Annual Meeting Webinar
H. A. (Buz) Jinnah, M.D., Ph.D.
Emory University, Atlanta
hjinnah@emory.edu

Webinar Housekeeping Information

- Signing in
  we have more than 100 participants
  everyone is muted, except speakers
  contact Jody or Gamze by email if needed

- Questions & comments
  type in the Questions box
  questions addressed after each speaker
 *do not use the Chat box*

- This webinar is being recorded

Agenda

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
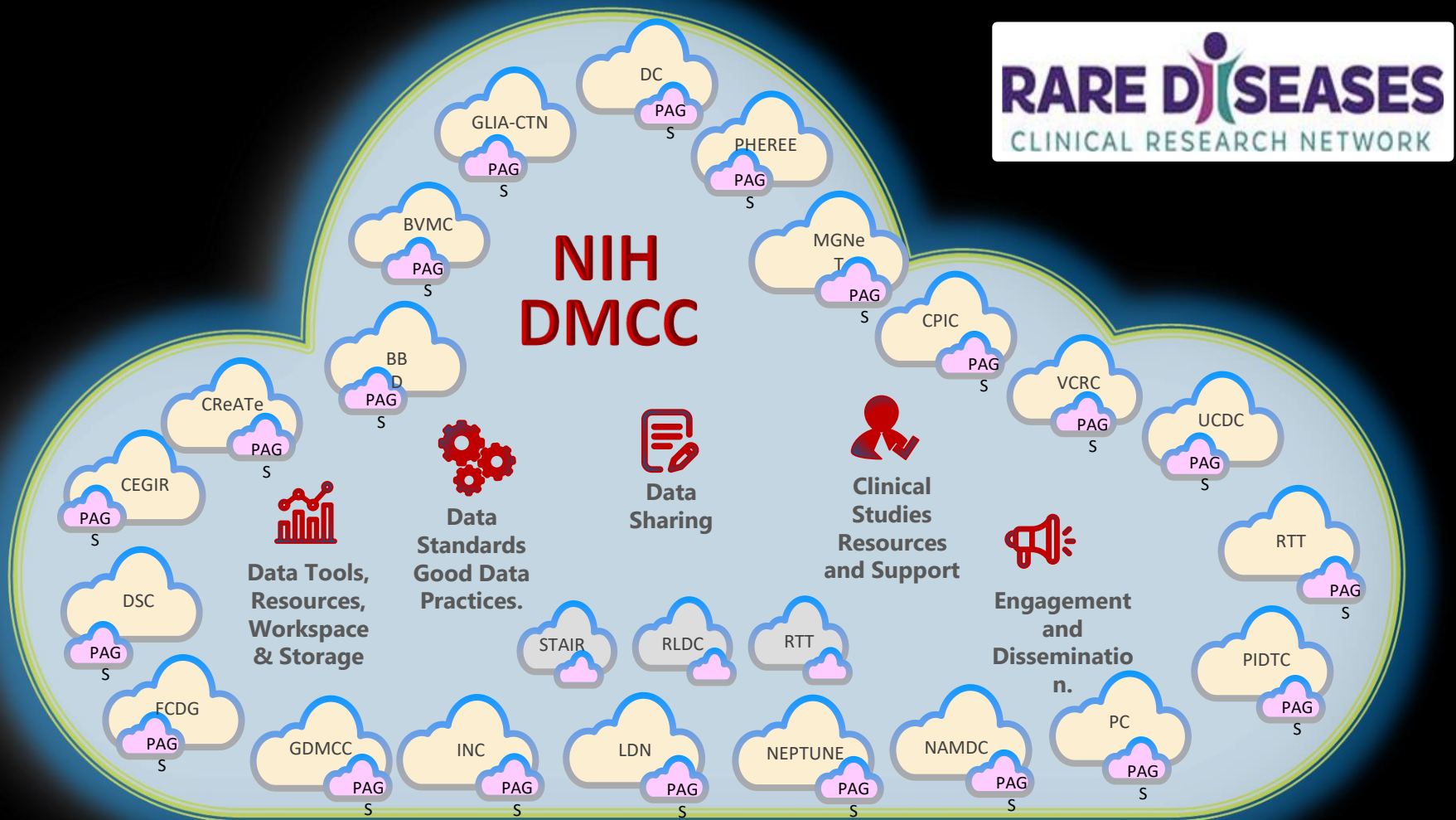
Dystonia Coalition:
Who is involved?

Emory · Active · Affiliate · Closed

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

R E V I E W

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, PhD[14]

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

Giovanni Defazio, MD,
PhD
Mark Hallett, MD
Hyder A. Jinnah, MD,
PhD
Alfredo Berardelli, MD

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," "bilateral spasms," "synchronous spasms," "stereotyped spasm 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

RESEARCH ARTICLE

Clinimetric Testing of the Comprehensive Cervical Dystonia Rating Scale

Cynthia L. Comella MD,[1]* Joel S. Perlmutter, MD,[2] Hyder A. Jinnah, MD, PhD,[3] Tracy A. Waliczek, AS,[1] Ami R. Rosen, MS, CGC,[3] Wendy R. Galpern, MD,[4] Charles A. Adler, MD, PhD,[5] Richard L. Barbano,[6] Stewart A. Factor, DO,[3] Christopher G. Goetz, MD,[1] Joseph Jankovic, MD,[7] Stephen G. Reich, MD,[8] Ramon L. Rodriguez, MD,[9] William L. Severt, MD, PhD,[10] Mateusz Zurowski, MD, MSc,[11] Susan H. Fox, MB ChB, MRCP, PhD,[11] and Glenn T. Stebbins, PhD[1]

Measuring Severity in Dystonias:
Blepharospasm rating scale

Mov Disord 2015

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

Giovanni Defazio, MD, PhD,[1]* Mark Hallett, MD,[2] Hyder A. Jinnah, MD, PhD,[3] Glenn T. Stebbins, MD, PhD,[4] Angelo F. Gigante, MD,[1] Gina Ferrazzano, MD,[5] Antonella Conte, MD,[5,6] Giovanni Fabbrini, MD,[5,6] and Alfredo Berardelli, MD[5,6]

Measuring Severity in Dystonias:
Digital measures for blepharospasm

Objective, computerized video-based rating of blepharospasm severity

David A. Peterson, PhD
Gwen C. Littlewort, PhD
Marian S. Bartlett, PhD
Antonella Macerollo, MD
Joel S. Perlmutter, MD
H.A. Jinnah, MD, PhD
Mark Hallett, MD
Terrence J. Sejnowski, PhD

Correspondence to
Dr. Peterson:
dap@salk.edu

ABSTRACT

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

Methods: We evaluated video recordings of a standardized clinical ex
with blepharospasm in the Dystonia Coalition's Natural History an
closures were measured on a frame-by-frame basis with softwar
Expression Recognition Toolbox (CERT). The proportion of eye closu
3 commonly used clinical rating scales: the Burke-Fahn-Marsden Dy
Dystonia Rating Scale, and Jankovic Rating Scale.

Results: CERT was reliably able to find the face, and its eye closure n
all of the clinical severity ratings (Spearman ρ = 0.56, 0.52, anc
Marsden Dystonia Rating Scale, Global Dystonia Rating Scale, a
respectively, all $p < 0.0001$).

Conclusions: The results demonstrate that CERT has convergent val
ical rating scales and can be used with video recordings to measu
severity automatically and objectively. Unlike EMG and kinematics,
tional video recordings and can therefore be more easily adop

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

Natural History of the Dystonias:
Progressive worsening over time

OPEN ACCESS

ORIGINAL RESEARCH

Risk of spread in adult-onset isolated focal dystonia: a prospective international cohort study

Brian D Berman [ID],[1] Christopher L Groth,[2] Stefan H Sillau,[1] Sarah Pirio Richardson,[3] Scott A Norris,[4] Johanna Junker,[5,6] Norbert Brüggemann [ID],[5,6] Pinky Agarwal,[7] Richard L Barbano,[8] Alberto J Espay,[9] Joaquin A Vizcarra,[10] Christine Klein,[6] Tobias Bäumer,[6] Sebastian Loens,[6] Stephen G Reich,[11] Marie Vidailhet,[12] Cecilia Bonnet,[12] Emmanuel Roze,[12] Hyder A Jinnah,[13] Joel S Perlmutter[14]

Natural History of the Dystonias:
Focus on cervical dystonia

Mov Disord 2016

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 Vidailhet, 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] Ludy 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. Perlmutter[1,25]

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
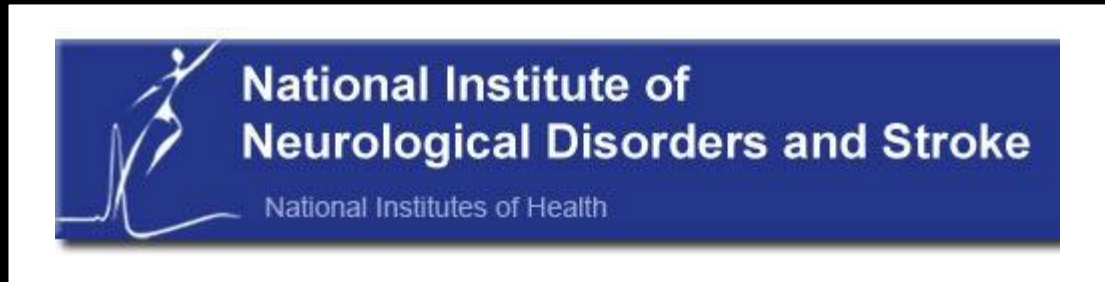
Career Development Award

- 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

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Special thanks to two people who make everything happen!

Gamze Kilic-Berkmen, PhD
DC Program Manager, Emory University
dystoniacoalition@emory.edu

Jody Roosevelt
Manager of Science & Technology, DMRF
jroosevelt@dystonia-foundation.org