Annual Meeting Webinar
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We have more than 100 participants. Everyone is muted, except speakers. Contact Jody or Gamze by email if needed.

Type in the Questions box. Questions addressed after each speaker. Do not use the Chat box.

This webinar is being recorded.
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| 9:00-9:20 AM | Introduction to the DC  
*H.A. Jinnah, MD, PhD* |
| 9:30-9:45 AM | Patient Advocacy Group Updates  
*J. Hieshetter and K. Kuman* |
| 9:50-10:10 AM | Natural History Project: Progress & Next Steps  
*J.S. Perlmutter, MD* |
| 10:20-10:40 AM | Biobank Project: Progress & Next Steps  
*C. Cruchaga, PhD* |
| 10:50-11:10 AM | BREAK |
| 11:10-11:30 AM | Patient-Centered Outcomes Project  
*S. Pirio Richardson, MD* |
| 11:40 AM-12:00 PM | Objective Measures Project  
*D. Peterson, PhD* |
| 12:10-12:40 PM | Q&A, Closing Remarks |
Dystonia Coalition: What is it?

- Not a research study
- Consortium for multicenter studies
  infrastructure for clinical & translational research
  address gaps in clinical trial readiness
- Support began 2009
  NIH Rare Diseases Clinical Research Network
  private foundations
  pharmaceutical companies
Dystonia Coalition: Rare Diseases Clinical Research Network

Data Sharing
Clinical Studies
Resources and Support

Engagement and Dissemination

Data Tools, Resources, Workspace & Storage

Data Standards
Good Data Practices.

Clinical Studies
Resources and Support

NIH DMCC
Dystonia Coalition: Who is involved?
Dystonia Coalition:
What have we done so far?

- Completed Several Major Clinical Studies
  - all address key bottlenecks in trial readiness
  - all have international participation

- Seeded Numerous Smaller Pilot Studies
  - 40 “investigator-initiated” pilot projects
  - 14 “career development awards”
  - 22 grant proposals (10 funded; NIH, Europe)

- More than 100 publications
  - *Brain*, *JAMA*, *J Neurosci*, *Mov Disord*, *Neurol*
Diagnostic Criteria for Dystonias: Why is this so important?

- Clinical trials cannot proceed without this appropriate patient selection uniform study populations

- Basic science cannot proceed without this genetic studies imaging studies biomarker studies physiological studies
Diagnostic Criteria for Dystonias: Defining dystonia and its subgroups

Phenomenology and Classification of Dystonia: A Consensus Update

Alberto Albanese, MD,1,2* Kailash Bhatia, MD, FRCP,3 Susan B. Bressman, MD,4 Mahlon R. DeLong, MD,5 Stanley Fahn, MD,6 Victor S.C. Fung, PhD, FRACP,7 Mark Hallett, MD,8 Joseph Jankovic, MD,9 Hyder A. Jinnah, PhD,10 Christine Klein, MD,11 Anthony E. Lang, MD,12 Jonathan W. Mink, MD, PhD,13 Jan K. Teller, PhD14

Cited ~800 times already
Diagnostic Criteria for Dystonias: Laryngeal dystonia

Consensus-Based Attributes for Identifying Patients With Spasmodic Dysphonia and Other Voice Disorders

Christy L. Ludlow, PhD; Rickie Domangue, PhD; Dinesh Sharma, PhD; H. A. Jinnah, MD, PhD; Joel S. Perlmutter, MD; Gerald Berke, MD, PhD; Christine Sapienza, PhD; Marshall E. Smith, MD; Joel H. Blumin, MD; Carrie E. Kalata, MS; Karen Blindauer, MD; Michael Johns, MD; Edie Hapner, PhD; Archie Harmon, PhD; Randal Paniello, MD; Charles H. Adler, MD, PhD; Lisa Crujido, MS; David G. Lott, MD; Stephen F. Bansberg, MD; Nicholas Barone, PhD; Teresa Drulia, PhD; Glenn Stebbins, PhD
Diagnostic Criteria for Dystonias: Blepharospasm

Development and validation of a clinical guideline for diagnosing blepharospasm

ABSTRACT

**Objective:** To design and validate a clinical diagnostic guideline for aiding physicians in confirming or refuting suspected blepharospasm.

**Methods:** The guideline was developed and validated in a 3-step procedure: 1) identification of clinical items related to the phenomenology of blepharospasm, 2) assessment of the relevance of each item to the diagnosis of blepharospasm, and 3) evaluation of the reliability and diagnostic sensitivity/specificity of the selected clinical items.

**Results:** Of 19 clinical items initially identified, 7 were admitted by content validity analysis to further assessment. Both neurologists and ophthalmologists achieved satisfactory interobserver agreement for all 7 items, including "involuntary eyelid narrowing/closure due to orbicularis oculi spasms," "bilaterial spasms," "synchronous spasms," "stereotyped spasms pattern," "sensory trick," "inability to voluntarily suppress the spasms," and "blink count at rest." Each selected item yielded unsatisfactory accuracy in discriminating patients with blepharospasm from healthy subjects and patients with other eyelid disturbances. Combining the selected items, however, improved diagnostic sensitivity/specificity. The best combination, yielding 93% sensitivity and 90% specificity, was an algorithm starting with the item "stereotyped, bilateral, and synchronous orbicularis oculi spasms inducing eyelid narrowing/closure" and followed by recognition of "sensory trick" or, alternatively, "increased blinking."

**Conclusion:** This study provides an accurate and valid clinical guideline for diagnosing blepharospasm. Use of this guideline would make it easier for providers to recognize dystonia in clinical and research settings. *Neurology* 2013;81:236-240
Measuring Severity in Dystonias: Why is this so important?

- Clinical trials must have measurable endpoints
  *proof of efficacy*

- Basic science needs clinical correlates
  *imaging studies*
  *biomarker studies*
  *physiological studies*
Measuring Severity in Dystonias: Cervical dystonia clinical rating scale

Clinimetric Testing of the Comprehensive Cervical Dystonia Rating Scale

Cynthia L. Comella MD, Joel S. Perlmutter, MD, Hyder A. Jinnah, MD, PhD, Tracy A. Waliczek, AS, Ami R. Rosen, MS, CGC, Wendy R. Galpern, MD, Charles A. Adler, MD, PhD, Richard L. Barbano, Stewart A. Factor, DO, Christopher G. Goetz, MD, Joseph Jankovic, MD, Stephen G. Reich, MD, Ramon L. Rodriguez, MD, William L. Severt, MD, PhD, Mateusz Zurowski, MD, MSc, Susan H. Fox, MB ChB, MRCP, PhD, and Glenn T. Stebbins, PhD
Measuring Severity in Dystonias: 
Blepharospasm rating scale

Development and Validation of a Clinical Scale for Rating the Severity of Blepharospasm

Giovanni Defazio, MD, PhD, Mark Hallett, MD, Hyder A. Jinnah, MD, PhD, Glenn T. Stebbins, MD, PhD, Angelo F. Gigante, MD, Gina Ferrazzano, MD, Antonella Conte, MD, Giovanni Fabbrini, MD, and Alfredo Berardelli, MD
Measuring Severity in Dystonias: Digital measures for blepharospasm

Objective, computerized video-based rating of blepharospasm severity

ABSTRACT

Objective: To compare clinical rating scales of blepharospasm severity measured automatically from patient videos with contemporary facial movement analysis.

Methods: We evaluated video recordings of a standardized clinical examination with blepharospasm in the Dystonia Coalition’s Natural History and Treatment Studies. Eye closures were measured on a frame-by-frame basis with software (CERT). The proportion of eye closure compared to the three commonly used clinical rating scales: the Burke-Fahn-Marsden Dystonia Rating Scale, Dystonia Rating Scale, and Jankovic Rating Scale.

Results: CERT was reliably able to find the face, and its eye closure measurements correlated with all of the clinical severity ratings (Spearman $\rho = 0.56$, 0.52, and 0.55, respectively, all $p < 0.0001$).

Conclusions: The results demonstrate that CERT has convergent validity with clinical rating scales and can be used with video recordings to measure blepharospasm severity automatically and objectively. Unlike EMG and kinematics, functional video recordings and can therefore be more easily adopted.

Neurology 2016; 87:2146-2153
Natural History of the Dystonias: Why is this so important?

- Essential to delineate phenotypic spectrum
  - recognize common comorbidities
  - identify common patterns
  - establish meaningful subgroups

- Essential for clinical trials
  - baseline data for designing clinical trials
  - encourage efforts to find disease-modifying therapies
  - encourage efforts to find a cure
Risk of spread in adult-onset isolated focal dystonia: a prospective international cohort study

Brian D Berman, Christopher L Groth, Stefan H Sillau, Sarah Pirio Richardson, Scott A Norris, Johanna Junker, Norbert Brüggemann, Pinky Agarwal, Richard L Barbano, Alberto J Espay, Joaquin A Vizcarra, Christine Klein, Tobias Bäumer, Sebastian Loens, Stephen G Reich, Marie Vidailhet, Cecilia Bonnet, Emmanuel Roze, Hyder A Jinnah, Joel S Perlmutter
Clinical and Demographic Characteristics Related to Onset Site and Spread of Cervical Dystonia

Scott A. Norris, MD,1* H. A. Jinnah, MD, PhD,2 Alberto J. Espay, MD, MSc,3 Christine Klein, MD,4 Norbert Brüggemann, MD,4 Richard L. Barbano, MD, PhD,5 Irene Andonia C. Malaty, MD,6 Ramon L. Rodriguez, MD,6 Marie Vidalhret, MD,7 Emmanuel Roze, MD, PhD,7 Stephen G. Reich, MD,8 Brian D. Berman,9 Mark S. LeDoux, MD, PhD,10 Sarah Pirio Richardson, MD,11 Pinky Agarwal, MD,12 Zoltan Mari, MD,13 William G. Ondo, MD,14 Lucy C. Shih, MD,15 Susan H. Fox, MRCP, PhD,16 Alfredo Berardelli, MD,17 Claudia M. Testa, MD, PhD,18 Florence Ching-Fen Cheng, MBBS, FRACP,19 Daniel Truong, MD,20 Fatta B. Nahab, MD,21 Tao Xie, MD, PhD,22 Mark Hallett, MD,23 Ami R. Rosen, MS,24 Laura J. Wright,1 and Joel S. Perlmutter1,25
Dystonia Coalition:
What have we done so far?

● Several Major Clinical Studies
  all address key bottlenecks in trial readiness
  all have international participation

● Seeded Numerous Pilot Studies
  14 “investigator-initiated” pilot projects
  14 “career development awards”
  22 grant proposals (10 funded; NIH, Europe)

● More than 100 publications
  *J Neurosci, Brain, Neurol, Mov Disord*
Pilot Projects Program

● Goal
  *foster promising clinical/translational studies*

● Sponsorship
  *NIH, Patient Advocacy Groups, Industry*

● History
  *40 projects, 32 different sites, 6 countries*

● Future
  *Multiple applications currently under review*
Career Development Award

- **Goal**
  encourage junior investigators

- **Sponsorship**
  NIH, Patient Advocacy Groups

- **History**
  14 candidates supported in 4 countries

- **Future**
  Multiple applications now under review
Dystonia Coalition: Current Projects

- Natural History Project
  Define phenotypic spectrum and evolution of dystonias

- Biobank Project
  Shared resource for DNA and other biomarker materials

- Patient-Centered Outcomes Project
  Develop an app-based patient tool to chart symptoms

- Objective Measures Project
  Develop digital tools to measure dystonia
Sponsors

- National Institute of Neurological Disorders and Stroke
- Office of Rare Diseases Research
- Rare Diseases Clinical Research Network

- Other supporters
  - Industry
  - Professional societies
  - Patient advocacy groups
Special thanks to two people who make everything happen!

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