Natural History Project

Joel Perlmutter
Jo Wright

Washington University in St. Louis

Sponsored by the NINDS and ORDR-NCATS at NIH, PAG, Industry, Professional Societies, and/or other sources.
Natural History Project

Goal: Collect clinical and exam data to better understand:

- phenotypic spectrum of all dystonias
- how symptoms change over time
- how other family members are affected
- researchers to use data for research
Natural History Recruitment Goals
(isolated dystonia): 200 cases/year

**New cases**
- Focal
- Multifocal
- Segmental
- Generalized
- Hemidystonia

**Follow-up cases**
- Focal
- Multifocal
- Segmental
- Generalized
- Hemidystonia

- Must have started in:
  - Face (Craniofacial/Blepharospasm/Oromandibular)
  - Larynx (Laryngeal)
  - Limbs (Limb dystonia)
Natural History: To Date

➢ The Natural History Study began recruitment in 2010
   ➢ Natural History/Biorepository, 2010
   ➢ Natural History Early Stage/Late Stage, 2016
   ➢ Natural History Project, 2019

➢ Minimal changes to data collection and video protocols
➢ No change for sample Coriell collection
➢ Follow-up visits, determined by a sliding scale since 2016

<table>
<thead>
<tr>
<th>If onset of symptoms was</th>
<th>Subsequent follow-up visit should be</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to &lt; 3 years ago</td>
<td>1 year from last visit</td>
</tr>
<tr>
<td>3 to &lt; 5 years ago</td>
<td>2 years from last visit</td>
</tr>
<tr>
<td>5 to &lt; 7 years ago</td>
<td>3 years from last visit</td>
</tr>
<tr>
<td>At least 7 years ago</td>
<td>4 years from last visit</td>
</tr>
</tbody>
</table>
Natural History Enrollment: 2010-2020

42 Clinical Sites recruited 3262 Cases, 1101 follow-ups as of 5/31/2020
## Distribution of Isolated Dystonia

<table>
<thead>
<tr>
<th>Types of Isolated Dystonias enrolled</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal Dystonia</td>
<td>2349</td>
</tr>
<tr>
<td>Generalized Dystonia</td>
<td>147</td>
</tr>
<tr>
<td>Hemidystonia</td>
<td>14</td>
</tr>
<tr>
<td>Multifocal Dystonia</td>
<td>219</td>
</tr>
<tr>
<td>Segmental Dystonia</td>
<td>709</td>
</tr>
</tbody>
</table>
# Distribution of Focal Dystonia Subtypes

All subjects categorized by site affected

<table>
<thead>
<tr>
<th>Body Site</th>
<th>Affected at onset of illness</th>
<th>Affected at time of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foot</td>
<td>91</td>
<td>181</td>
</tr>
<tr>
<td>Hand</td>
<td>453</td>
<td>786</td>
</tr>
<tr>
<td>Jaw</td>
<td>145</td>
<td>302</td>
</tr>
<tr>
<td>Larynx</td>
<td>359</td>
<td>607</td>
</tr>
<tr>
<td>Lower Face</td>
<td>234</td>
<td>657</td>
</tr>
<tr>
<td><strong>Neck</strong></td>
<td><strong>1900</strong></td>
<td><strong>2397</strong></td>
</tr>
<tr>
<td>Pelvis</td>
<td>11</td>
<td>46</td>
</tr>
<tr>
<td>Shoulder</td>
<td>154</td>
<td>690</td>
</tr>
<tr>
<td>Tongue</td>
<td>43</td>
<td>133</td>
</tr>
<tr>
<td>Trunk</td>
<td>51</td>
<td>218</td>
</tr>
<tr>
<td>Upper Arm</td>
<td>141</td>
<td>337</td>
</tr>
<tr>
<td>Upper Face</td>
<td>591</td>
<td>866</td>
</tr>
<tr>
<td>Upper Leg</td>
<td>43</td>
<td>91</td>
</tr>
</tbody>
</table>
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

Movement Disorders 2013
Spread of Cervical Dystonia

Norris SA et al, Mov Disord 2017
DC: Natural History

Berman BD et al, JNNP 2020
Cervical dystonia severity tools

- Organizing center
  *Cynthia Comella, MD*

- Revise current TWSTRS
  *include non-motor elements validate training tape*

Comella C et al, Mov Disord, 2016
Natural History Available Data -1

Completed by Neurologist
- Global Dystonia Rating Scale (GDRS)
- Burke-Fahn Marsden Dystonia Scale (BFM)

Completed by participant
- Short Form Health Survey 36 (SF-36)
- Beck Depression Inventory II (BDI-II)
- Hospital Anxiety and Depression Scale (HADS)
- Liebowitz Social Anxiety Scale (LSAS)
- Patient Health Questionnaire 9 (PHQ-9)
Natural History Available Data -2

Completed by Coordinator
➢ DCP Data Collection Form
  demographic, medical history, medications, exam, family history

➢ Neurological Exam Video
  over 3,000 videos available

➢ Biospecimens
  over 3,000 DNA samples available
Data Accessibility - Who

- Enrolling Sites
  - Access to site data and videos

- New Research Projects
  - IRB approval
  - Data Access Agreement form
  - Executive Committee approval
    - Data
    - Videos (restricted access)
    - Biospecimens

- REDCap Data Interface (Pentaho)
  *Publically available non-PHI data*
Data Accessibility - Where

- Washington University in St. Louis
  - REDCap
  - Video Repository
  - REDCap Data Interface (Pentaho)
    - Publically available de-identified data

- NINDS Coriell Institute for Medical Research, New Jersey
  - DNA samples
  - De-identified data

- Data Management and Coordinating Center (DMCC), Cincinnati Children’s Hospital Medical Center
  - De-identified data
Data Accessibility – Video Repository

Restricted access
Data Sharing/Access

Public Access: REDCap Data Interface (Pentaho)

http://clinportalquery.wustl.edu/pentaho/Home?userid=DYSTONIA_OPENI&password=DYSTONIA
(Firefox or Chrome, not IE)

Full Data or Video Access

➢ Application
➢ Data access agreement
  
  no secondary release
  return results/acknowledgment
➢ IRB approval
➢ Executive Committee approval
➢ Only project specific data release
➢ Video: only streaming, not downloading
Investigator Responsibilities

➢ Use data for proposed studies only
➢ No secondary release
➢ No attempt to identify participants
➢ Adequate staff training
➢ Share findings with Dystonia Coalition and publish data
➢ Acknowledge source
Data Utilization

➢ Use data for proposed studies only
➢ No secondary release
➢ No attempt to identify participants
➢ Adequate staff training
➢ Share findings with Dystonia Coalition and publish data
➢ Acknowledge source
Q & A

Natural History (NH) Project
Project Management Center: Washington University in St. Louis
Project Leader: Joel Perlmutter, MD (perlmutterjoel@wustl.edu)
Data Manager: Jo Wright (laurajwright@wustl.edu)