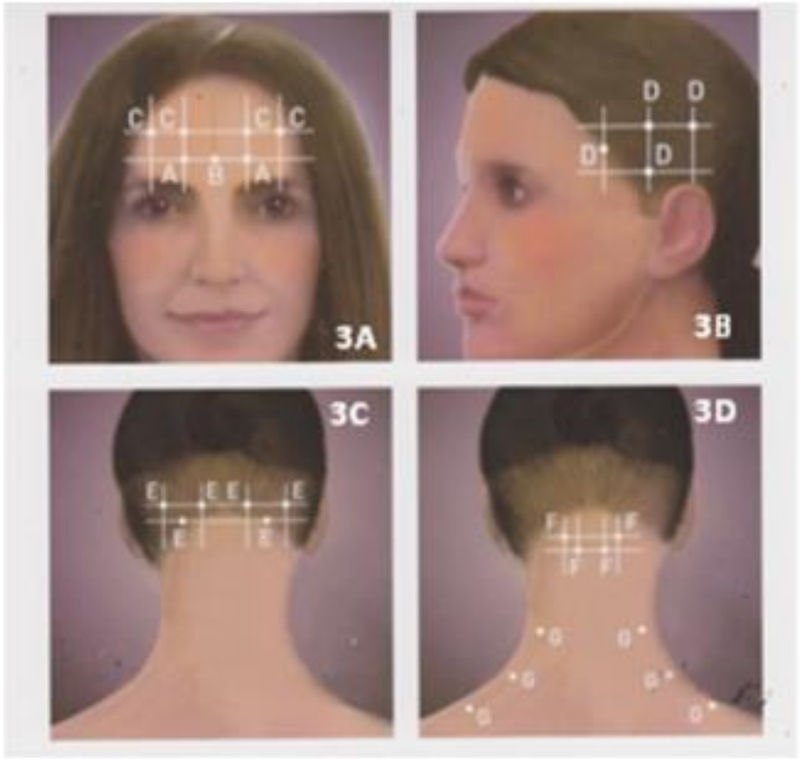
- Effetto diretto ?

Jankovic e Schwartz, 1990

Freund e Schwarz, 2003

Sycha et al, 2004

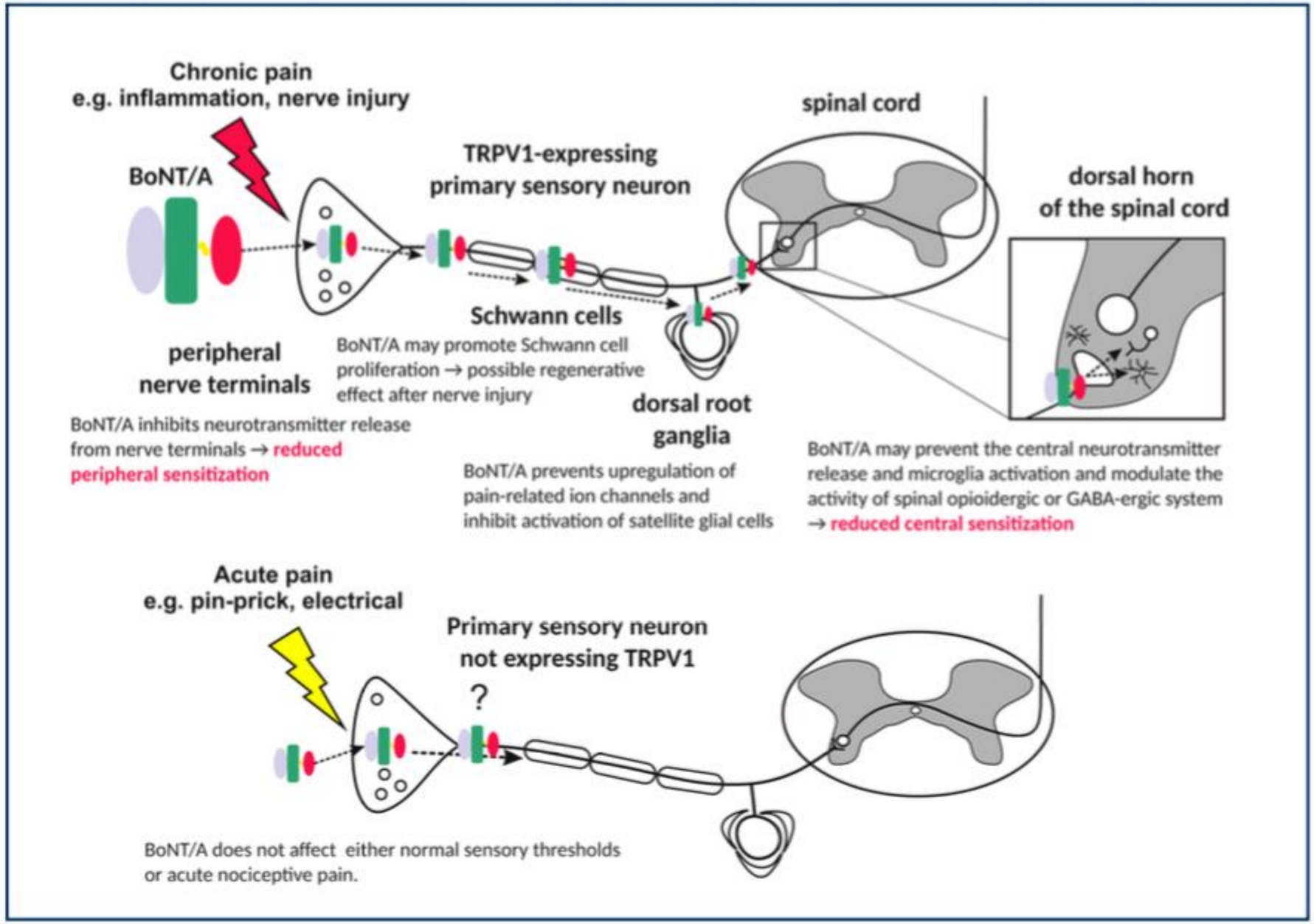
UNIVERSITÀ DEL PIEMONTE ORIENTALE



Order	Muscle	Total Recommended Dosage, Number of Sites**
A	Corrugator*	10 Units divided in 2 sites
B	Procerus*	5 Units in 1 site
C	Frontalis*	20 Units in 4 sites
D	Temporalis*	40 Units in 8 sites
E	Occipitalis*	30 Units divided in 6 sites
F	Cervical paraspinsal*	20 Units divided in 4 sites
G	Trapezius*	30 Units divided in 6 sites
Total Dose		155 Units divided in 31 sites
*Dose distributed bilaterally		**Each IM injection site = 0.1 mL = 5 units BOTOX®

UNIVERSITÀ DEL PIEMONTE ORIENTALE

A. Wheeler, H.S. Smith / Toxicology 306 (2013) 124–146



UNIVERSITÀ DEL PIEMONTE ORIENTALE

Matak et al, 2019

toxins

MDPI

Article

Effectiveness of Botulinum Toxin on Pain in Stroke Patients Suffering from Upper Limb Spastic Dystonia

Carlo Trompetto [1,2], Lucio Marinelli [1,3,*], Laura Mori [1,2], Luca Puce [1], Chiara Avanti [1], Elena Saretti [1], Giulia Biasotti [1], Roberta Amella [1], Filippo Cotellessa [1], Domenico A. Restivo [4] and Antonio Currà [5]

Toxins **2022**, *14*, 39. https://doi.org/10.3390/toxins14010039

Clinical efficacy of botulinum toxin type A in patients with traumatic brain injury, spinal cord injury, or multiple sclerosis: An observational longitudinal study

Alessio Baricich[1,2], Marco Battaglia[1,2]*, Daria Cuneo[3], Lucia Cosenza[4], Marzia Millevolte[5], Michela Cosma[6], Mirko Filippetti[7], Stefania Dalise[8], Valentina Azzollini[8], Carmelo Chisari[8], Stefania Spina[9], Nicoletta Cinone[9], Lorenza Scotti[10], Marco Invernizzi[1,11], Stefano Paolucci[12], Alessandro Picelli[7] and Andrea Santamato[9]

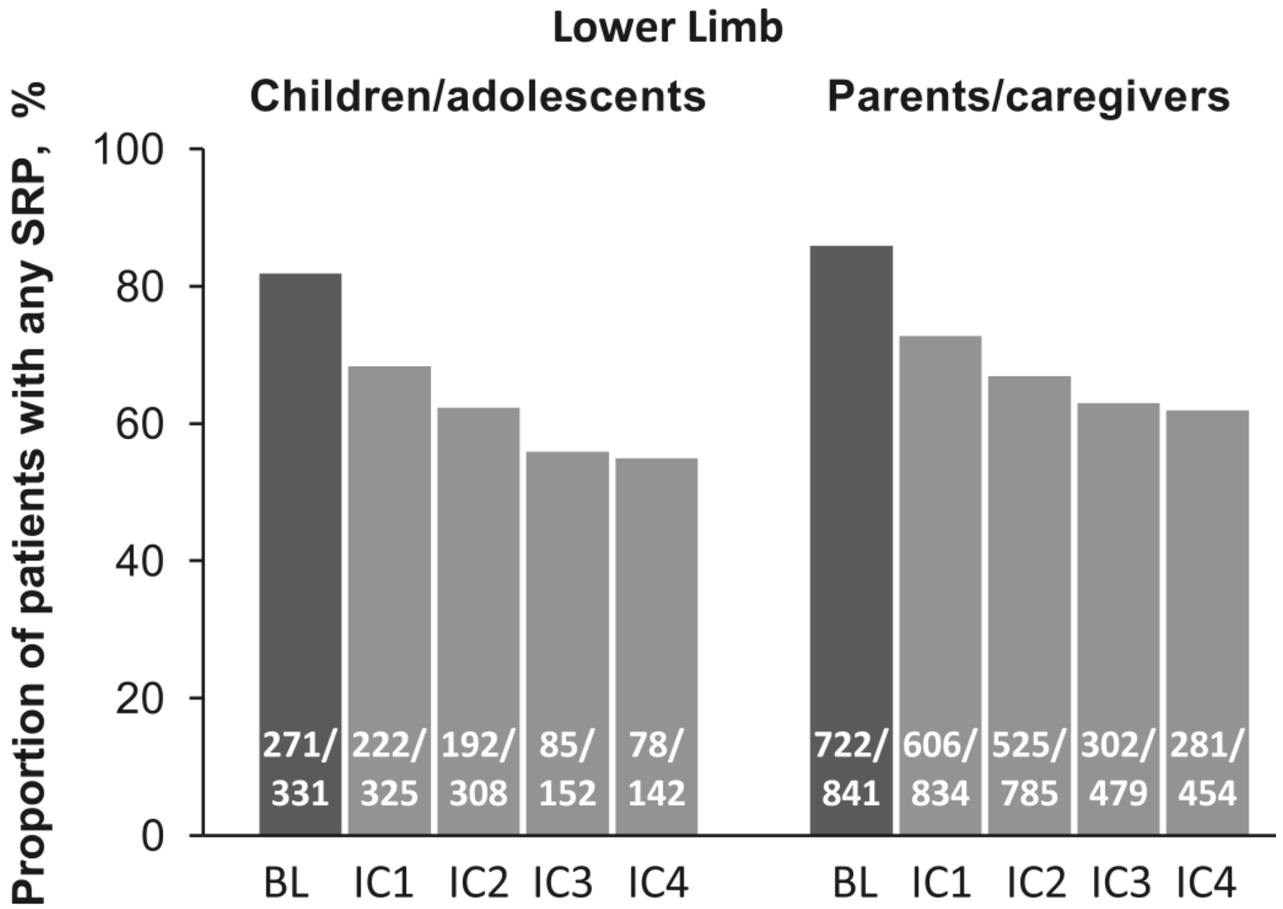
Time	MAS		*F*-test	NRS		*F*-test
	beta (se)	*p*-value	*p*-value	beta (se)	*p*-value	*p*-value
T0	ref			ref		
T1	−0.99 (0.10)	**<0.0001**	**<0.0001**	−1.69 (0.25)	**<0.0001**	**<0.0001**
T2	−0.51 (0.10)	**<0.0001**		−1.03 (0.26)	**<0.0001**	

frontiers | Frontiers in Neurology

TYPE Original Research
PUBLISHED 06 April 2023
DOI 10.3389/fneur.2023.1133390

Spasticity-related pain in children/adolescents with cerebral palsy. Part 2: IncobotulinumtoxinA efficacy results from a pooled analysis

Michaela Bonfert[a], Florian Heinen[a,*], Petr Kaňovský[b], A. Sebastian Schroeder[a], Henry G. Chambers[c], Edward Dabrowski[d], Thorin L. Geister[e], Angelika Hanschmann[e], Michael Althaus[e], Marta Banach[f] and Deborah Gaebler-Spira[g]



Journal of Pediatric Rehabilitation Medicine: An Interdisciplinary Approach Throughout the Lifespan 16 (2023) 83–98
DOI:10.3233/PRM-220020

BoNT-A and pain reduction in CP

- Highly significant effect of extra-articular BoNT-A in non-ambulatory CCP
  - Reduction in muscle tone
  - Reduction of mechanical stimulus to the pain afferent system in the soft tissues surrounding the hip joint
  - Reduction of compression on the blood vessels and nerves (nociceptive stimulus)
  - Direct peripheral analgesic and anti-inflammatory activity

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Lundy et al, Dev. Med. Child Neurol. 2009, 51, 705–710

Administration of type a botulinum toxin after total hip replacement

M. BERTONI [1], A. CASTAGNA [1], A. BARICICH [2], G. BERTI [1], S. LAZZARETTI [1], C. MORANDI [1]

EUR J PHYS REHABIL MED 2008;44:461-5

Published in final edited form as:
Br J Med Med Res. ; 4(1): . doi:10.9734/BJMMR/2014/4897.

Efficacy of Long-term Effect and Repeat Intraarticular Botulinum toxin in Patients with Painful Total Joint Arthroplasty: A Retrospective Study

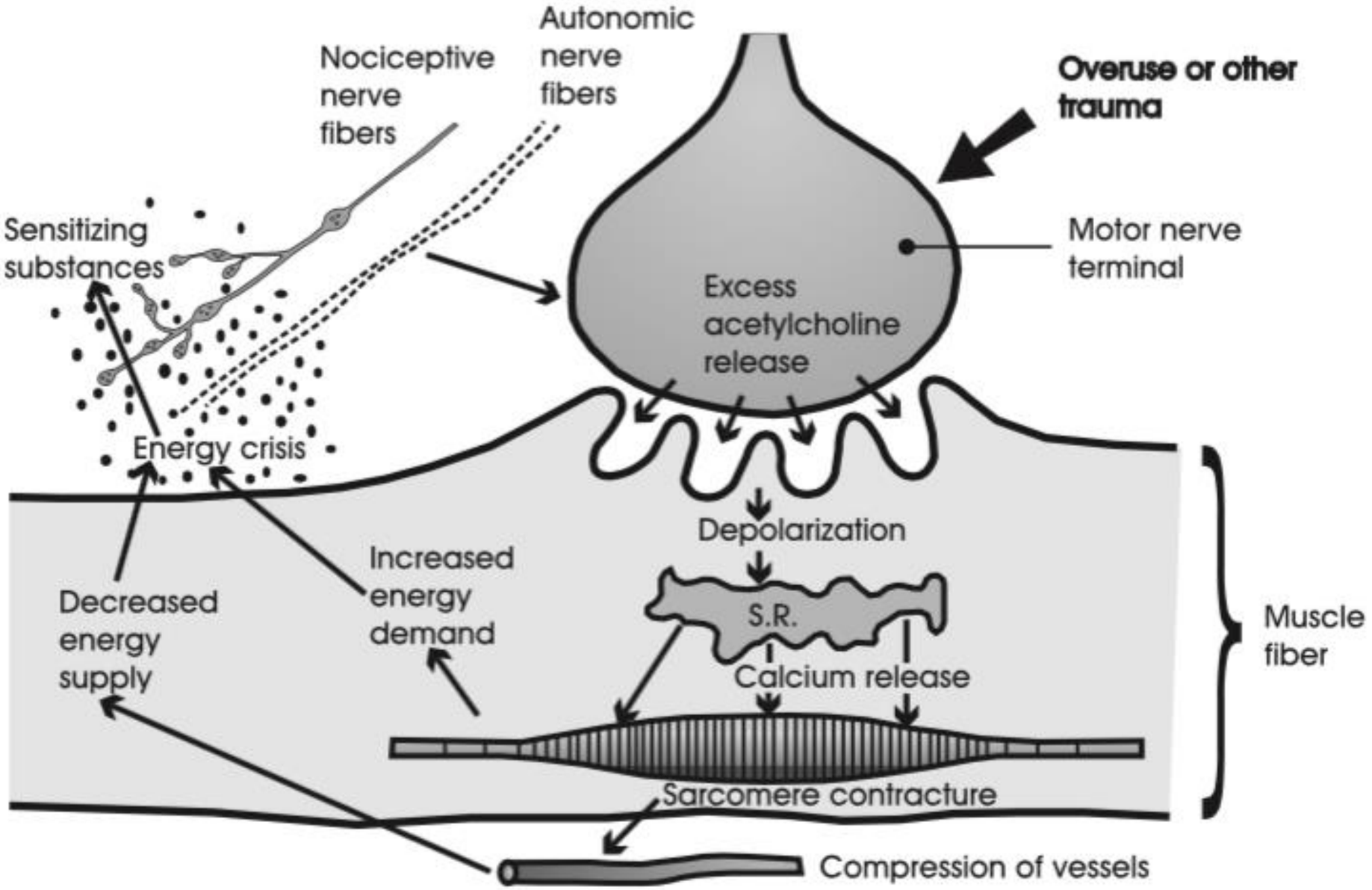
Jasvinder A. Singh[1,2,3,*]

[1]Medicine Service and Center for Surgical Medical Acute Care Research and Transitions (C-SMART), Birmingham VA Medical Center, Birmingham, AL; USA

[2]Department of Medicine, University of Alabama, and Division of Epidemiology, School of Public Health, University of Alabama at Birmingham, Birmingham, AL; USA.

[3]Department of Orthopedic Surgery, Mayo Clinic School of Medicine, Rochester, MN, USA

UNIVERSITÀ DEL PIEMONTE ORIENTALE



UNIVERSITÀ DEL PIEMONTE ORIENTALE

Toxicon 147 (2018) 120–128

Contents lists available at ScienceDirect

Toxicon

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

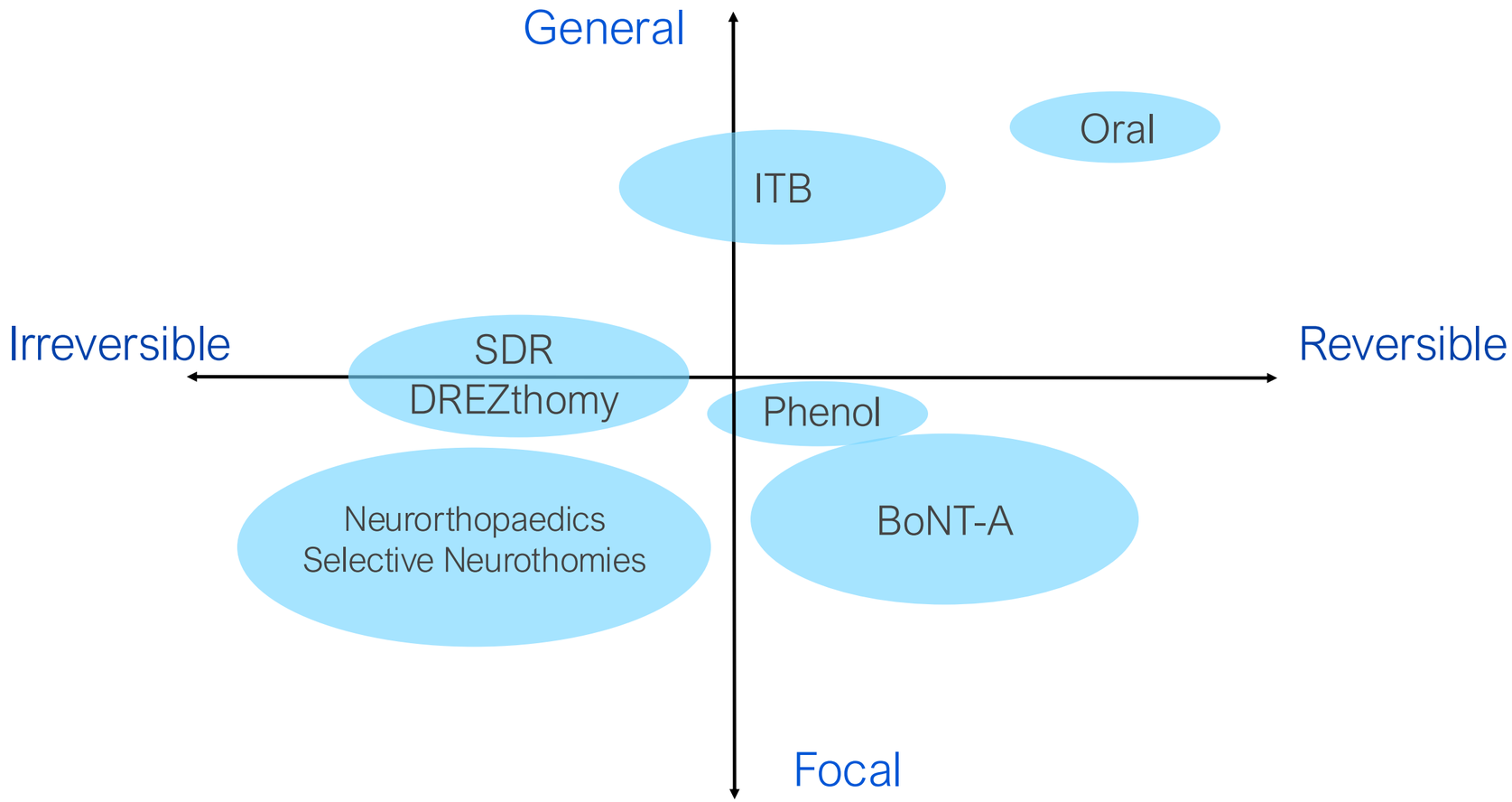
Botulinum toxin treatment of pain syndromes –an evidence based review

Yasaman Safarpour [a], Bahman Jabbari [b, *]

[a] Department of Medicine, Division of Nephrology, University of California, Irvine (UCI), CA, USA
[b] Department of Neurology, Yale University School of Medicine, New Haven, CT, USA

Spasticità generalizzata

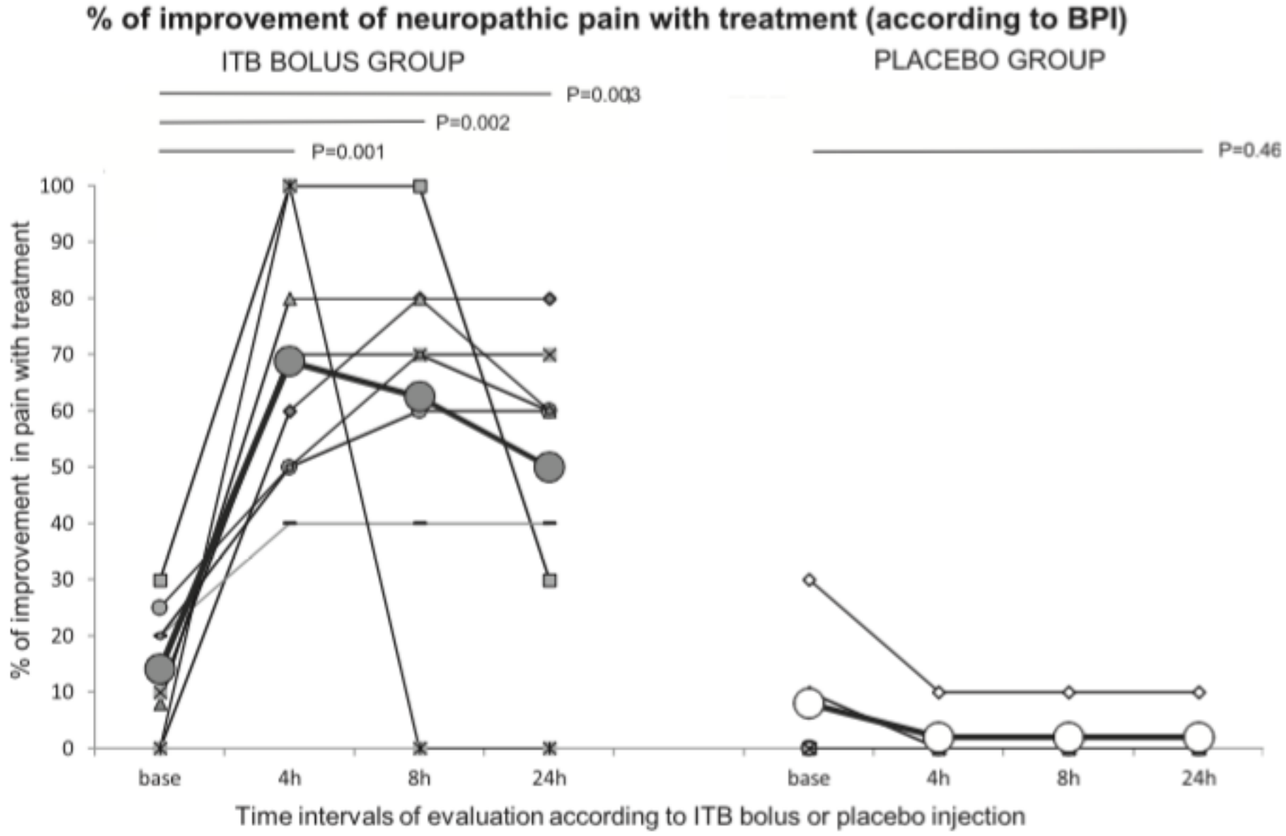
Spasticity Treatment Compass



UNIVERSITÀ DEL PIEMONTE ORIENTALE

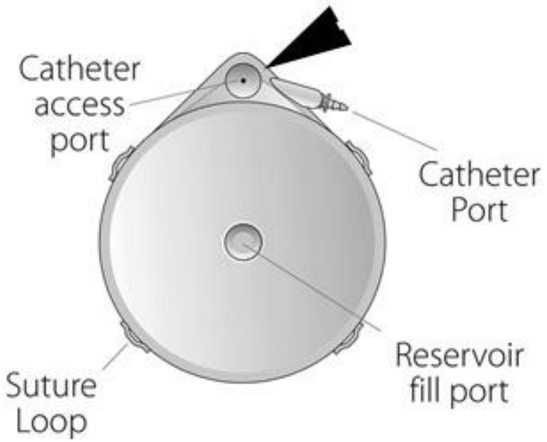
Analgesic effect of intrathecal baclofen bolus on neuropathic pain in spinal cord injury patients

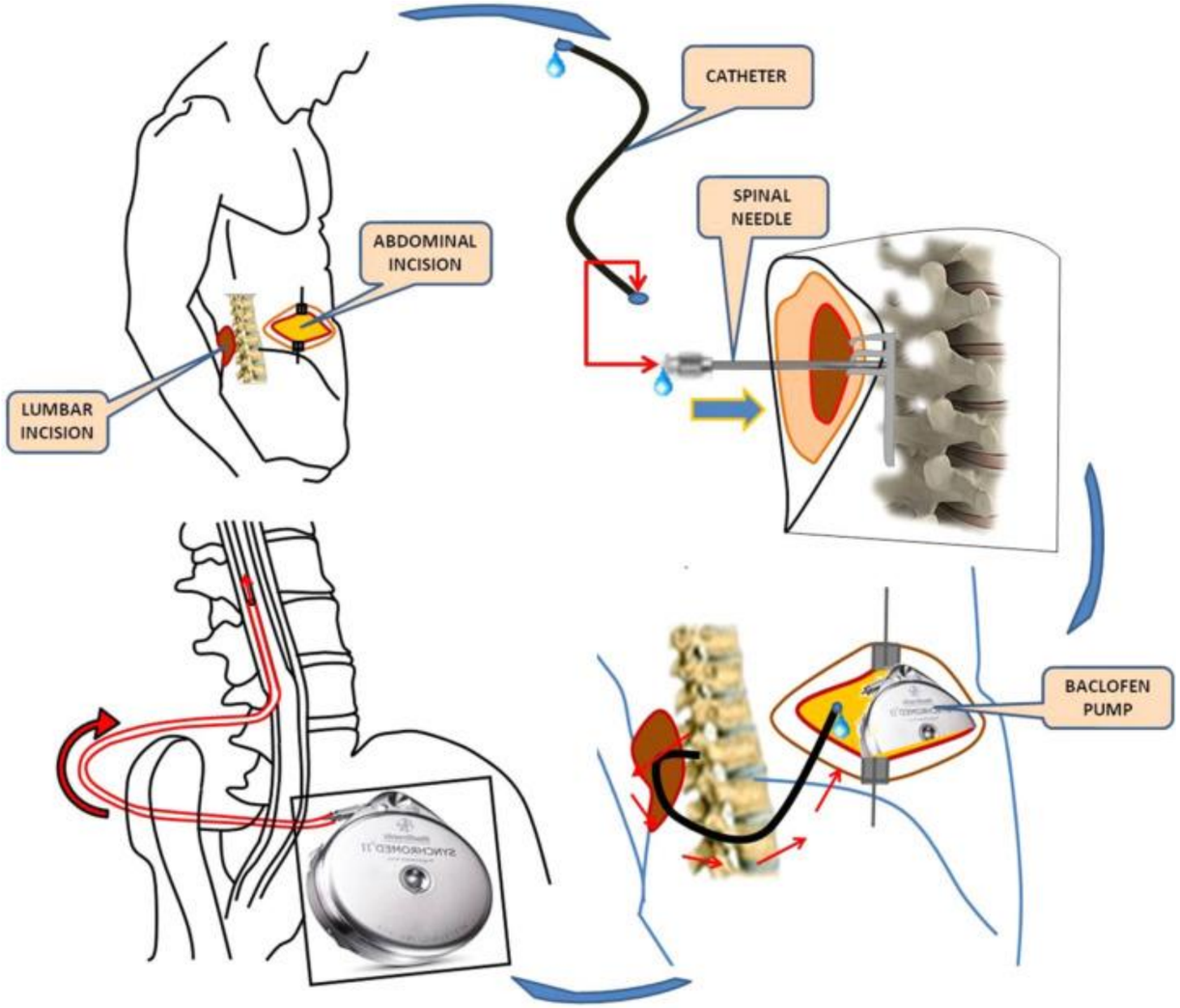
Hatice Kumru[a,c,d,*], Jesus Benito-Penalva[b,c,d], Markus Kofler[a], Joan Vidal[b,c,d]



Brain Research Bulletin 140 (2018) 205–211

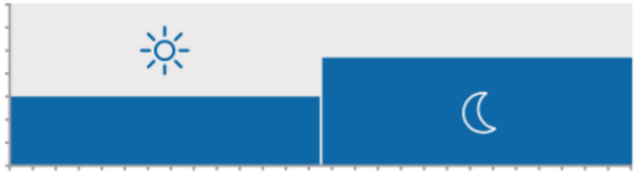
ITB pump





UNIVERSITÀ DEL PIEMONTE ORIENTALE

Simple Continuous



Day/Night

Periodic Bolus

UNIVERSITÀ DEL PIEMONTE ORIENTALE

PM R 8 (2016) 553-562

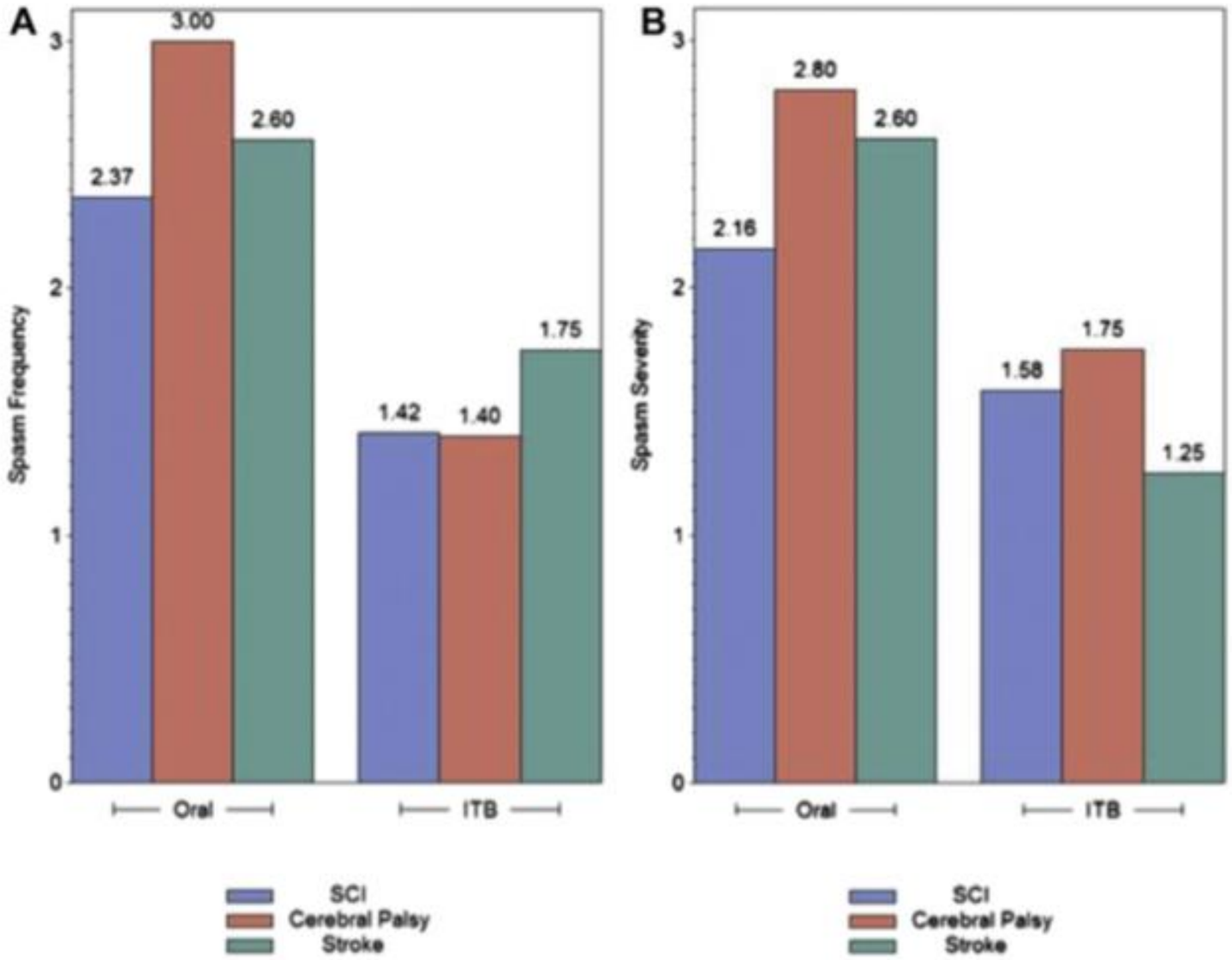
www.pmrjournal.org

Original Research

Intrathecal Versus Oral Baclofen: A Matched Cohort Study of Spasticity, Pain, Sleep, Fatigue, and Quality of Life

Zachary L. McCormick, MD, Samuel K. Chu, MD, Danielle Binler, MS, Daniel Neudorf, DO, Sunjay N. Mathur, MD, Jungwha Lee, PhD, MPH, Christina Marciniak, MD

Z.L. McCormick et al. / PM R 8 (2016) 553-562



UNIVERSITÀ DEL PIEMONTE ORIENTALE

Baclofen treatment questionnaire results for all patients

	Intrathecal		Oral		Intrathecal vs Oral
	Mean	SD	Mean	SD	*P* Value
Penn Spasm Frequency Scale (PSFS)					
Spasm Frequency Score	1.44	0.92	2.37	1.12	<.01
Spasm Severity Score	1.44	0.92	2.16	0.83	<.01
Brief Pain Inventory (BPI)					
Average NRS pain score	3.79	2.72	5.42	2.81	.22
Worst NRS pain score in last 24 hours	4.21	2.99	6.58	3.31	.13
Least NRS pain score in last 24 hours	2.16	2.43	3.05	2.39	.54
NRS pain score currently	3.05	2.74	4.79	3.24	.20
Pain severity score	3.3	2.54	4.96	2.65	.19
Last 24 hours, pain interfered with:					
General Activity	2.84	3.25	3.16	3.34	.45
Mood	2.89	3.36	2.89	3.97	.80
Relations with other people	1.84	2.75	1.58	2.46	.21
Sleep	4.37	3.71	3.58	3.88	.81
Enjoyment of life	3.11	3.14	3.37	2.75	.38
Pain Interference score	2.84	2.71	2.72	2.42	.99
Epworth Sleepiness Scale (ESS)					
Total score	7.72	6.25	8.16	5.86	.70
Fatigue Severity Scale (FSS)					
Average score	3.26	1.71	3.36	1.52	.68
Life Satisfaction Questionnaire (LSQ)					
Average score	4.14	0.86	4.03	1.25	.39
Diener Satisfaction with Life Scale (SWLS)					
Total score	20.74	6.22	21.63	8.45	.35

SD = standard deviation.

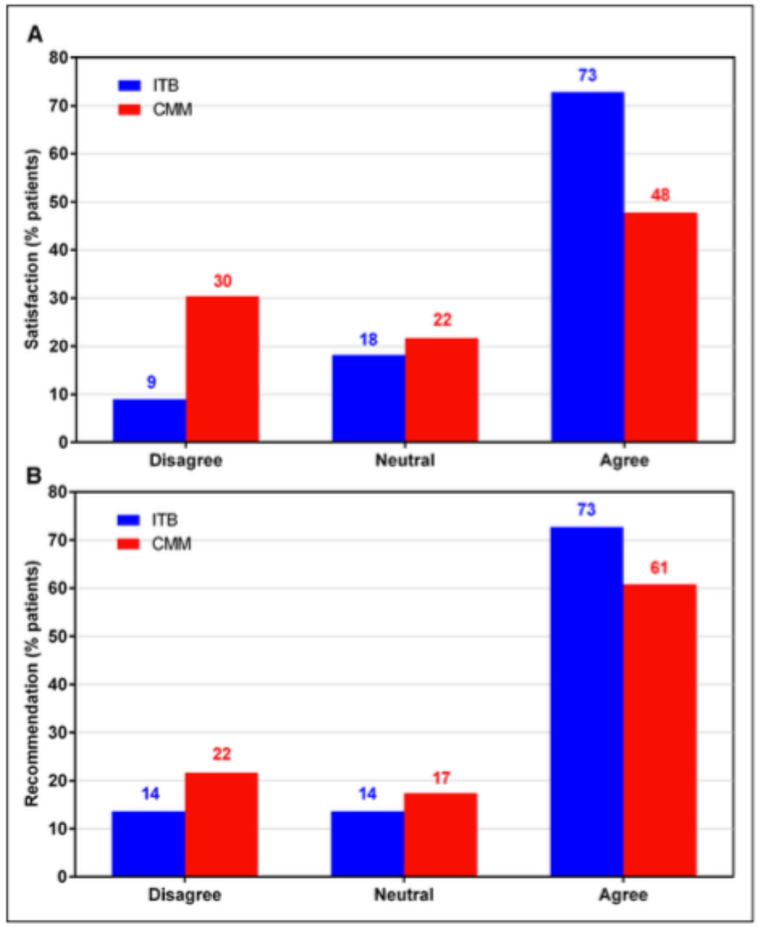
UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

OPEN

Effect of Intrathecal Baclofen on Pain and Quality of Life in Poststroke Spasticity

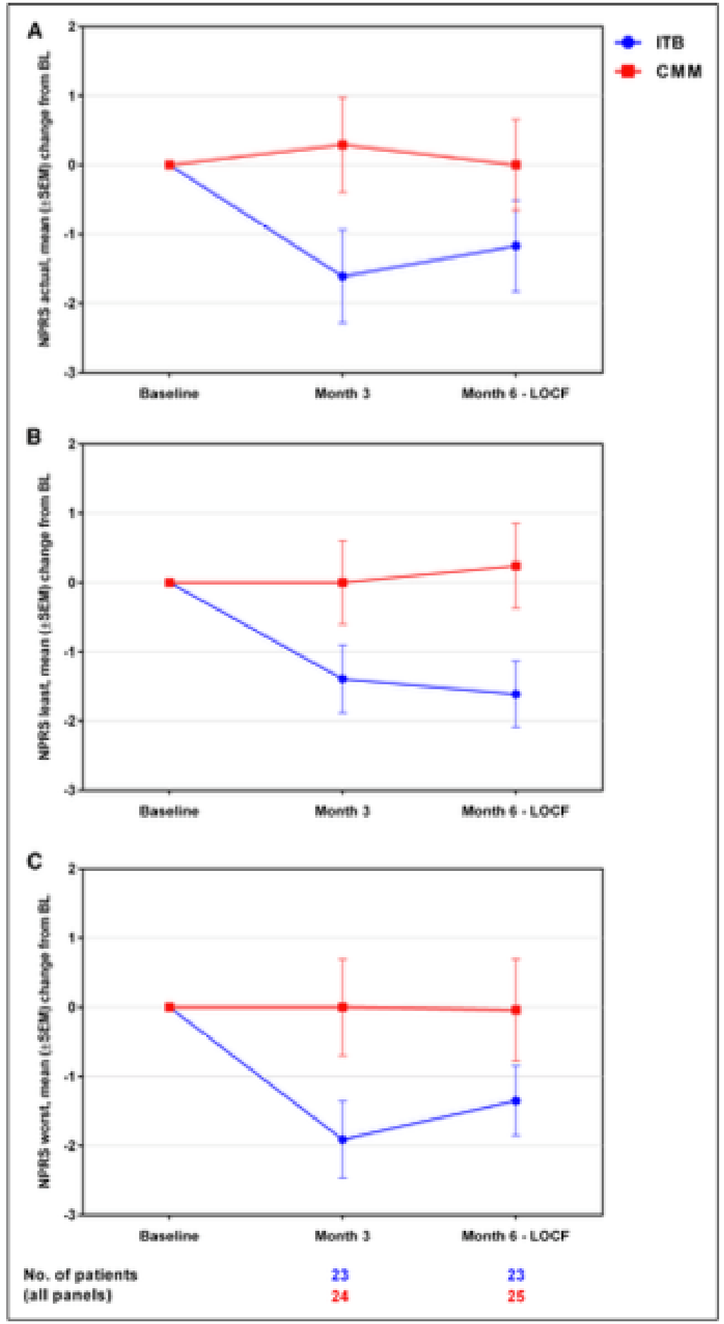
A Randomized Trial (SISTERS)

Michael Creamer, DO; Geoffrey Cloud, MB BS; Peter Kossmehl, MD; Michael Yochelson, MD; Gerard E. Francisco, MD; Anthony B. Ward, MD; Jörg Wissel, MD; Mauro Zampolini, MD; Abdallah Abouihia, MSc; Alessandra Calabrese, PhD; Leopold Saltuari, MD



(*Stroke*. 2018;49:2129-2137. DOI: 10.1161/STROKEAHA.118.022255.)

UNIVERSITÀ DEL PIEMONTE ORIENTALE



UPO
UNIVERSITÀ DEL PIEMONTE ORIENTALE

(*Stroke*. 2018;49:2129-2137. DOI: 10.1161/STROKEAHA.118.022255.)

Annals of Physical and Rehabilitation Medicine xxx (2018) xxx–xxx

Available online at ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

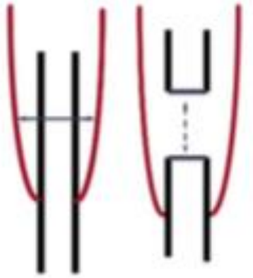
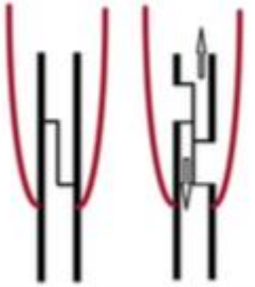
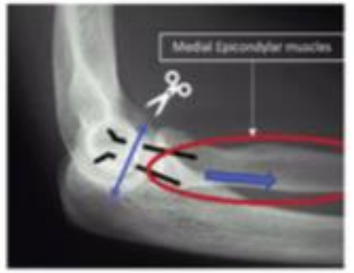
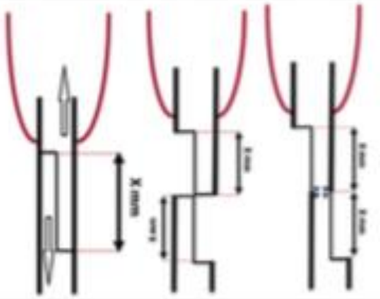
Review

Orthopaedic surgery for patients with central nervous system lesions: Concepts and techniques

F. Genêt [a,b,*], P. Denormandie [b,c], M.A. Keenan [d]

- Componenti statiche prevalenti
- Situazione clinica “stabilizzata”

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Technique	Simple tenotomy	Simple Intramuscular tenotomy	Z Intramuscular tenotomy	Proximal muscle release (Forearm - Page-Scaglietti procedure)	Z tenotomy
Schematic representation — Muscle — Tendon					
Location	Tendon	Myotendinous Union	Myotendinous Union	Proximal insertion of the muscle	Tendon
Procedure	Surgically or percutaneously	Surgically or percutaneously	Surgically or percutaneously	Surgically	Surgically (needs suture)
Expected lengthening		15-20 mm (10-15°)	20-50 mm (20-50°)	10 to 60 mm (10 to 60°)	No limit: X mm tendon lengthening = X° gain in range of motion gain
Immobilization	Cast 10 days (Skin and pain management)	Cast 35 days with weight bearing	Cast 35 days with weight bearing	Cast 21 days (Early muscular contractions under cast)	Cast 35 days with weight bearing

Genet et al, 2018

Conclusioni

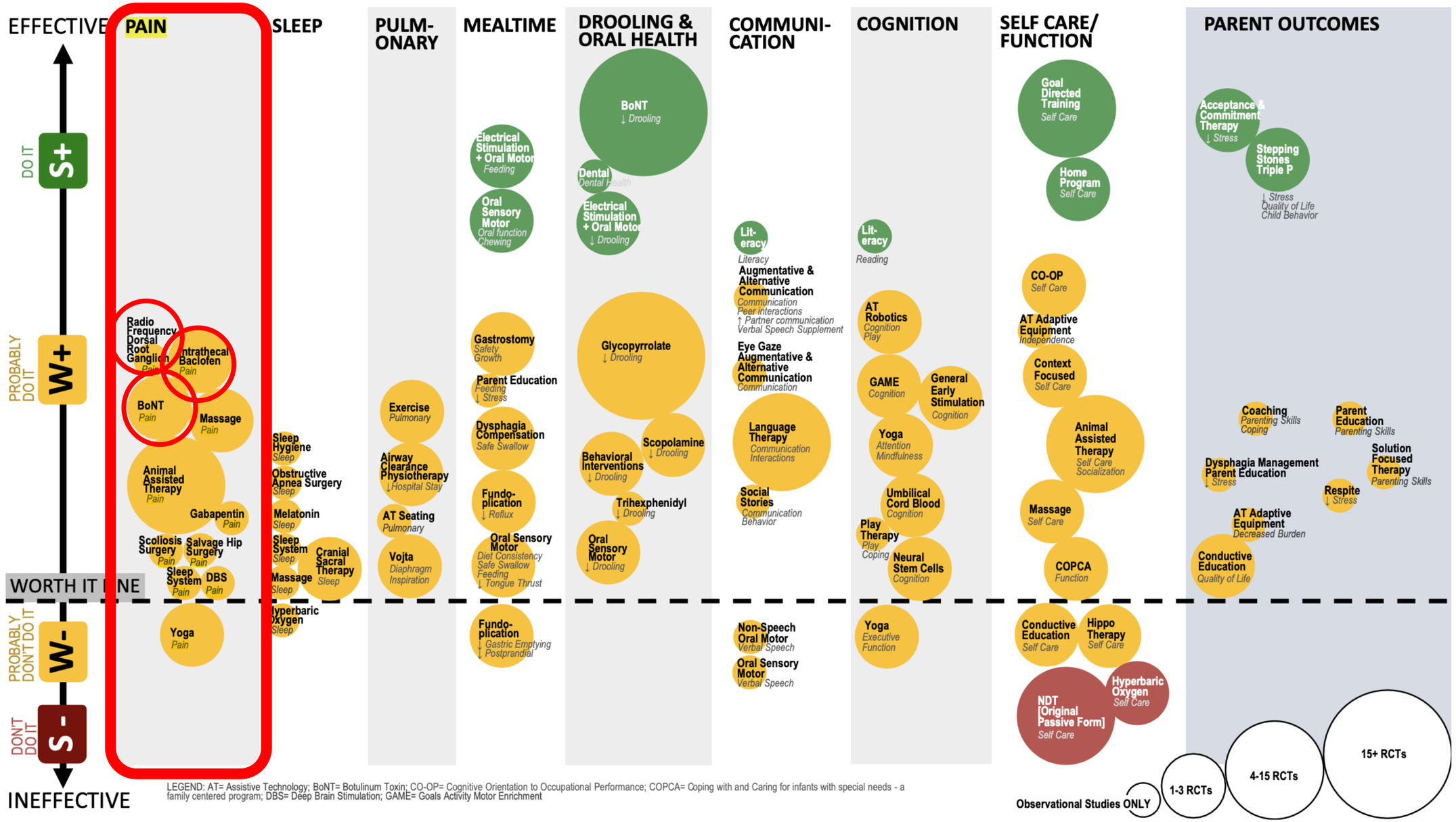
- La presenza di spasticità è frequentemente associata alla presenza di dolore
- “Mixed pain syndrome”

- Trattamento della spasticità può essere correlato a riduzione della sintomatologia algica

UNIVERSITÀ DEL PIEMONTE ORIENTALE

Conclusioni -2

- Necessità di corretto inquadramento diagnostico e fisiopatologico
- Utilizzo delle opzioni terapeutiche più indicate (anche in combinazione)



LEGEND: AT= Assistive Technology; BoNT= Botulinum Toxin; CO-OP= Cognitive Orientation to Occupational Performance; COPCA= Coping with and Caring for infants with special needs - a family centered program; DBS= Deep Brain Stimulation; GAME= Goals Activity Motor Enrichment

Curr Neurol Neurosci Rep (2020) 20: 3

frontiers | Frontiers in Rehabilitation Sciences

TYPE Perspective
PUBLISHED 19 April 2023
DOI 10.3389/fresc.2023.1135593

OPEN ACCESS

EDITED BY
James Abbas,
University of Arkansas, United States

REVIEWED BY
Michel Lemay,
Temple University, United States

*CORRESPONDENCE
Jacob Graves McPherson
✉ mcpherson.jacob@wustl.edu

Precision neuromodulation: Promises and challenges of spinal stimulation for multi-modal rehabilitation

Maria F. Bandres[1,2], Jefferson L. Gomes[2], Gerson N. Moreno Romero[1†], Avery R. Twyman[1†] and Jacob Graves McPherson[1,2,3,4,5*]

UNIVERSITÀ DEL PIEMONTE ORIENTALE

alessio.baricich@med.uniupo.it