Distonias

Dra Sara Casagrande

Membro Titular da ABN

Neurologista do Grupo de Distúrbios de Movimento e Estimulação Cerebral Profunda - HC/FMUSP

Neurologista do Núcleo de Neuromodulação - Hospital Beneficência Portuguesa

Sócia Propietária da Clínica Dommo

Hermann Oppenheim

Über eine eigenartige Krampfkrankheit des kindlichen and jugendlichen Alters (dysbasia lordotica progressiva, dystonia musculorum deformans). Neurol Centralbl 1911;30:1090-1107.

About a unique cramping sickness observed in children and teenagers (Dysbasia lordotica progressiva, Dystonia musculorum deformans)

Klein C, Fahn S. Translation of Oppenheim's 1911 paper on dystonia. Mov Disord. 2013 Jun 15;28(7):851-62.

1911: Oppenheim
1975: first international dystonia symposium
1976: Fahn and Eldridge's first definition and classification for dystonias

D

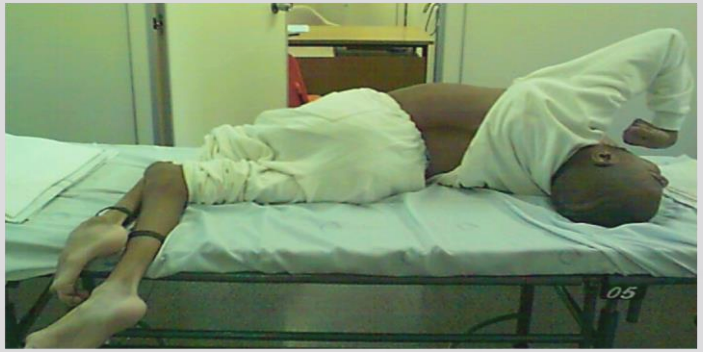
Mov Disord. 2013 June 15; 28(7): 863–873. doi:10.1002/mds.25475.

Phenomenology and classification of dystonia: a consensus update

Alberto Albanese[1], Kailash Bhatia[2], Susan B. Bressman[3], Mahlon R. DeLong[4], Stanley Fahn[5], Victor S.C. Fung[6], Mark Hallett[7], Joseph Jankovic[8], H.A. Jinnah[9], Christine Klein[10], Anthony E. Lang[11], Jonathan W. Mink[12], and Jan K. Teller[13]

Contrações musculares sustentadas ou intermitentes, causando movimentos repetitivos e/ou posturas anormais

Movimentos em torção típicos (velocidade)
Pode estar associado a tremor
Associado a espasticidade (distonias secundárias)
Gatilhos de piora



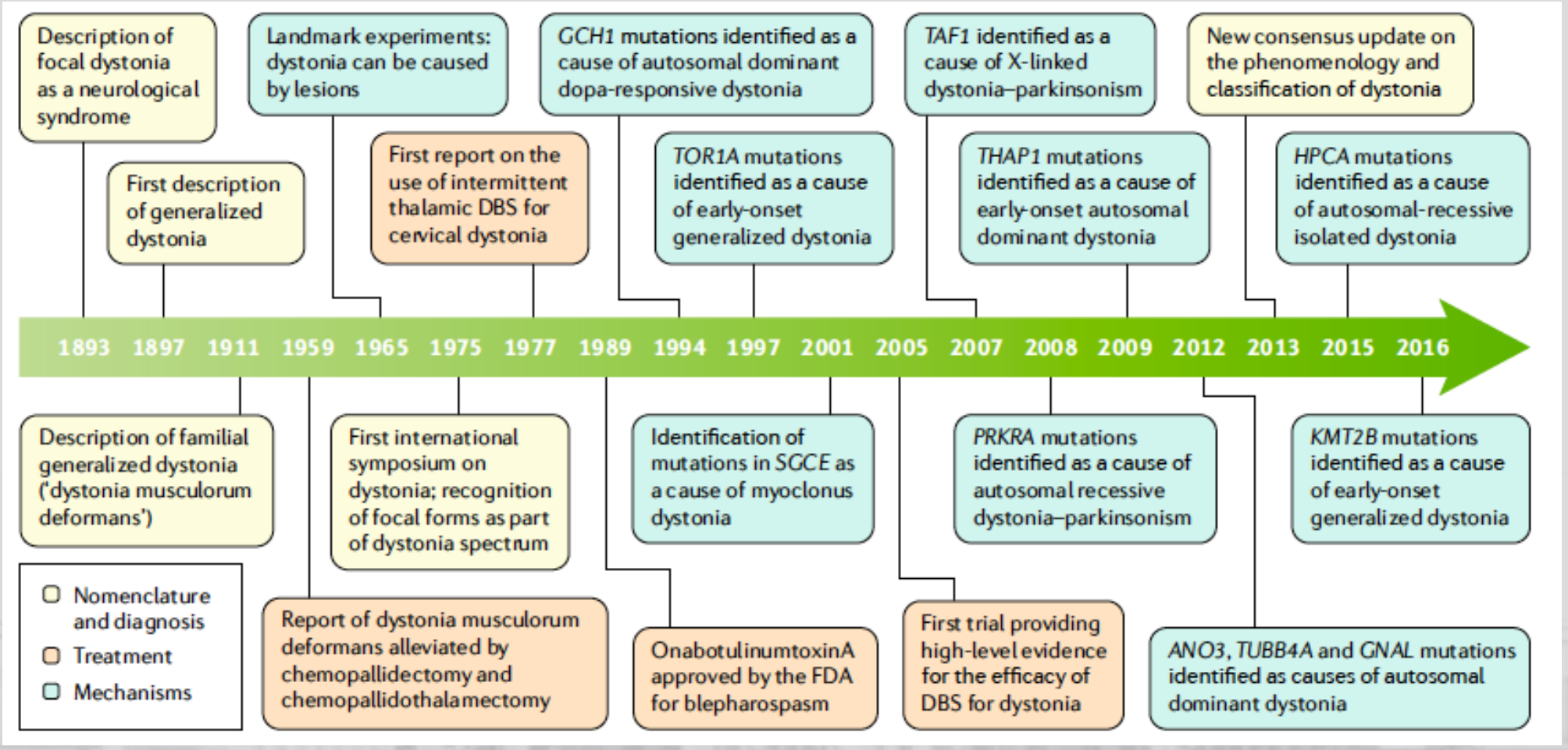
"Dystonia is not a entity and not a syndrome but a collection of syndromes" Alberto Albanese (MSD Congress , 2017)

"Dystonic movements are the most common of involuntary movements to be misdiagnosed" (Stanley Fahn, 1984)

Macerollo A, Superbo M, Gigante AF, et al J Clin Neurosci 2015

Prevalence

- 42/100.000 (Defazio G. 2021)
- 16.4/100.000 (Steeves et al. 2012)
- 732/100.000 (adultos) (Muller, J. et al. 2002)


Description of focal dystonia as a neurological syndrome
First description of generalized dystonia
Landmark experiments: dystonia can be caused by lesions
First report on the use of intermittent thalamic DBS for cervical dystonia
GCH1 mutations identified as a cause of autosomal dominant dopa-responsive dystonia
TOR1A mutations identified as a cause of early-onset generalized dystonia
TAF1 identified as a cause of X-linked dystonia–parkinsonism
THAP1 mutations identified as a cause of early-onset autosomal dominant dystonia
New consensus update on the phenomenology and classification of dystonia
HPCA mutations identified as a cause of autosomal-recessive isolated dystonia
1893
1897
1911
1959
1965
1975
1977
1989
1994
1997
2001
2005
2007
2008
2009
2012
2013
2015
2016
Description of familial generalized dystonia ('dystonia musculorum deformans')
First international symposium on dystonia; recognition of focal forms as part of dystonia spectrum
Identification of mutations in SGCE as a cause of myoclonus dystonia
PRKRA mutations identified as a cause of autosomal recessive dystonia–parkinsonism
KMT2B mutations identified as a cause of early-onset generalized dystonia
Nomenclature and diagnosis
Treatment
Mechanisms
Report of dystonia musculorum deformans alleviated by chemopallidectomy and chemopallidothalamectomy
OnabotulinumtoxinA approved by the FDA for blepharospasm
First trial providing high-level evidence for the efficacy of DBS for dystonia
ANO3, TUBB4A and GNAL mutations identified as causes of autosomal dominant dystonia

Benson *et al.*
Orphanet Journal of Rare Diseases (2022) 17:130
https://doi.org/10.1186/s13023-022-02270-4

Orphanet Journal of Rare Diseases

RESEARCH Open Access

Development of a patient journey map for people living with cervical dystonia

Monika Benson[1,2], Alberto Albanese[2,3], Kailash P. Bhatia[4], Pascale Cavillon[5], Lorraine Cuffe[6], Kathrin König[7], Carola Reinhard[2,8] and Holm Graessner[2,8*]

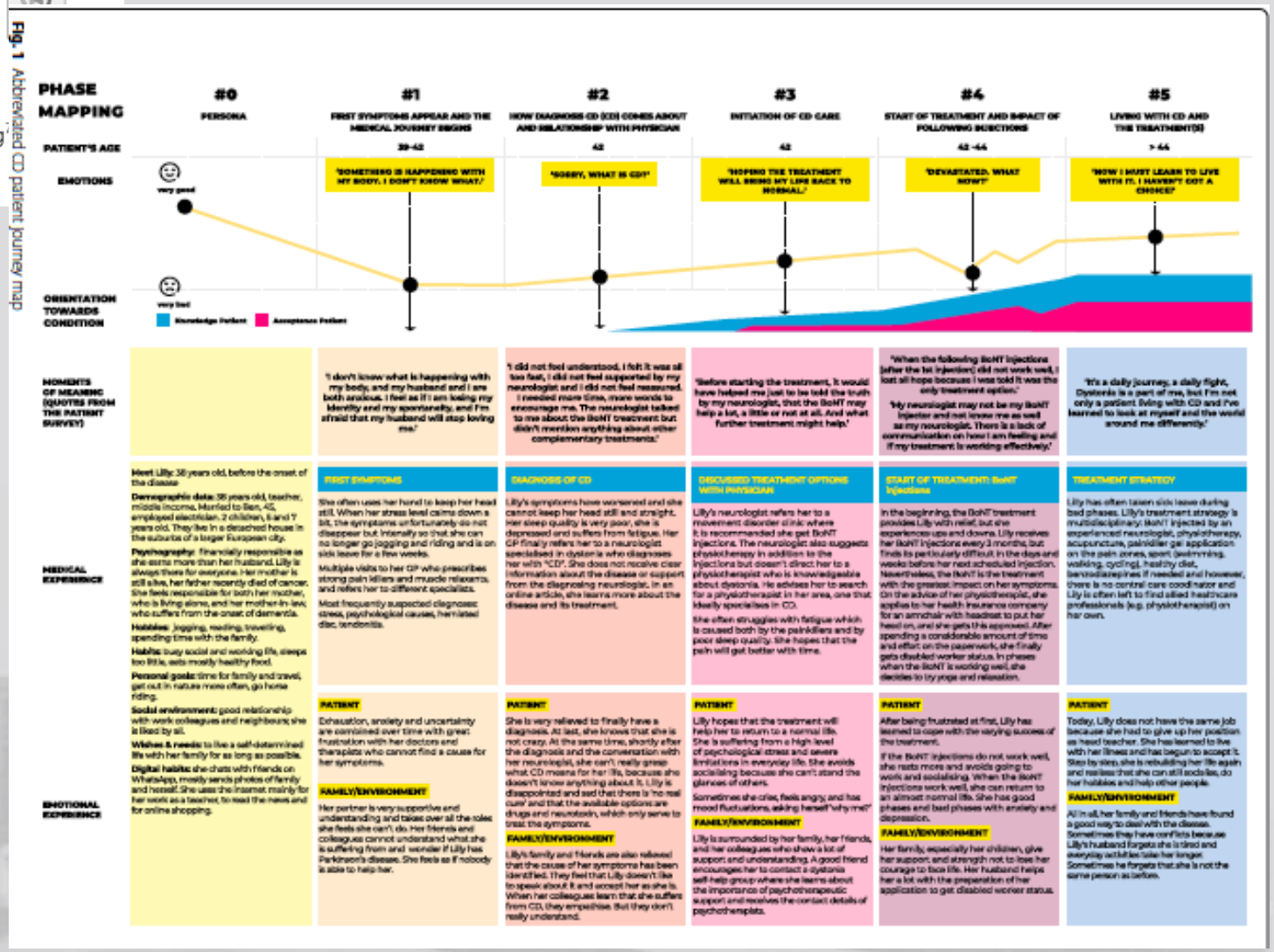
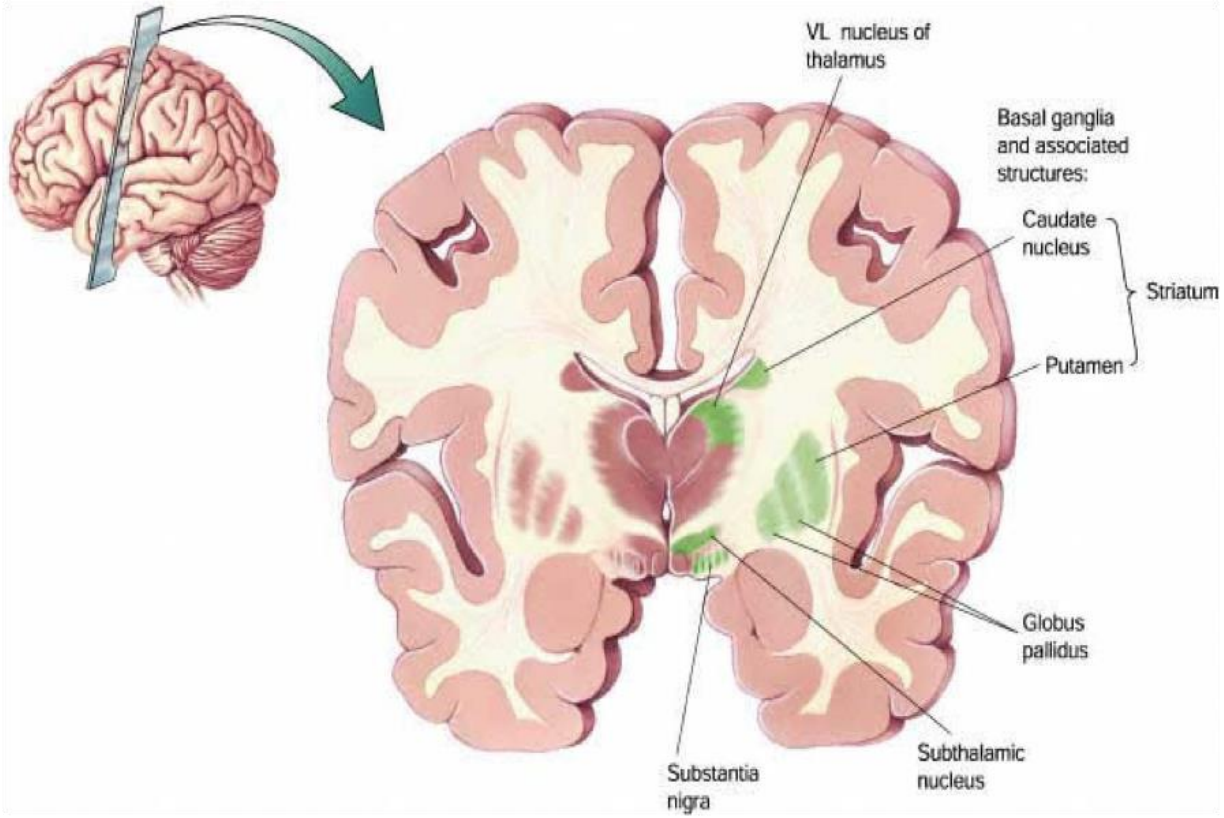
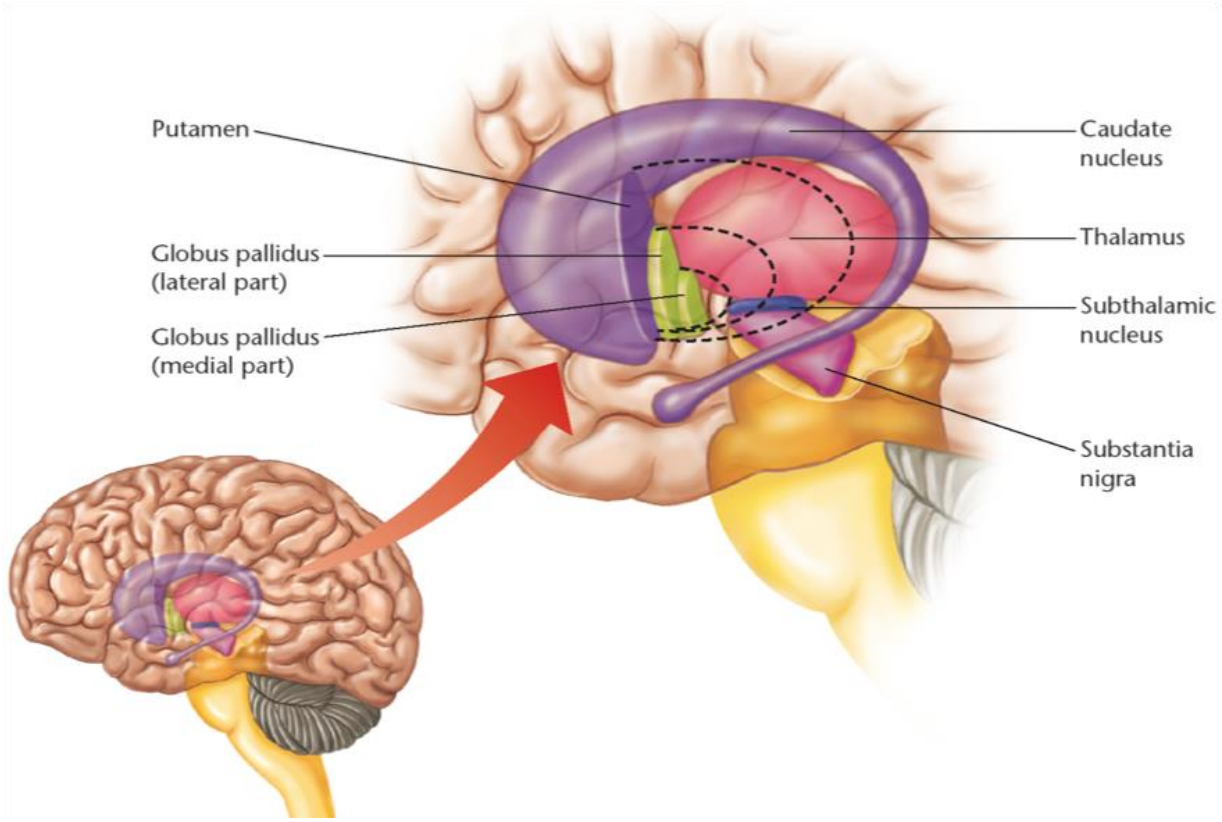


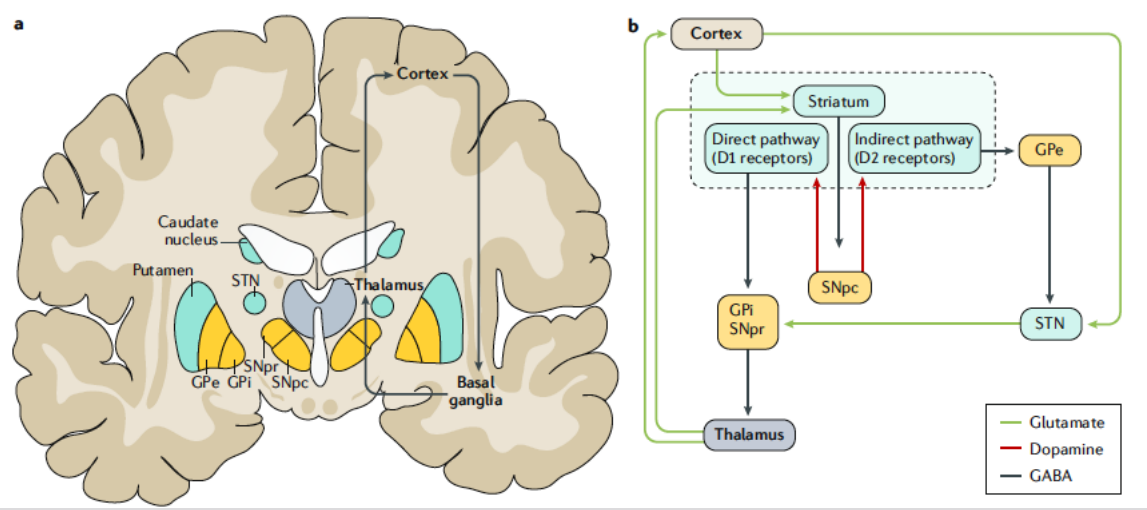
Fig. 1 Abbreviated CD patient journey map

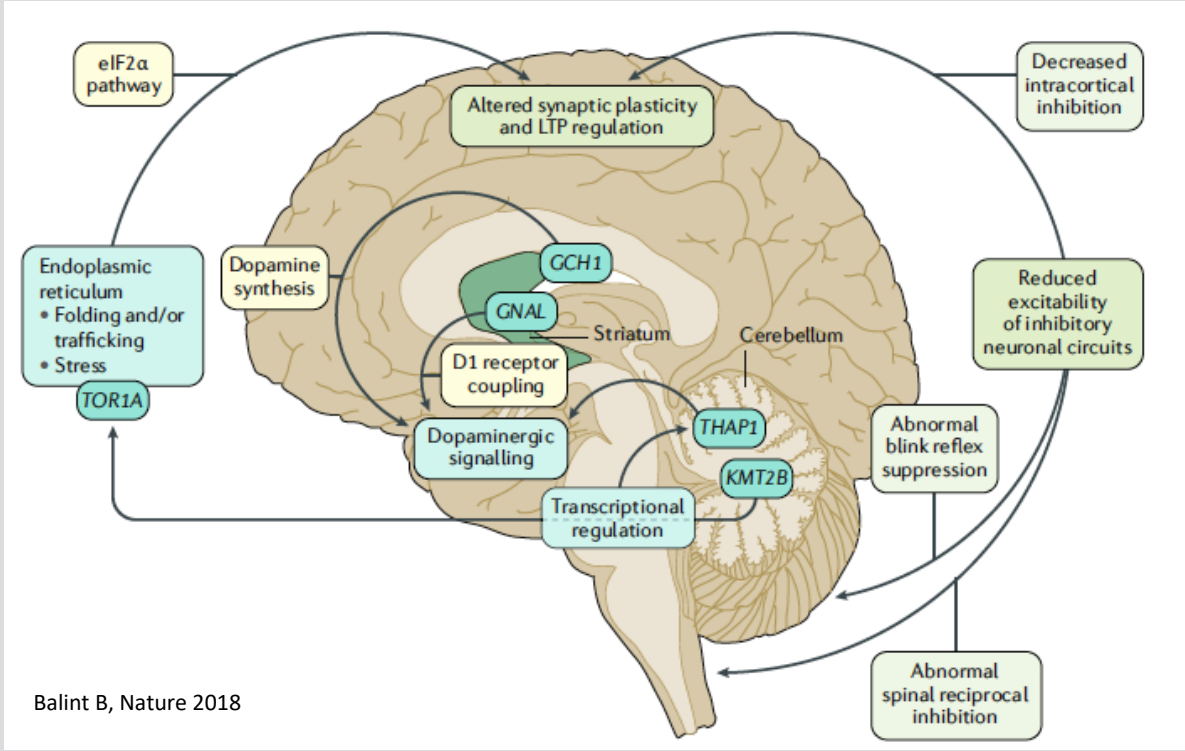
Núcleos da Base - Anatomia



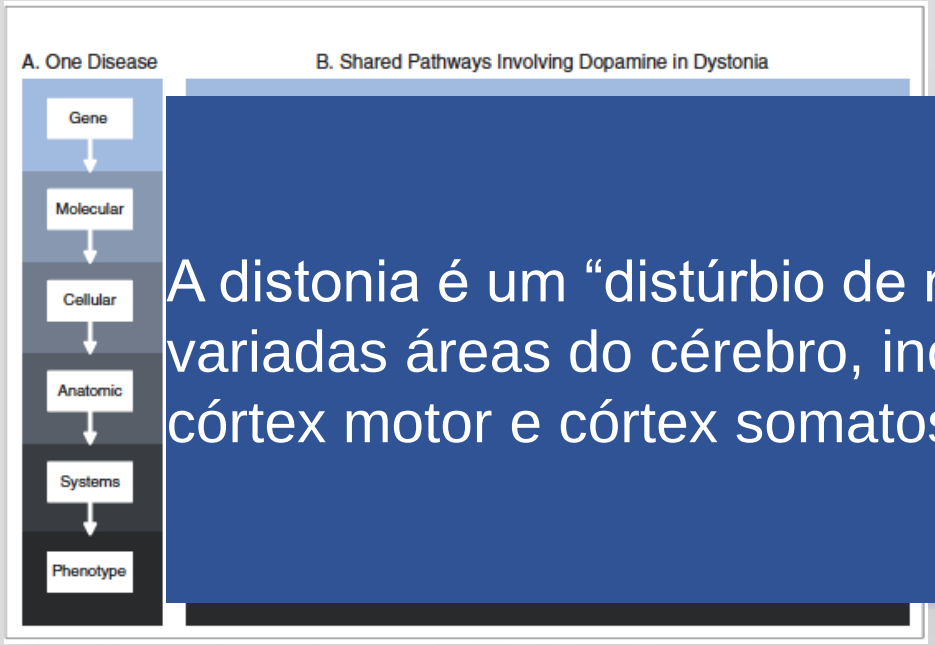


Fisiopatologia Complexa





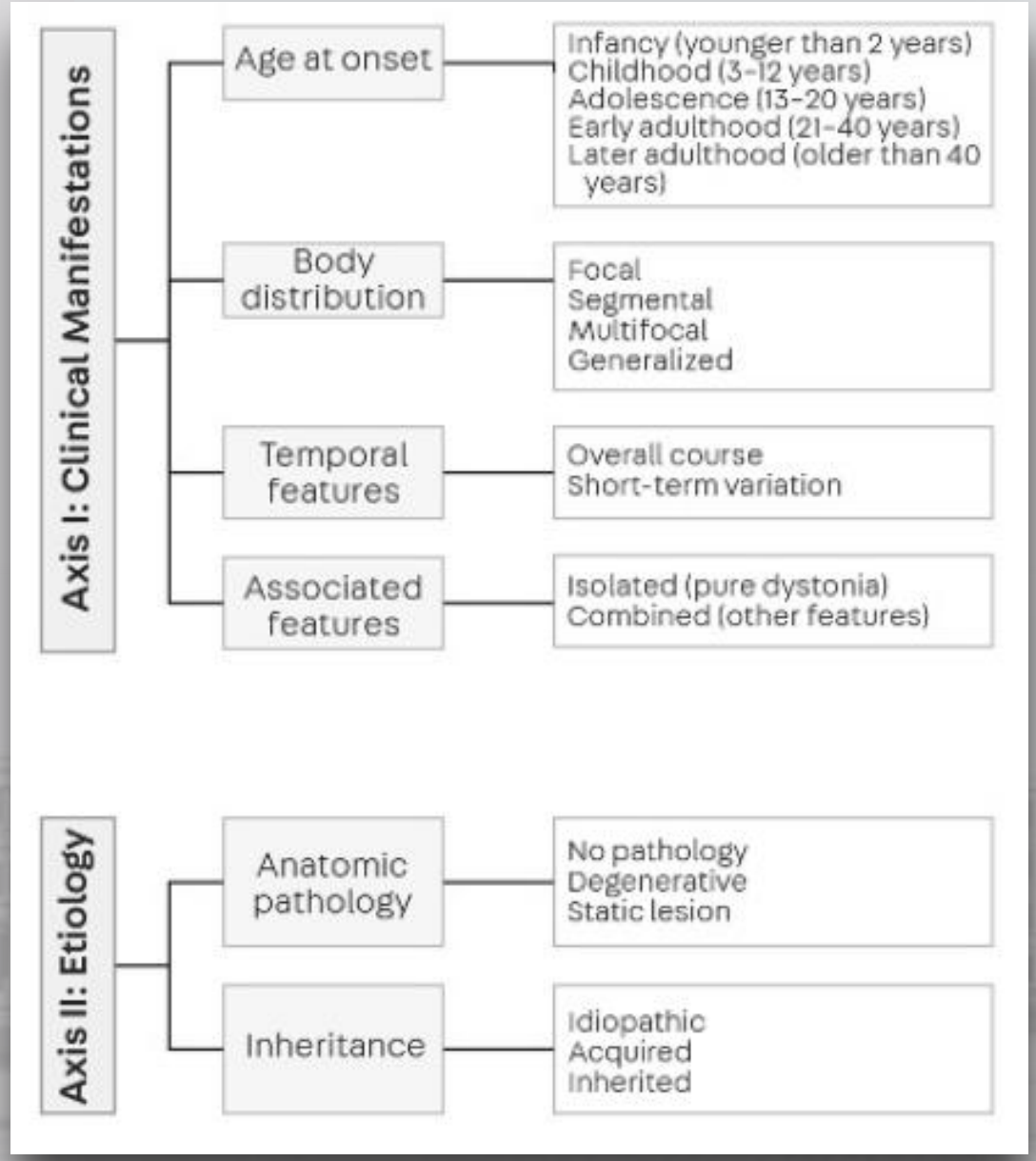
Balint B, Nature 2018



A distonia é um “distúrbio de rede” resultante da disfunção em múltiplas e variadas áreas do cérebro, incluindo o cerebelo, córtex pré-frontal, mesencéfalo, córtex motor e córtex somatossensorial.

Jinnah HA, Neurobiology of Disease 129 (2019) 159–168

Axis I e II



Idade de início

Região do Corpo

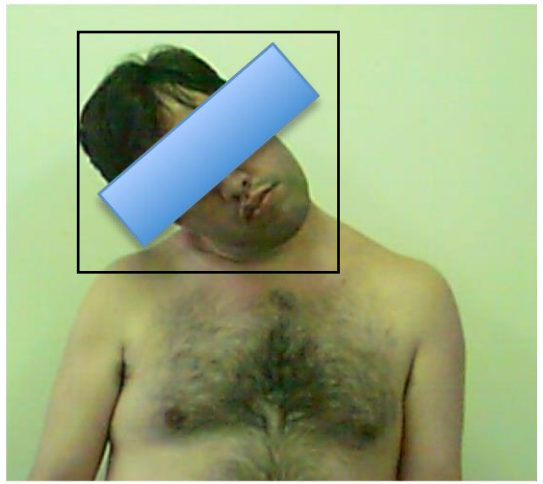
Evolução

Sintomas associados

Anatômico-estrutural

Herança

Focal



Distonia Cervical
Blefaroespasmo
DOM
Caimbra do escrivão

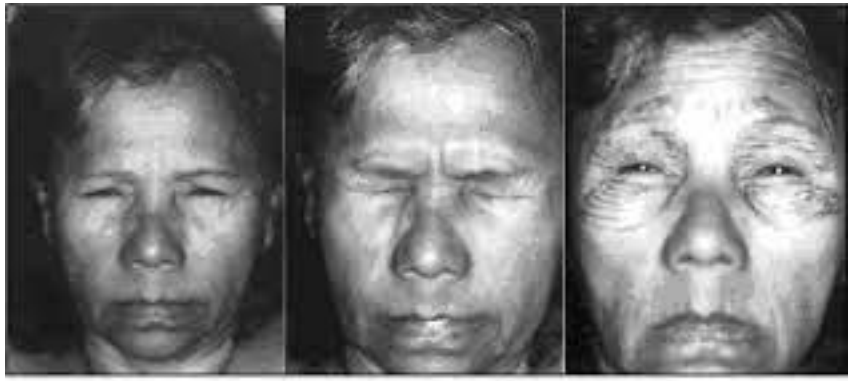
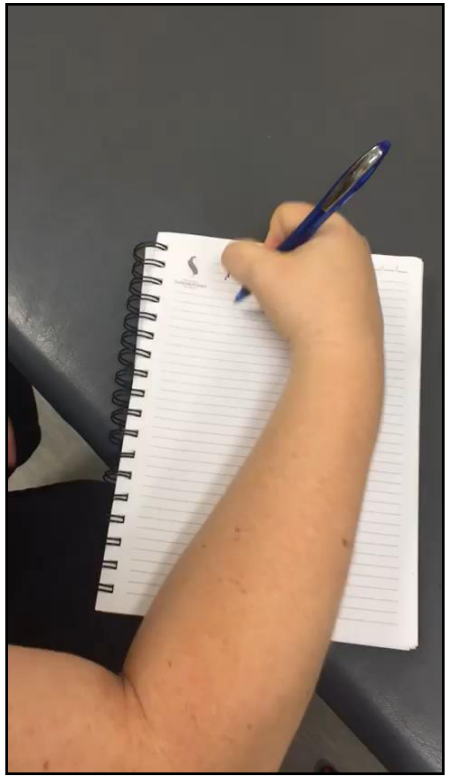
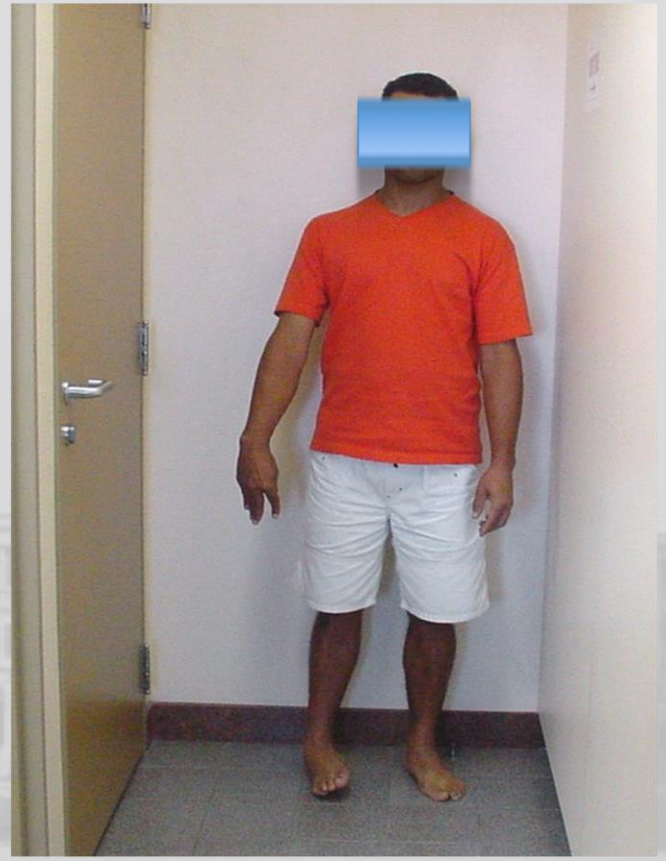


Fig 1. A: Pré-Operatório do Paciente 1. B: Paciente 1 na vigência de espasmo palpebral. C: Marcação pré-operatória das miectomias.



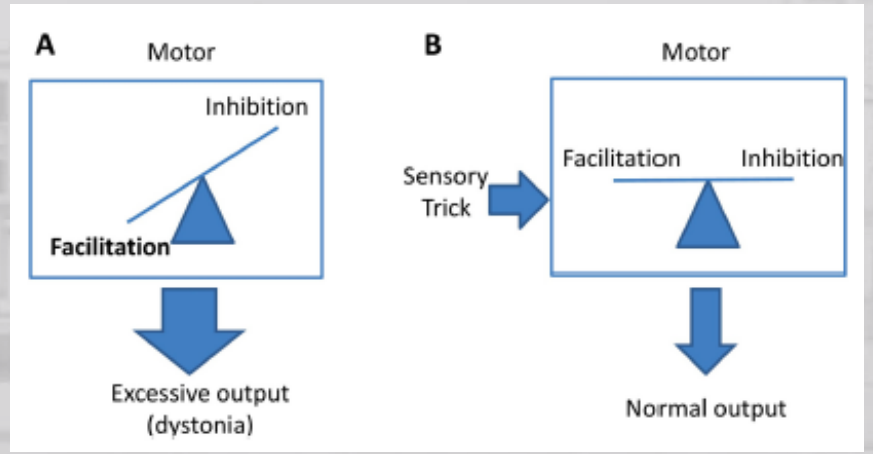
Teive, H. A. G., & Chen, C. C. (2020). Isolated focal dystonia: The mysterious pathophysiology is being unraveled. Neurology, 10.1212/WNL.0000000000010818. doi:10.1212/wnl.00000000000108

Segmentar



Distonia Combinada

Uma característica peculiar das distonias é a possibilidade de aliviar o movimento anormal por meio de “truques” sensoriais (sensory tricks) que geralmente são estúmulos sensoriais ou proprioceptivos



Movement disorders

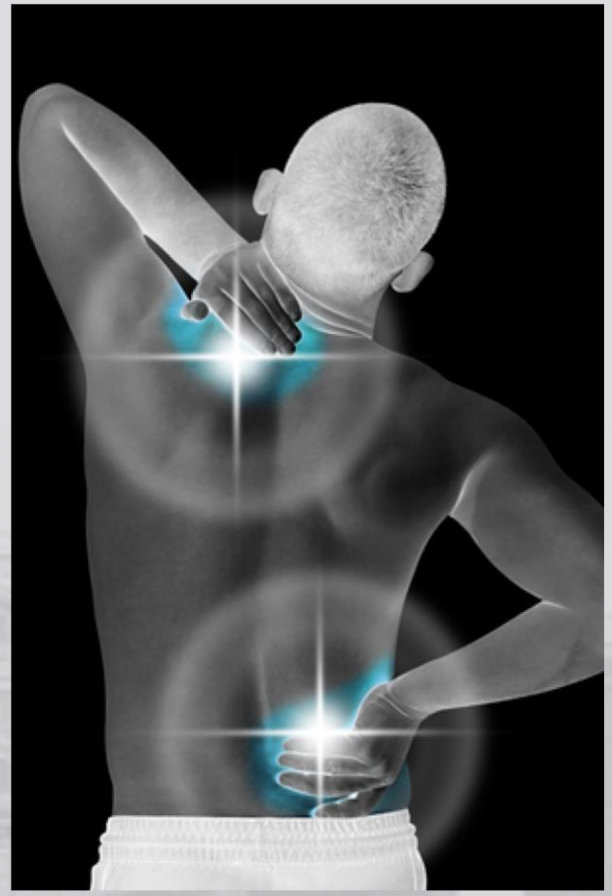
REVIEW

Tricks in dystonia: ordering the complexity

Vesper Fe Marie Llaneza Ramos,[1] Barbara I Karp,[2] Mark Hallett[1]

Casagrande SCB et al, Neurology 2017

Symptom X Syndrome



Sintomas não motores

Neurological Sciences
https://doi.org/10.1007/s10072-021-05452-3

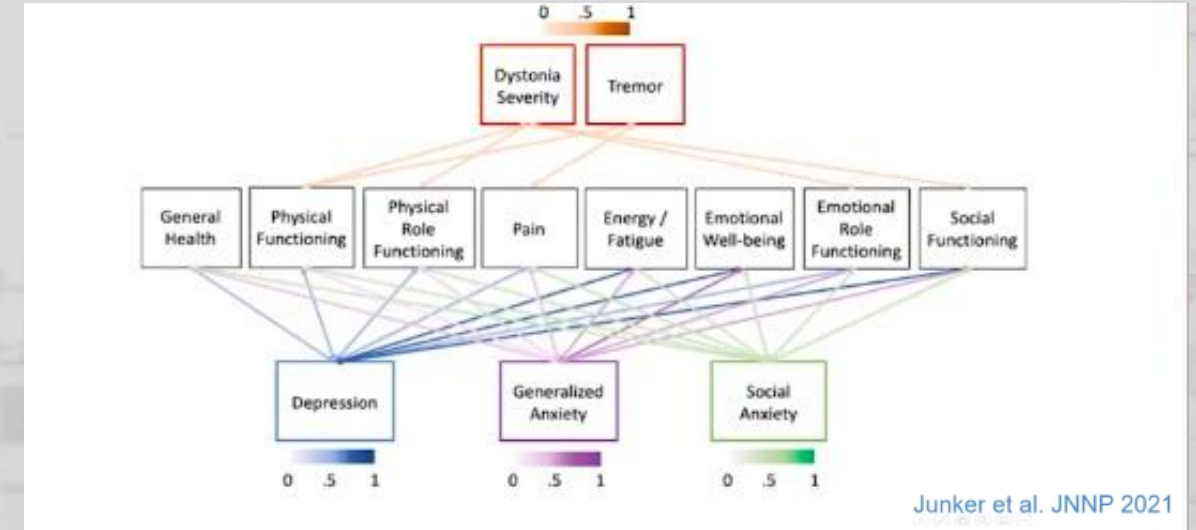
ORIGINAL ARTICLE

High prevalence of self-reported non-motor symptoms and lack of correlation with motor severity in adult patients with idiopathic isolated dystonia

Francisco Pereira da Silva-Júnior[1,2] · Camila Oliveira dos Santos Alves[2] · Sônia Maria Cesar Azevedo Silva[3,4] · Vanderci Borges[3] · Henrique Ballalai Ferraz[3] · Maria Sheila Guimarães Rocha[5] · João Carlos Papaterra Limongi[1] · Egberto Reis Barbosa[1] · Patrícia de Carvalho Aguiar[2,3]

Received: 6 April 2021 / Accepted: 27 June 2021

Non-motor symptom	Prevalence (%)
Sensory symptoms	
Pain	72.5
Tingling/burning	22.5
Olfactory disturbance	14.7
Taste disturbance	12.7
Neuropsychiatric symptoms	
Sadness/anhedonia	41.2
Lack of interest	37.3
Anxiety	63.7
Lack of concentration	31.4
Difficulty recalling information	44.1
Hallucinations	2
Sleep problems	
Excessive sleepiness	28.4
Difficulty falling asleep	38.2
Difficulty staying asleep	30.4
Vivid dreams	17.6
Autonomic symptoms	
Diziness/vertigo	23.5
Excessive sweating	23.5
Heart palpitations	23.5
Urinary retention	0
Urinary incontinence	6.9
Gastrointestinal symptoms	
Nausea	6.9
Constipation*	21.6
Fecal incontinence*	3.9
Sexual dysfunction	
Loss of libido	22.5
Erectile dysfunction*†	4.9
Miscellaneous	
Fatigue	35.3
Dyspnea	21.6
Loss of appetite	12.7
Excessive hunger	9.8
Unexplained loss of weight	13.7



Junker et al. JNNP 2021

Zurowski M, McDonald W, Fox S, Marsh L.
Psychiatric comorbidities in dystonia: emerging concepts. Mov Disord 2013

Movement disorders
Original research

Quality of life in isolated dystonia: non-motor manifestations matter

Johanna Junker [1, 2], Brian D Berman [3], James Hall [4], Deena W Wahba [5], Valerie Brandt [6], Joel S Perlmutter [7], Joseph Jankovic [8], Irene A Malaty [9], Aparna Wagle Shukla [9], Stephen G Reich [10], Alberto J Espay [11], Kevin R Duque [11], Neepa Patel [12], Emmanuel Roze [13, 14], Marie Vidailhet [13, 14], H.A. Jinnah [15], Norbert Brüggemann [1, 2, 16]

Correspondence to MD Norbert Brüggemann, Department of Neurology and Institute of Neurogenetics, University of Luebeck, 23538, Luebeck, Schleswig-Holstein, Germany; norbert.brueggemann@neuro.uni-luebeck.de

Abstract

Objective To evaluate the relationship between health-related quality of life (HR-QoL) and both physical and psychiatric factors in a large, international, multicentre cohort of patients with isolated dystonia, the Dystonia Coalition.

Methods Natural history data from 603 patients with isolated dystonia (median age 57 years (IQR: 48 to 64 years), 67.0% women) were prospectively acquired and analysed. HR-QoL (RAND 36-Item Health Survey), severity of depressive symptoms, generalised anxiety (Hospital Anxiety and Depression Scale) and social anxiety (Liebowitz Social Anxiety Scale) were assessed. Dystonia severity (Burke-Fahn-Marsden Dystonia Rating Scale) and dystonic tremor were examined. Statistical predictors of HR-QoL were calculated using saturated path analysis.

Results Reduced HR-QoL was strongly associated with the degree of depressive symptoms and generalised and social anxiety (8/8 RAND 36 subscales, $p \leq 0.001$). Increased dystonia severity was associated with worse physical functioning, physical and emotional role functioning and social functioning (all $p \leq 0.001$). The presence of tremor correlated with worse physical functioning and pain (all $p \leq 0.006$). Younger age was associated with reduced emotional well-being and vitality (all $p \leq 0.006$). There were no HR-QoL differences between sexes.

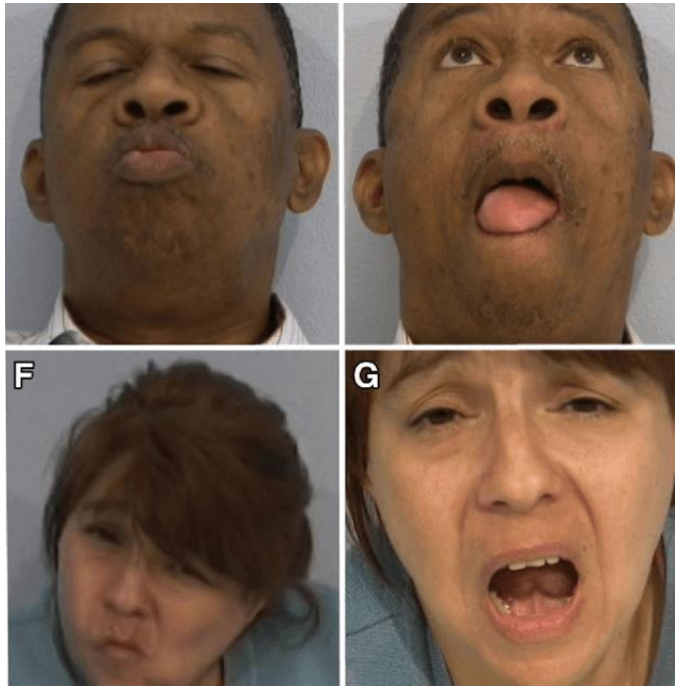
Conclusion HR-QoL in isolated dystonia is strongly associated with psychiatric and physical features. While current standard of care focus on motor aspects of dystonia, comprehensive care should address both physical and mental aspects of health.

Síndrome Tardia

REVIEW

Tardive syndromes

Eoin Mulroy,[1] Bettina Balint,[1,2] Kailash P Bhatia[1]



- Forma Clássica: movimentos coreiformes acometendo região orobucolingual, tronco ou extremidades que surgem em associação com o uso crônico de bloqueadores de receptores dopaminérgicos.
- Discinesia Tardia (coreoatetoico e estereotipias) X Síndrome Tardia

Discinesia Tardia

- DT podem emergir durante o uso do agente causador ou emergir mesmo após a descontinuação do tratamento. Paradoxalmente a droga causadora pode reduzir ou mascarar os sintomas.
- O tempo de exposição para o aparecimento do quadro é variável e pode ser de apenas algumas semanas. A suspensão súbita de um neuroléptico pode desencadear DT (redução gradual é recomendada).
- Para o diagnóstico de uma síndrome tardia, deve haver a persistência dos movimentos anormais por pelo menos 1 mês após a suspensão da medicação causadora (Critérios do DSM-5)
- .Em estudo de longo prazo, foi observada tendência de redução dos sintomas após quatro anos, mas resolução permanente é rara (Gardos et al. The natural history of tardive dyskinesia. J Clin Psychopharmacol ,1988)
- Glazer WM et al (J Clin Psychiatry. 1993): o risco de DT persistente é de 50 % em pacientes com mais de 10 a de exposição

Principais drogas relacionadas a ST

Main Drugs that can cause Tardive Dyskinesia.

Class of Drug	Examples of Drugs causing Tardive Dyskinesia
First Generation Antipsychotic	Haloperidol, Chlorpromazine, Thioridazine, Thiothixine, Pimozide, Perphenazine,Trifluoperazine
Second Generation Antipsychotic	Risperidone, Paliperidone, Iloperidone, Loxapine, Olanzapine, Aripiprazole, Ziprasidone, Asenapine, Lurasidone, Quetiapine, Clozapine
Antiemetic	Metoclopramide, prochlorperazine
Antidepressants	Trazodone, Amitriptyline, Clomipramine, Amoxapine, Fluoxetine, Sertraline
Calcium Channel Blockers (rare)	Cinnarizine, Flunarizine

Frei, K., Parkinsonism and Related Disorders, https://doi.org/10.1016/j.parkreldis.2018.11.017

Classificação Genética

Isolated

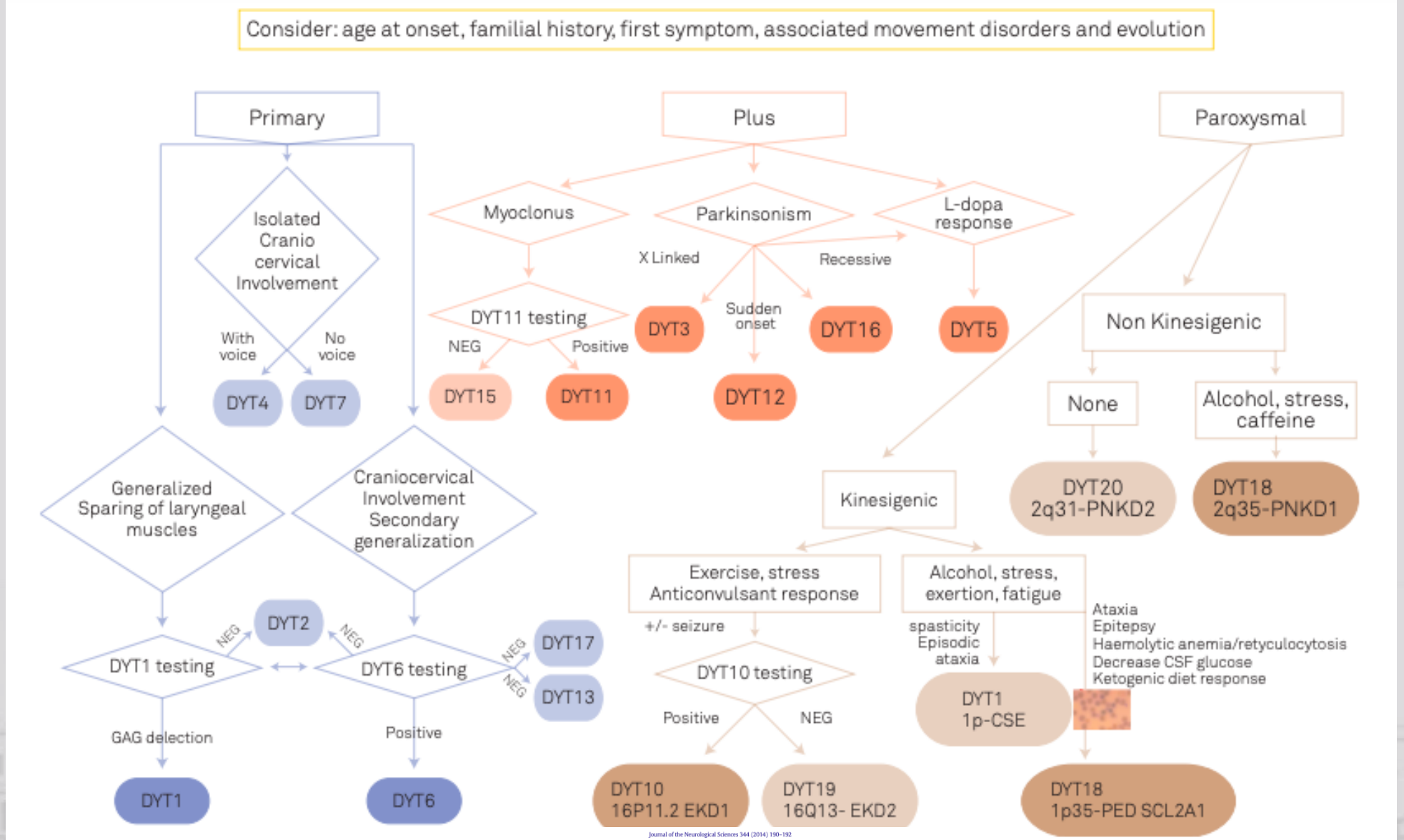
Classification	Chromosome Gene mutation Gene product	Pattern of inheritance	Onset	Distribution, additional features
DYT1	9q34, GAG deletion, missense mutations, *TOR1A*/TorsinA	AD	C	Distal limbs, generalized 10-fold higher prevalence in AJ vs NJ populations
DYT2	1p35.1 *HPCA*/hippocalcin	AR	C	Upper limbs, cranial-cervical, generalized, spanish gypsies, sephardic Jews
DYT6	8q21-22 *THAP1*	AD	A,C	Cervical, cranial, brachial German-American Mennonite-Amish
DYT7	18p	AD	A	Cervical, cranial, spasmodic dysphonia, hand tremor
DYT13	1p36.13-32	AD	A,C	Cranial-cervical and upper limb
DYT17	20p11.22-q13.12	AR	C	Cervical dystonia, dysphonia, segmental, generalized
DYT21	2q14.3-q21.3	AD	A	Late-onset
DYT23	9q34.11, *CIZ1*	AD	A	Cervical
DYT24	3, *ANO3*	AD	C,A	Cranial-cervical-laryngeal, tremor, myoclonus
DYT25	18p, *GNAL*	AD	A	Cervical>cranial>arm>laryngeal
DYT27	*2q37.3 ATP1A2, COL6A3*	AR	C,A	Cranial-cervical, upper limbs, and trunk

A = adult onset; AJ = Ashkenazi Jewish; AD = autosomal dominant; AR = autosomal recessive; C = childhood onset; NJ = Non-Jewish

Classification	Chromosome Gene mutation Gene product	Pattern of inheritance	Onset	Distribution, additional features
DYT28	19q13.2 *KMT2B*	AD	C	Cranial-oromandibular-cervical-laryngeal, generalized, onset in leg, developmental delay, bulbous nose, elongated face, microcephaly, short stature, oculomotor apraxia, galloping tongue, open mouth, risus sardonicus
DYT29	1p35.3 *MECR*	AR	C	Generalized, optic atrophy and BG abnormalities
DYT30	20p13 *VPS16*	AD	C	Oromandibular, cervical, bulbar, or upper limb dystonia, progressing to generalized dystonia

Combined

Classification	Chromosome Gene mutation Gene product	Pattern of inheritance	Onset	Distribution, additional features
DYT3-PARK-TAF1	Xq *TAF1*	XR	A	Parkinsonism Filipinos (Lubag), mosaic striatal gliosis
DYT4-TUBB4A	19p13.3-p13.2 *TUBB4* (β-tubulin 4a)	AD	C,A	Whispering dysphonia, cranial, cervical, limb, hobby horse gait disorder, facial atrophy, ptosis, edentulous
DYT5a-PARK-GCH1	14q22.1 *GCH1* cyclohydrolase I	AD	C	Dopa-responsive dystonia, diurnal fluctuation, gait disorder, parkinsonism, myoclonus, spasticity
DYT5b-PARK-TH	11p15.5 tyrosine hydroxylase	AR	C	Dopa-responsive dystonia, gait disorder, parkinsonism, myoclonus, spasticity
DYT11-SGCE	7q21.3 *SGCE* Epsilon-sarcoglycan	AD	C	Myoclonus-dystonia, alcohol-responsive, OCD, drug addiction
DYT12-PARK-ATP1A3	19q13.2 *ATP1A3* Na+/K+-ATPase	AD	C,A	Rapid-onset-dystonia-parkinsonism, cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss syndrome, (CAPOS), alternating hemiplegia of childhood
DYT15	18p11	AD	C	Myoclonus-dystonia
DYT16-PRKRA	2q31.2 *PRKRA*	AD	C	Predominantly lower limb, axial, oromandibular, and laryngeal dystonia, parkinsonism, unresponsive to levodopa
DYT26	22q12 *KCTD17*	AD	C,A	Myoclonus-dystonia Cranial-cervical
DYT3-PARK-TAF1	Xq *TAF1*	XR	A	Parkinsonism Filipinos (Lubag), mosaic striatal gliosis
DYT4-TUBB4A	19p13.3-p13.2 *TUBB4* (β-tubulin 4a)	AD	C,A	Whispering dysphonia, cranial, cervical, limb, hobby horse gait disorder, facial atrophy, ptosis, edentulous
DYT5a-PARK-GCH1	14q22.1 *GCH1* cyclohydrolase I	AD	C	Dopa-responsive dystonia, diurnal fluctuation, gait disorder, parkinsonism, myoclonus, spasticity
DYT5b-PARK-TH	11p15.5 tyrosine hydroxylase	AR	C	Dopa-responsive dystonia, gait disorder, parkinsonism, myoclonus, spasticity
DYT11-SGCE	7q21.3 *SGCE* Epsilon-sarcoglycan	AD	C	Myoclonus-dystonia, alcohol-responsive, OCD, drug addiction
DYT12-PARK-ATP1A3	19q13.2 *ATP1A3* Na+/K+-ATPase	AD	C,A	Rapid-onset-dystonia-parkinsonism, cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss syndrome, (CAPOS), alternating hemiplegia of childhood
DYT15	18p11	AD	C	Myoclonus-dystonia
DYT16-PRKRA	2q31.2 *PRKRA*	AD	C	Predominantly lower limb, axial, oromandibular, and laryngeal dystonia, parkinsonism, unresponsive to levodopa
DYT26	22q12 *KCTD17*	AD	C,A	Myoclonus-dystonia Cranial-cervical



Journal of the Neurological Sciences 344 (2014) 190–192

OPEN ACCESS Freely available online
Tremor and Other Hyperkinetic Movements

Brief Reports

DYT6 in Brazil: Genetic Assessment and Clinical Characteristics of Patients

Carlos Henrique F. Camargo[1,2*], Sarah Teixeira Camargos[3], Salmo Raskin[4], Francisco Eduardo C. Cardoso[3] & Hélio Afonso G. Teive[1]

[1] Movement Disorders Unit, Neurology Service, Hospital de Clínicas, Federal University of Paraná, Curitiba, Brazil, [2] Neurology Service, Medicine Department, Hospital Universitário, State University of Ponta Grossa, Ponta Grossa, Brazil, [3] Movement Disorders Unit, Neurology Service, Hospital das Clínicas, Belo Horizonte, Brazil, [4] Genetika Laboratory and Catholic University of Paraná, Curitiba, Brazil

Contents lists available at ScienceDirect
Journal of the Neurological Sciences
journal homepage: www.elsevier.com/locate/jns

Short communication

Novel *THAP1* variants in Brazilian patients with idiopathic isolated dystonia

Francisco Pereira da Silva-Junior [a], Camila Oliveira dos Santos [b], Sonia Maria Cesar Azevedo Silva [c,d], Egberto Reis Barbosa [a], Vanderci Borges [d], Henrique Ballalai Ferraz [d], João Carlos Papaterra Limongi [a], Maria Sheila Guimarães Rocha [e], Patricia de Carvalho Aguiar [b,d,*]

SPECIAL ARTICLE

New algorithm for the diagnosis of hereditary dystonia

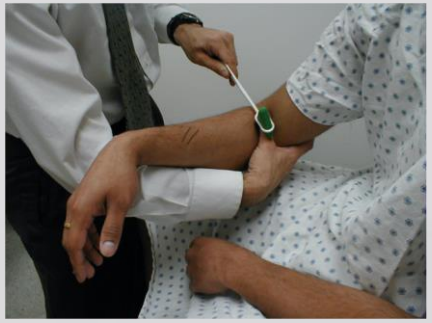
Novo algoritmo para o diagnóstico de distonias hereditárias

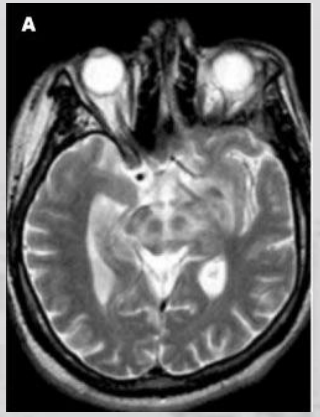
Sarah Camargos, Francisco Cardoso

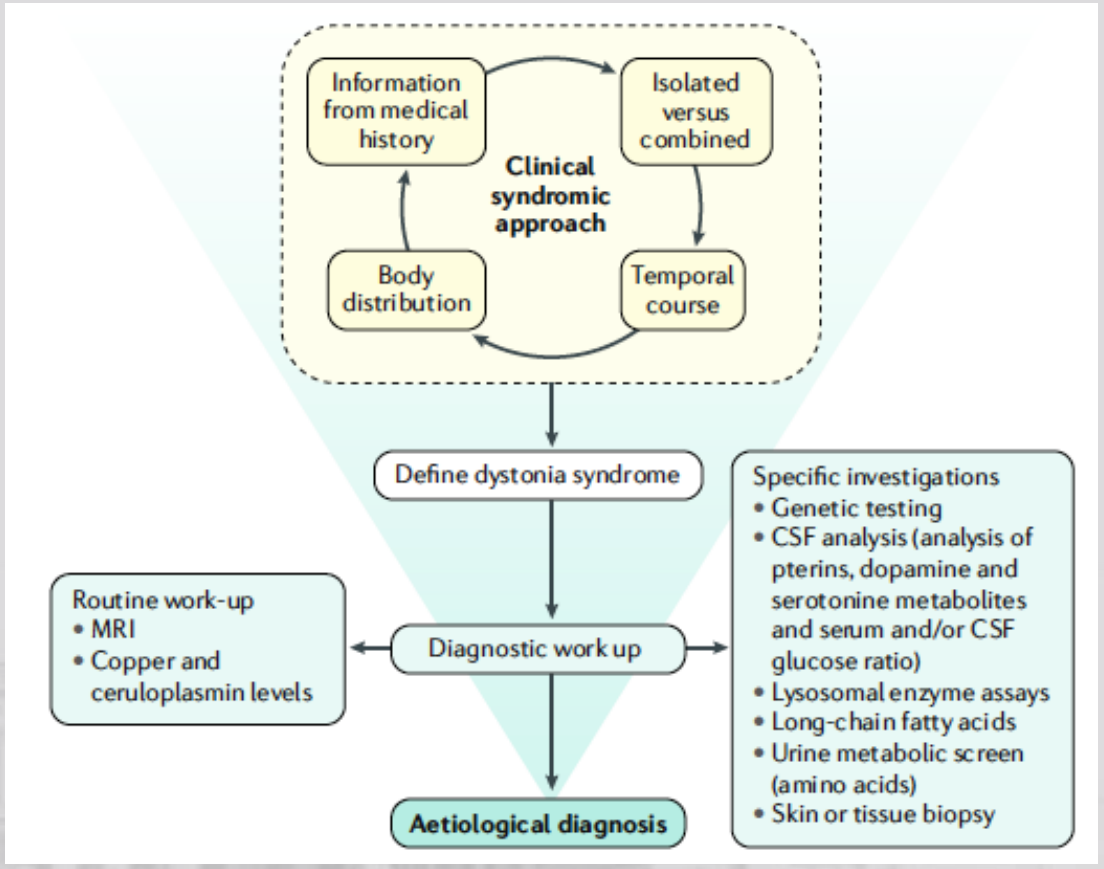
Exames

Identificar causas secundárias e possivelmente tratáveis

Diagnósticos diferenciais







Balint B, Nature 2018

Parkinsonism and Related Disorders 111 (2023) 105449

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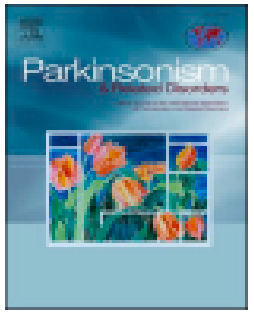
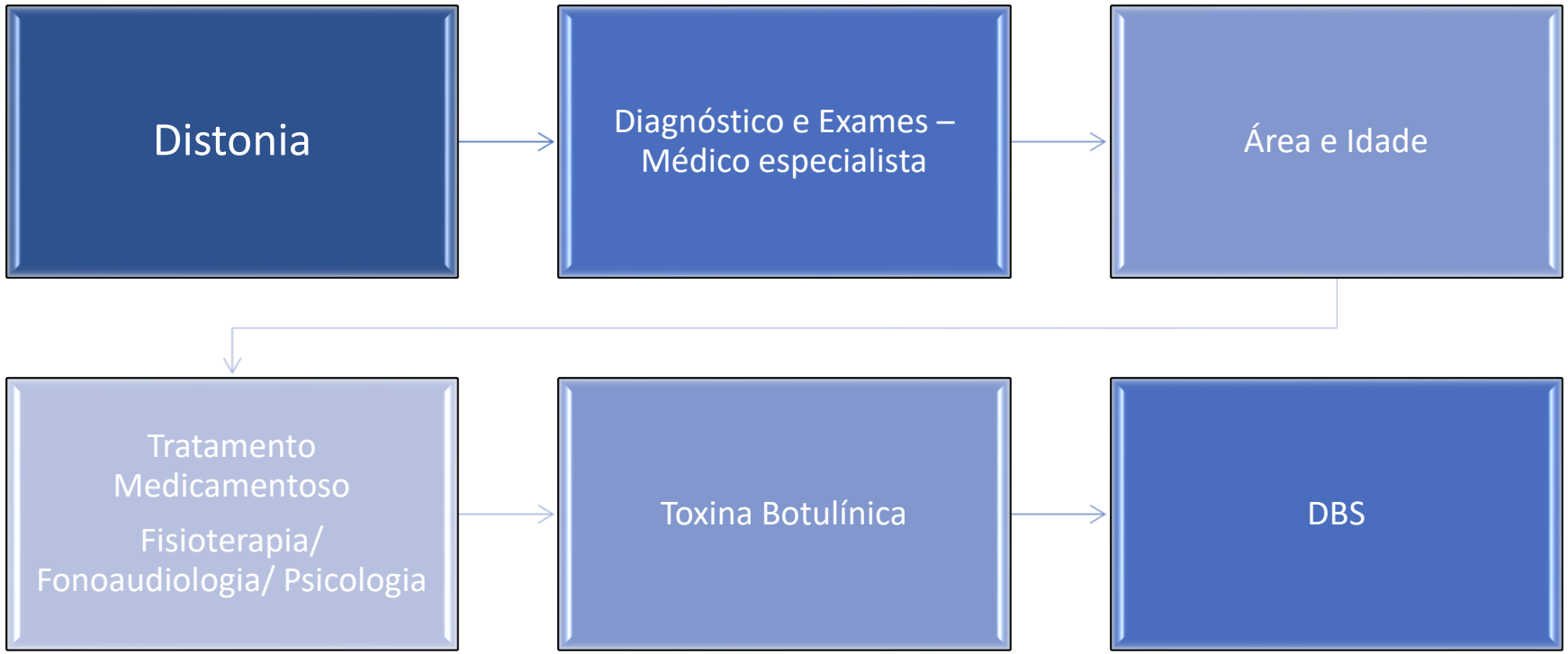
journal homepage: www.elsevier.com/locate/parkreldis

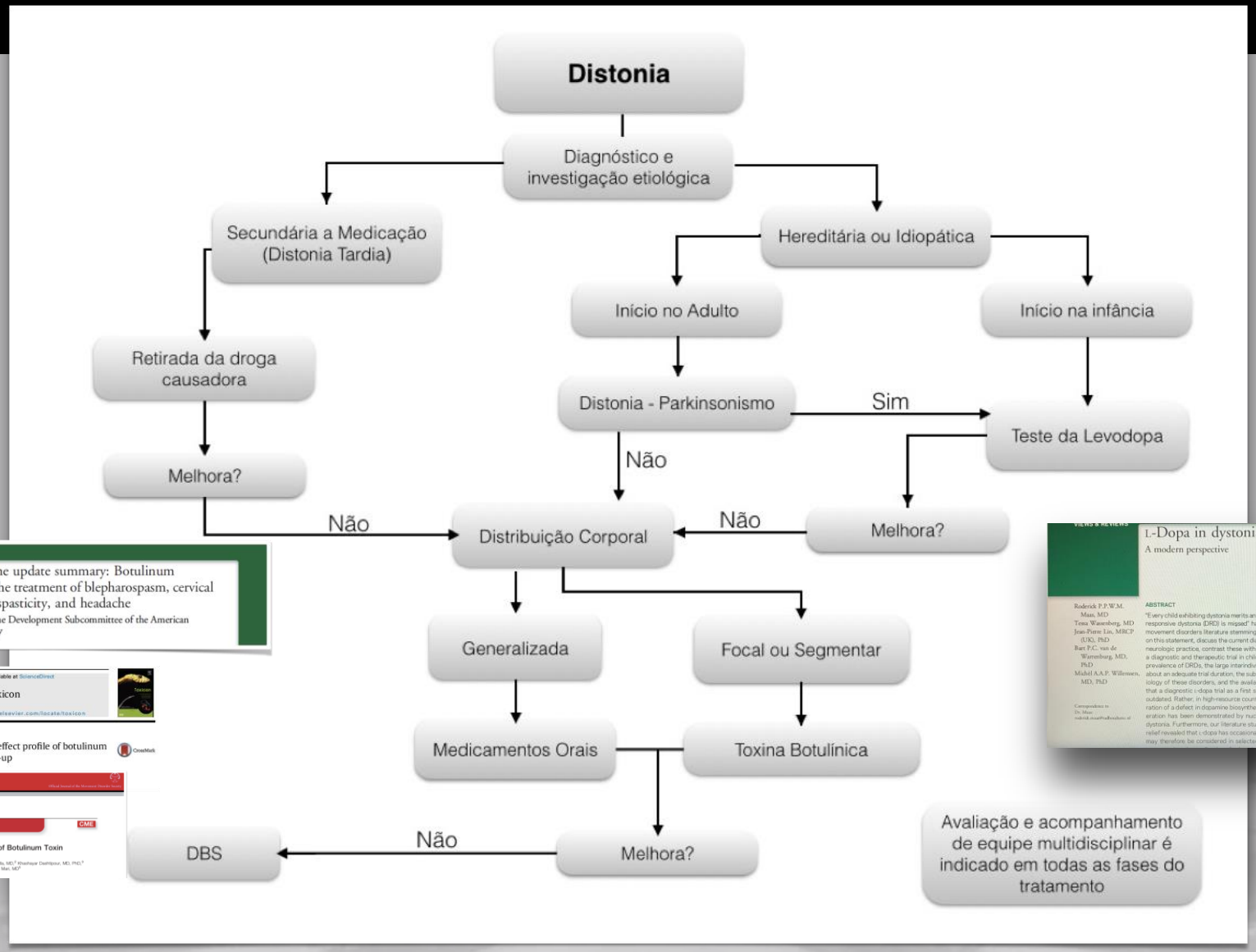


It's time to offer genetic testing to all individuals diagnosed with cerebral palsy

Tratamento Clínico



Treatment of Dystonia



SPECIAL ARTICLE

Practice guideline update summary: Botulinum neurotoxin for the treatment of blepharospasm, cervical dystonia, adult spasticity, and headache

Report of the Guideline Development Subcommittee of the American Academy of Neurology


Toxicon

Long-term efficacy, safety, and side effect profile of botulinum toxin in dystonia: A 20-year follow-up


Movement Disorders

REVIEW

Diffusion, Spread, and Migration of Botulinum Toxin

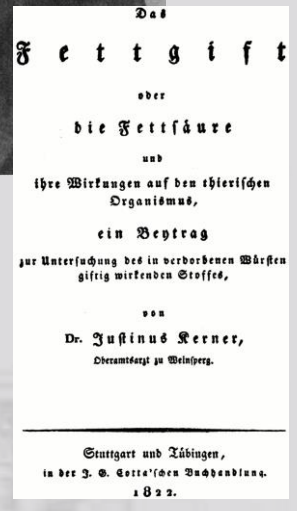
L-Dopa in dystonia

A modern perspective

Toxina Botulínica

- 1793 : primeiro surto - “veneno da salsicha” :
  distúrbios gastrointestinais, diplopia, midríase e paralisia muscular
- 1820: Justinus Kerner
- 1897 : Van Ermengem (Bélgica) *“Clostridium botulinum"*
- 1977 : Allan Scott, oftalmologista americano - estrabismo
  1989 *Oculinum*® *Botox*®
- 1985 : Fahn - Blefaro/ Tsui - Dist cer

“A transmissão neural é interrompida pela toxina da mesma forma que a ferrugem faz com um condutor elétrico “



Das

Fettgift

oder

die Fettsäure

und

ihre Wirkungen auf den thierischen Organismus,

ein Beytrag

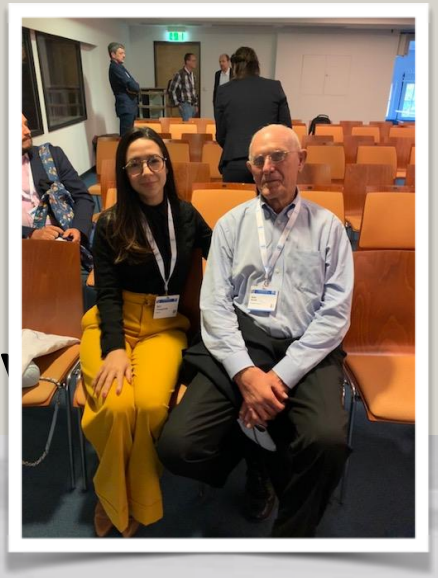
zur Untersuchung des in verdorbenen Würsten giftig wirkenden Stoffes,

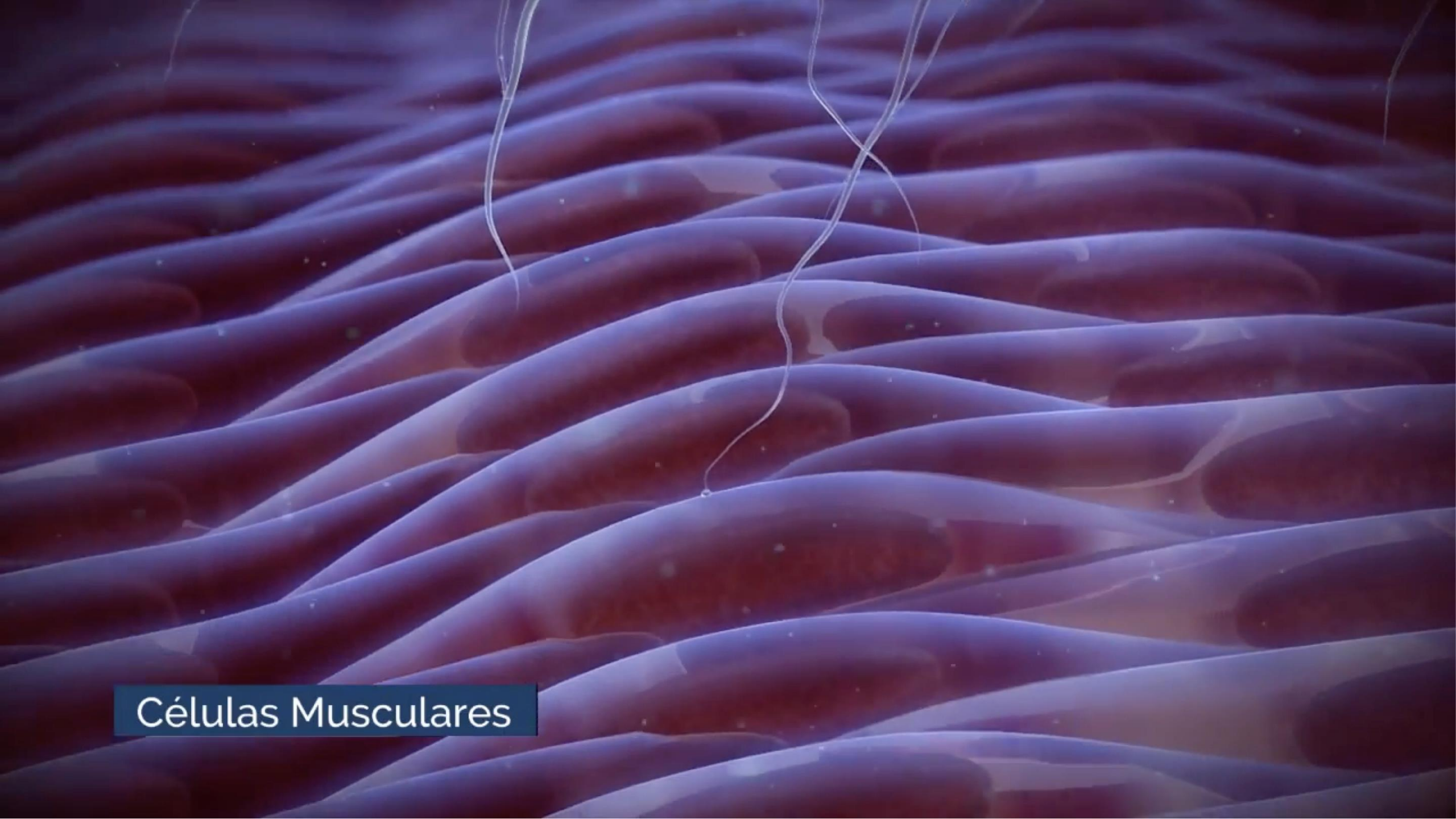
von

Dr. Justinus Kerner,

Oberamtsarzt zu Weinsperg.

Stuttgart und Tübingen,
in der J. G. Cotta'schen Buchhandlung.
1822.




Células Musculares

Técnicas para guiar a aplicação : Ultrassonografia , melhorando a acurácia e Evitando efeitos colaterais

Efeitos Adversos

- Dor/ Hematoma/Edema discreto
- Atrofia muscular
- Paresia Excessiva dos Músculos Injetados
- Difusão da TB para Músculos Adjacentes (Ptose, Diplopia, Disfagia - relativamente comuns)
- Alergia (raro)
- Resistencia *

Reavaliação pós toxina / pré nova aplicação

Contents lists available at ScienceDirect

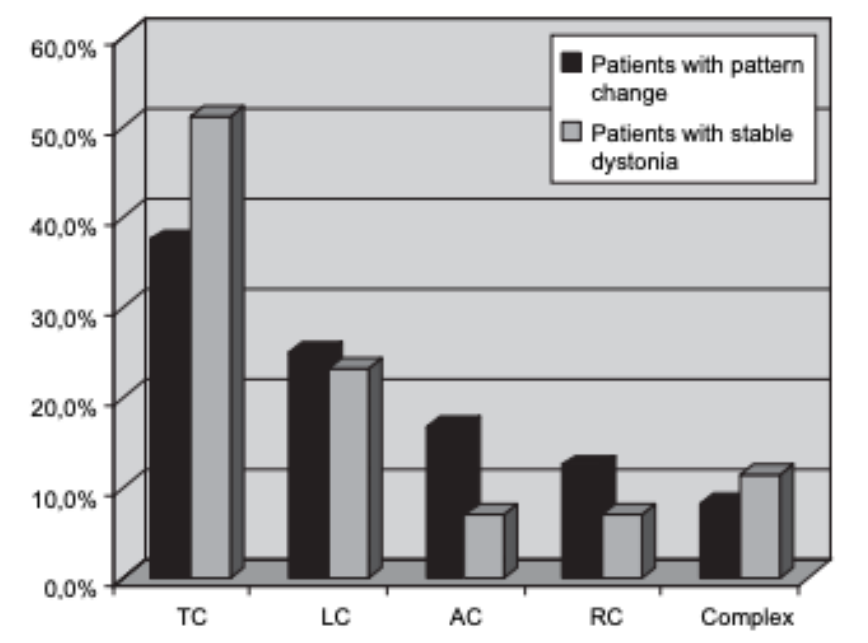
Parkinsonism and Related Disorders

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

Clinical changes of cervical dystonia pattern in long-term botulinum toxin treated patients☆

Fernanda Martins Maia*, Aline Kozoroski Kanashiro, Hsin Fen Chien, Lílian Regina Gonçalves, Egberto Reis Barbosa

Movement Disorders Clinics, Department of Neurology, Hospital das Clinicas, University of São Paulo, School of Medicine, São Paulo, Brazil



Toxins **2015**, *7*, 2321-2335; doi:10.3390/toxins7062321

OPEN ACCESS

toxins

ISSN 2072-6651

www.mdpi.com/journal/toxins

Review

Pain Relief in Cervical Dystonia with Botulinum Toxin Treatment

Carlos Henrique Ferreira Camargo [1,2,*], Lígia Cattai [1,2] and Hélio Afonso Ghizoni Teive [2]

Table 2. Studies with BoNT for CD.

Study/Year	Patients	BoNT	Dose/Muscle (U)	Dose/Session (U)	Motor Response	Pain Relief
Tsui *et al.*, 1986 [66]	19	Botox®	50	100	63%	87%
Gelb *et al.*, 1989 [67]	20	Botox®	20–90	50–280	80%	50%
Jankovic *et al.*, 1990 [68]	232	Botox®	20–200	100–300 average 209	70.7%	76.4%
Blackie and Lees, 1990 [69]	50	Dysport®	120–480	average 875	83%	77%
Jankovic *et al.*, 1990 [70]	195	Botox®	25–100	average 209	90%	93%
Barbosa *et al.*, 1995 [33]	19	Botox®	-	100–270	100%	100%
Poewe *et al.*, 1998 [71]	75	Dysport®	75–300	300–1000	72%	16%–35%
Wissel *et al.*, 2001 [64]	68	Dysport®	100–350	500	86%	42%
Camargo *et al.*, 2008 [15]	85	Botox®		100–280	94.1%	84.4%

Desafios da Toxina Botulínica

- Dose inicial e dose efetiva mínima?
- Múltiplos pontos?
- Técninas para guiar: EMG e USG ?
- Não responsividade: Anticorpo (inco*, TxbB). Teste.
- Intervalo mínimo seguro : 12 semanas (injeçoes de reforço)*
- Mudança do padrão.
- Conversão ideal entre diferentes formulações ?
- Familiarização com as formulações
- Profissionais não especialistas
- Alto custo
- Novos sorotipos

Tratamento Adjuvantes

- Terapia Ocupacional
- Fisioterapia
- Fonoaudiologia
- TMS/TDCS
- Psicólogo/ Psiquiatra

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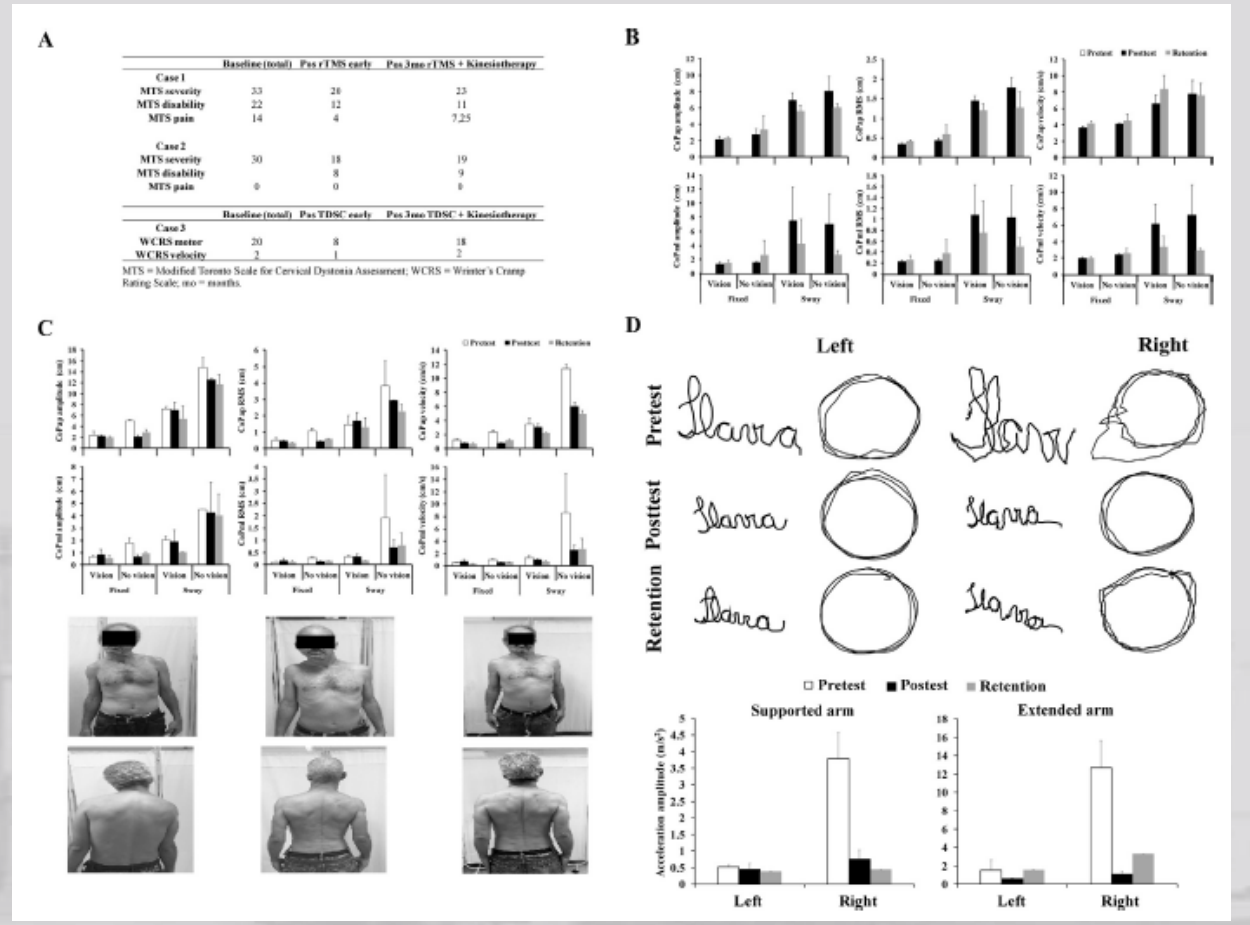
journal homepage: www.elsevier.com/locate/jocn

Case report

Non-invasive brain stimulation and kinesiotherapy for treatment of focal dystonia: Instrumental analysis of three cases

Carolina de Oliveira Souza [a,b,1], Juliana Goulardins [a,c,1], Daniel Boari Coelho [d,*,1], Sara Casagrande [b], Juliana Conti [b], João Carlos Papaterra Limongi [b], Egberto Reis Barbosa [b], Katia Monte-Silva [e], Clarice Tanaka [a,f]



Desafios do Tratamento

1. A distonia e a alteração funcional são difíceis de quantificar; escalas nao validadas.
2. Doença heterogênea: causa, anatomia, disfuncionalidade.
3. Muitos estudos usaram doses insuficientes de medicação ou follow up inadequado para avaliar o benefício do tto.
4. A maioria dos estudos não são DCRC
5. Amostra pequena > resultado difícil de interpretar

Inclusion and Exclusion Criteria for DBS in Dystonia

Helen Bronte-Stewart, MD, MSE,[1]* Takaomi Taira, MD,[2] Francesc Valldeoriola, MD,[3] Marcello Merello, MD, PhD,[4] William J. Marks, Jr., MD,[5] Alberto Albanese, MD,[6] Susan Bressman, MD,[7] and Elena Moro, MD, PhD[8]

[1]Department of Neurology and Neurological Sciences, Stanford University, Stanford, California, USA
[2]Department of Neurosurgery, Tokyo Women's Medical University, Tokyo, Japan
[3]Servei de Neurologia, Institut Clínic de Neurociències, Hospital Clínic, Barcelona, Spain
[4]FLENI, Department of Movement Disorders, Buenos Aires, Argentina
[5]Department of Neurology, University of California, San Francisco, California, USA
[6]Istituto Neurologico Carlo Besta and Università Cattolica, Milano, Italy
[7]Mirken Department of Neurology, Beth Israel Medical Center, New York, New York, USA
[8]Movement Disorders Center, Division of Neurology, TWH, University of Toronto, UHN, Toronto, Ontario, Canada

REVIEW ARTICLE

Eligibility Criteria for Deep Brain Stimulation in Parkinson's Disease, Tremor, and Dystonia

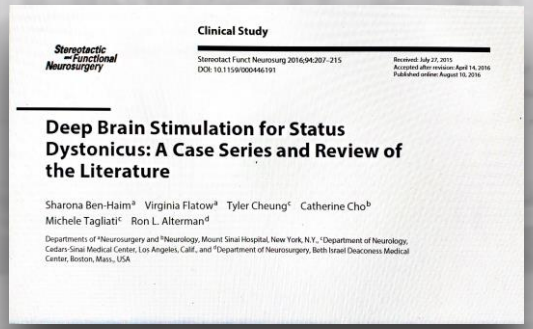
Renato P. Munhoz, Marina Picillo, Susan H. Fox, Veronica Bruno, Michel Panisset, Christopher R. Honey, Alfonso Fasano

Neuromodulation for Dystonia
Target and Patient Selection

Kelly A. Mills, MD[a], Philip A. Starr, MD, PhD[b,*], Jill L. Ostrem, MD[a]

Quando indicar?

- Sintomas refratários e incapacitantes. (Generalizada e Focal)
- Limitações funcionais (causadas por deficiência motora, dor e incapacidade)
- Gravidade ou escalas?
- Distonias Primárias X Secundárias (60% x 24%)



Clinical Study

Stereotactic Functional Neurosurgery

Stereotact Funct Neurosurg 2016;94:207–215
DOI: 10.1159/000446191

Received: July 27, 2015
Accepted after revision: April 14, 2016
Published online: August 10, 2016

Deep Brain Stimulation for Status Dystonicus: A Case Series and Review of the Literature

Sharona Ben-Haim[a] Virginia Flatow[a] Tyler Cheung[c] Catherine Cho[b]
Michele Tagliati[c] Ron L. Alterman[d]

Departments of [a]Neurosurgery and [b]Neurology, Mount Sinai Hospital, New York, N.Y., [c]Department of Neurology, Cedars-Sinai Medical Center, Los Angeles, Calif., and [d]Department of Neurosurgery, Beth Israel Deaconess Medical Center, Boston, Mass., USA

Fatores preditores

- Etiology
- Clinical aspects
- Age of Onset
- Genetic
- Spot

Defer GL, Wildner H, Marie RM, Remy P, Levivier M. Mov Disord. 1999
Renato P. Munhoz, Can J Neurol Sci. 2016; 43: 462-471
Niranjan A, Lunsford LD, Richardson RM (eds): Basel, Karger, 2018

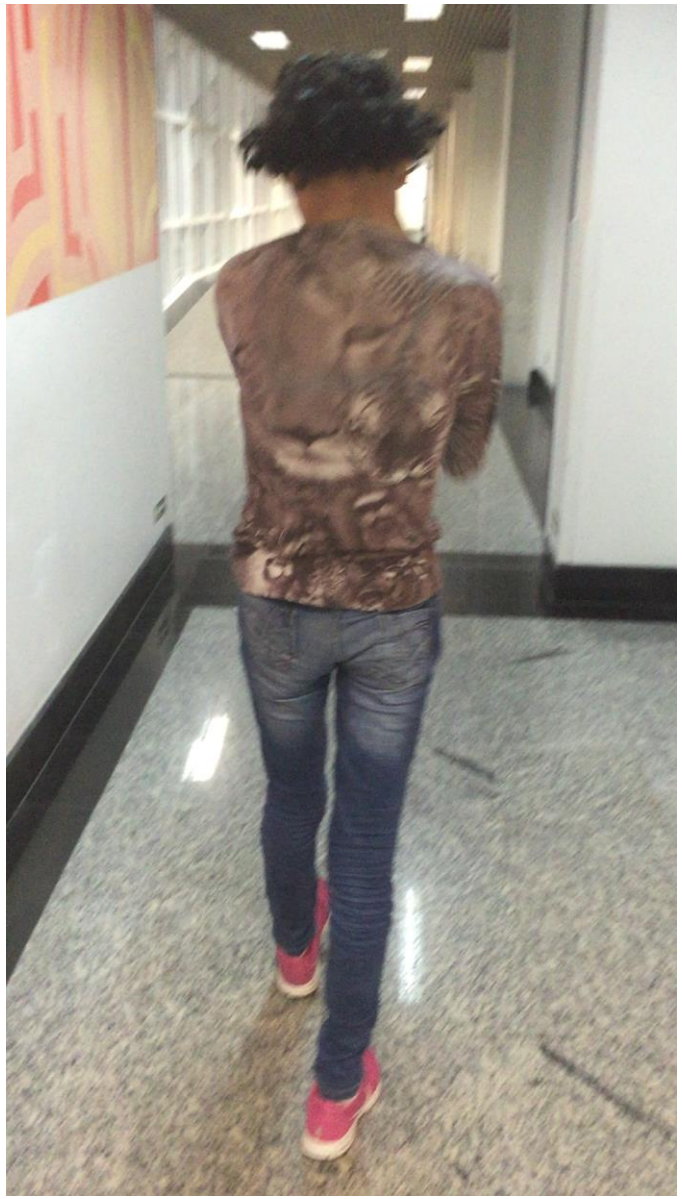
Etiology

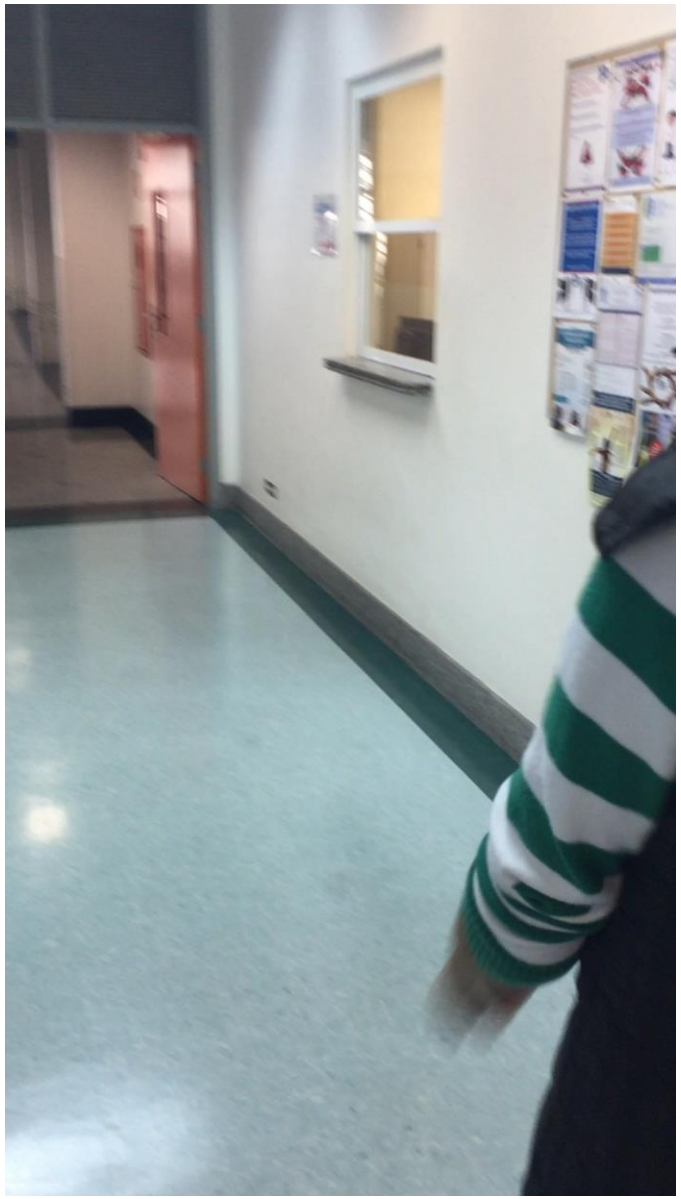
- Isolated dystonia TWSTRSs improvement 55%/ BFMDRS 60%**o**
- Cerebral Palsy
- Goals

Estudo Prospectivo (n 13) > **24% melhora** (1 ano) (melhora cervical e tronco)
Metanálise (n 68) > **23% melhora** (1 ano)
Correlação **com a severidade** da doença no pre-op
STIM CP

DBS Gpi > BFMm 80% melhora (6 mo-48mo) (Tardive Dyskinesia)
Estudo prospectivo (n 9) > BFMm 83% (41mo)

Rubens G. Cury, Suneil K Kalia, Binit B. Shah, Joohi Jimenez-Shahed, L.K. Prashanth & Elena Moro (2018): Surgical treatment of dystonia, Expert Review of Neurotherapeutics, DOI: 10.1080/14737175.2018.1478288





Does genetic influence DBS outcomes?

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J Neural Transm (Vienna). 2017 April ; 124(4): 417–430. doi:10.1007/s00702-016-1656-9.

Deep Brain Stimulation for Dystonia: A Novel Perspective on the Value of Genetic Testing

H. A. Jinnah, MD, PhD[1], Ron Alterman, MD[2], Christine Klein, MD, PhD[3], Joachim K. Krauss, MD[4], Elena Moro, MD[5], Marie Vidailhet, MD[6], and Robert Raike, PhD[7]

- **Estudos em DYT 1 e DYT 6 > BFM m melhora 42 a 80%**
- **DYT 6 > fala e deglutição**

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Deep Brain Stimulation in Rare Inherited Dystonias

Isabelle Beaulieu-Boire [a,b], Camila C. Aquino [b], Alfonso Fasano [b,*], Yu-Yan Poon [b], Melanie Fallis [b], Antony E. Lang [b], Mojgan Hodaie [c], Suneil K. Kalia [c], Andres Lozano [c], Elena Moro [d]

[a] Division of Neurology, Centre Hospitalier Universitaire de Sherbrooke, University of Sherbrooke, Sherbrooke, Québec, Canada
[b] Morton and Gloria Shulman Movement Disorders Clinic and the Edmond J. Safra Program in Parkinson's Disease, Toronto Western Hospital, Division of Neurology, University of Toronto, Toronto, Ontario, Canada
[c] Division of Neurosurgery, Toronto Western Hospital, University Health Network, Department of Surgery, University of Toronto, Toronto, Ontario, Canada
[d] Division of Neurology, CHU Grenoble, INSERM U836, Joseph Fourier University, Grenoble, France

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Treatment

ABSTRACT

Background: Rare causes of inherited movement disorders often present with a debilitating phenotype of dystonia, sometimes combined with parkinsonism and other neurological signs. Since these disorders are often resistant to medications, DBS may be considered as a possible treatment.
Methods: Patients with identified genetic diseases (ataxia-telangiectasia, chorea-achantocytosis, dopa-responsive dystonia, congenital nemaline myopathy, methylmalonic aciduria, neuronal ceroid lipofuscinosis, spinocerebellar ataxia types 2 and 3, Wilson's disease, Woodhouse–Sakati syndrome, methylmalonic aciduria, and X trisomy) and disabling dystonia underwent bilateral GPi DBS (bilateral thalamic Vim nucleus in 1 case). The primary outcome was the difference in the Burke–Fahn–Marsden Dystonia Rating Scale (BFMDRS) between baseline, 1 year and last available follow-up. Preoperative factors such as age at surgery, disease duration at surgery, proportion of life lived with dystonia and severity of dystonia were correlated to the primary outcome.
Results: Eleven patients were operated between February 2003 and December 2013. Age and duration of disease at time of surgery were 30 ± 19 and 12.5 ± 15.7 years, respectively. DBS effects on dystonia severity were variable but overall marginally effective, with a mean improvement of 7.9% (p = 0.39) at 1-year follow-up and 16.7% (p = 0.46) at last follow-up (mean 47.3 ± 19.9 months after surgery). No preoperative factors were identified to predict the surgical outcome.
Conclusion: Our findings support the current knowledge that DBS is modestly effective in treating rare inherited dystonias with a combined phenotype. However, the BFMDRS might not be the best tool to measure outcome in these severely affected patients.

...nent ...orders
...L PRACTICE

LETTERS: NEW OBSERVATIONS

Deep Brain Stimulation in Patients with Isolated Generalized Dystonia Caused by *PRKRA* Mutation

Sara Carvalho Barbosa Casagrande, MD,[1] Clarice Listik, MD,[1] Daniel Boari Coelho, PhD,[2] Joao Carlos Papaterra Limongi, MD, PhD,[1] Luis Augusto Teixeira, PhD,[2] Manoel Jacobsen Teixeira, MD, PhD,[3] Egberto Reis Barbosa, MD, PhD,[1] and Rubens Gisbert Cury, MD, PhD[1,]*

Table 2
Surgical targets, stimulation parameters and dystonia outcomes.

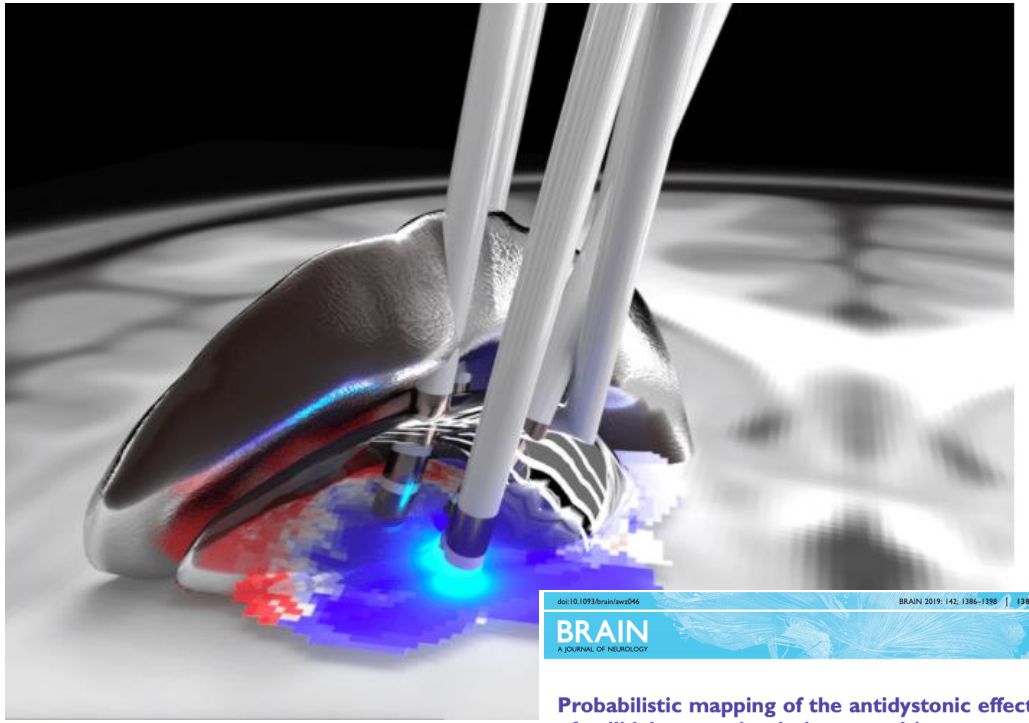
	Diagnosis	Surgical procedure		Duration of follow-up after surgery (months)	BFMDRS before DBS (movement/disability)	BFMDRS 1 year after DBS (movement/disability/% change)	BFMDRS at last evaluation (movement/disability/% change)	Last stimulation parameters			
		DBS implant	Unilateral or bilateral					Contacts	Amp (V)	Freq (Hz)	PW (μs)
1	Ataxia-telangiectasia	GPi	Bilateral	33	69/24	100,5/28 (+45.7/+16.7)	78/27 (+13.0/+12.5)	R 1- 5-C+ L 4- 5 +	1.9	130	60 210
2	Chorea-achantocytosis	GPi	Bilateral	45	14/16	14,5/8 (+3.6/–50.0)	3,5/20 (–75/+25)	R 1- C + L 5- C +	2.5 3.5	130 130	60 60
3	Congenital nemaline myopathy	GPi	Bilateral	36	51/13	50,5/11 (–1.0/–15.4)	NA	R C+ 5- L C+ 1-	2.0 2.0	130 130	120 120
4	Atypical dopa-responsive dystonia	GPi	Bilateral	51	Off med: 18/7 On med: 0/1 *UPDRS part III off med: 19 on med: 10*	Off med/on stim: 10/1 (–44.4/–85.7) *UPDRS part III off med/off stim: 29 off med/on stim: 23 on med/off stim: 16 on med/on stim: 12*	NA	R 3 + 2- L C+ 7-	5.2 5.5	60 60	60 60
5	Methylmalonic aciduria	Thalamic	Bilateral	20	68.5/30	65,5/30 (–4.4 /0.0)	NA				
6	Neuronal ceroid lipofuscinosis	GPi	Bilateral	12	34.5/12	24.5/13 (–29.0/+8.3)	NA	R C+2-3- L C+10-11-	3.0 3.0	130 130	60 60
7	Spinocerebellar ataxia 2	GPi STN	Bilateral Bilateral	36	15.5/4	21/11 (+35.5/+175.0)	21/8,5 (+35.5/+112.5)	R STN C+3- R GPI 3 + 2- L STN C+7- L GPi 7 + 6-	3.1 4.0 3.1 4.0	130 60 130 60	60 120 60 120
8	Spinocerebellar ataxia 3	GPi	Bilateral	12	20/6 TWSTRS 28	18 / 4 (–10.0/–33.3)	NA	R C+1-3- L C+5-7-	3.0 3.0	130 130	210 210
9	Wilson's disease	GPi	Bilateral	24	71.5/27	77/25 (+7.7/–7.4)	NA	R C+1- 2- L C+9- 10-	4.1 4.1	160 160	90 90
10	Woodhouse–Sakati syndrome	GPi	Bilateral	18	50/13	27/12 (–46.0/–7.7)	29/14 (–42.0/+7.7)	R C+ 0- L C+4-	4.5 4.5	60 60	60 60
11	X trisomy	GPi	Bilateral (only right functional)	5	52/12	29/12 (–44.2/0.0) (at 3 months)	NA	R C+2- L OFF	4.0	40	60

Amp, amplitude; BFMDRS, Burke–Fahn–Marsden Dystonia Rating Scale; DBS, deep brain stimulation; Freq, frequency; L, left side; med, medication; PW, pulse width; R, right side; TWSTRS, Toronto Western Spasmodic Torticollis Rating Scale.
Changes in BFMDRS expressed in percentage (+ means worsening of scores, - means improvement of scores).

Pre e pós

Complex and heterogeneous

- Benefits can vary
- Gradual clinical response (delay)
- Variable Stimulation Parameters/Programming



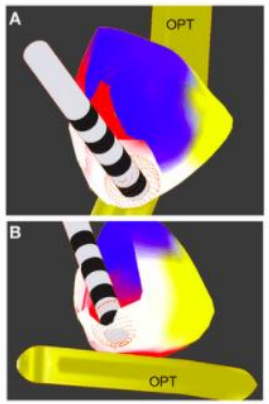
Parkinsonism & Related Disorders

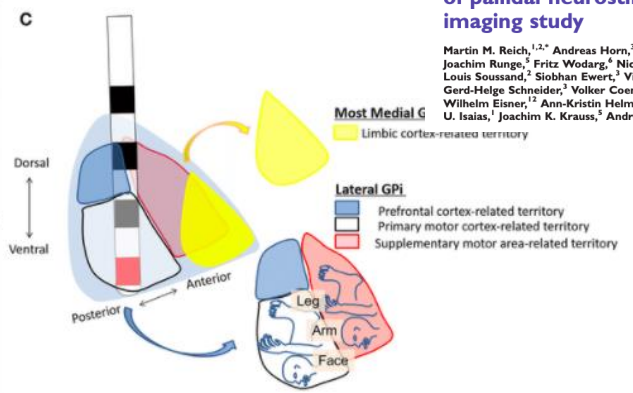
CORRESPONDENCE | VOLUME 45, P101-102, DECEMBER 01, 2017

Pallidal DBS for dystonia in the age of personalized medicine

K. Amande M. Pauls • Joachim K. Krauss • Andrea A. Kühn • ... Gereon R. Fink • Jens Volkmann • Lars Timmermann • Show all authors

Published: September 13, 2017 • DOI: https://doi.org/10.1016/j.parkreldis.2017.09.007 • Check for upd





BRAIN
A JOURNAL OF NEUROLOGY

Probabilistic mapping of the antidystonic effect of pallidal neurostimulation: a multicentre imaging study

Martin M. Reich, Andreas Horn, Florian Lange, Jonas Roothans, Steffen Paschen, Joachim Runge, Fritz Wodarg, Nicolo G. Pozzi, Karsten Witt, Robert C. Nickl, Louis Soussand, Siobhan Ewert, Virgina Maltese, Matthias Wittstock, Gerd-Helge Schneider, Volker Coenen, Philipp Mahlknecht, Werner Poewe, Wilhelm Eisner, Ann-Kristin Helmers, Cordula Matthies, Volker Sturm, Ioannis U. Isaias, Joachim K. Krauss, Andrea A. Kühn, Günther Deuschl and Jens Volkmann

| Deep brain stimulation of the globus pallidus internus (GPi). Electrodes are placed in th part of the GPi (the posterodorsolateral part of the GPi is partially removed). (A) Dorsopc (B) Ventroposterior view of the GPi. (C) Schematic drawing of GPi-DBS with active conta the posteroventrolateral GPi. Colors indicate the territories receiving limbic-(yellow), prefi (white), and supplementary motor (red) cortex-related inputs. OPT, optic tract.

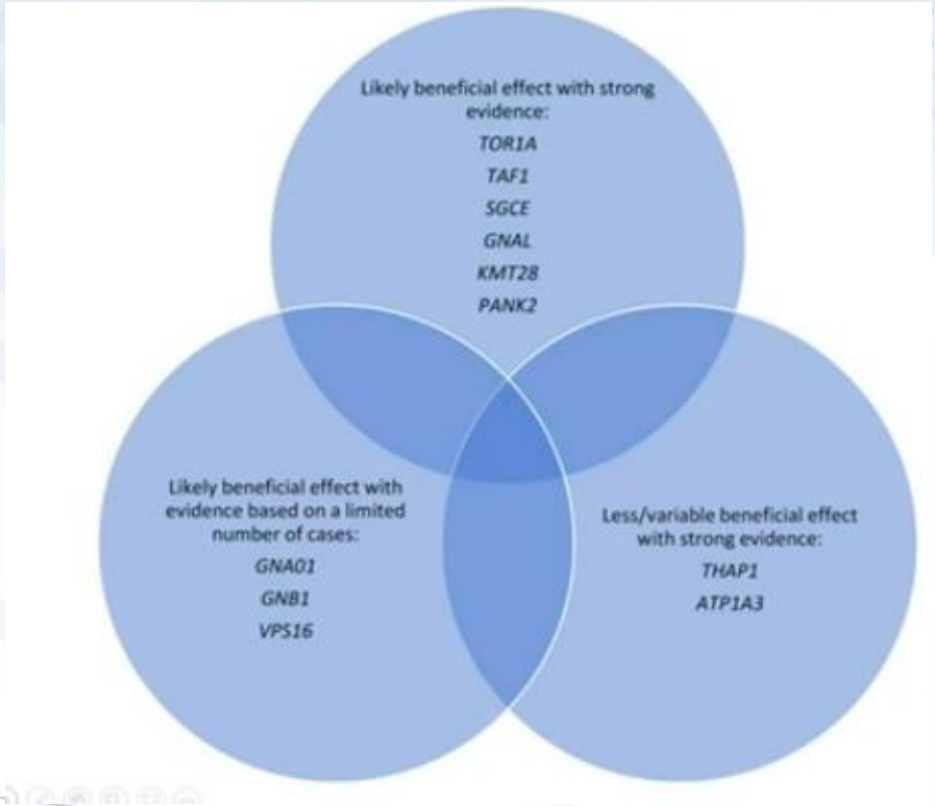
Therapeutic Perspective on Tardive Syndrome with Special Reference to Deep Brain Stimulation

Ryoma Morigaki, Hideo Mure, Ryuji Kaji, Shinji Nagahiro and Satoshi Goto

Published in final edited form as:
J Neural Transm (Vienna). 2017 April ; 124(4): 417–430. doi:10.1007/s00702-016-1656-9.

Deep Brain Stimulation for Dystonia: A Novel Perspective on the Value of Genetic Testing

H. A. Jinnah, MD, PhD[1], Ron Alterman, MD[2], Christine Klein, MD, PhD[3], Joachim K. Krauss, MD[4], Elena Moro, MD[5], Marie Vidailhet, MD[6], and Robert Raike, PhD[7]



Movement Disorders
CLINICAL PRACTICE
LETTERS: NEW OBSERVATIONS

Deep Brain Stimulation in Patients with Isolated Generalized Dystonia Caused by *PRKRA* Mutation

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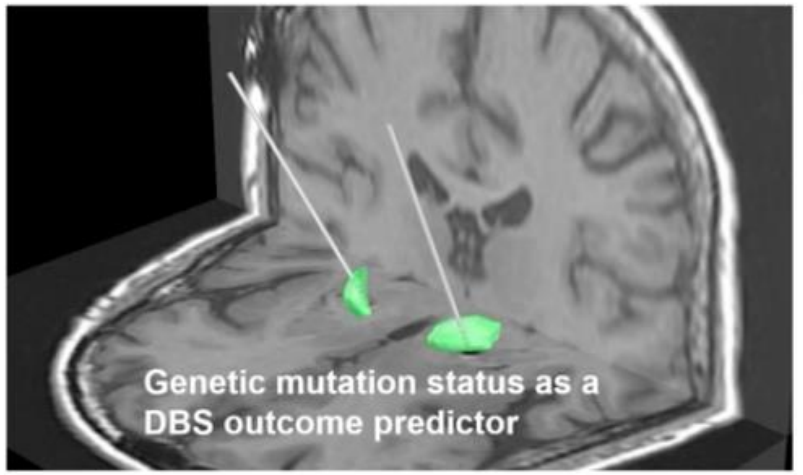

Tisch and Kumar Front Neurol 2020
Artusi et al. JNNP 2020

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