

# 6th INTERNATIONAL DYSTONIA SYMPOSIUM

1-3 JUNE 2023  
DUBLIN, IRELAND

## Day 1: Thursday, 1 June 2023

8:00 Welcome message Local organizing committee  
8:10 Meeting goals & plans Jinnah, Pisani, Teller

Traditionally, this meeting has focused on the science of dystonia. Since many other meetings have focused on clinical education and treatment of dystonia, this meeting maintains the tradition of focusing on scientific aspects. While we will certainly cover the clinical topics by way of introduction, most attention will be on scientific developments and needs.

### I. INTRODUCTION TO DYSTONIA

Chairs: Jinnah, Tijssen

#### Where are we now?

8:20 Definition and classification of dystonia: How well is the 2013 Consensus Plan working? Lang  
This introductory presentation is essential to ensure all attendees, both clinical and basic, are on the same page. The intent is not purely an educational lecture for trainees. Instead, the intent is to summarize the 2013 consensus definition of dystonia and its classification, to put the many subtypes into perspective. It would also be useful to address and how well we think the consensus plan has fared. This approach was born at the prior International Dystonia Symposium held in Barcelona, and several papers have assessed how well it has worked. In general, most of these have implied that it was largely successful, although some clarifications and changes may be warranted in the future.

8:45 Dystonia syndromes: Overlapping or distinct? Fung  
The intent of this presentation is to cover the common dystonia syndromes, as examples in support of the 2013 diagnosis and classification system. Again, the goal is to ensure all attendees, both clinical and basic, are using the same language. We encourage lots of short videos. This is not purely an educational lecture, as it may include newly described syndromes too, and now they might fit into the classification system.

9:10 What is the relationship between dystonia, tremor, Parkinson disease, and ataxia? Bhatia  
There has been a lot of discussion about the relationships between these movement disorders, both at the clinical and etiological levels. We hope a brief summary of these relationships will be useful to put dystonia into perspective, and to suggest potential shared biological mechanisms.

9:35 Current treatment for dystonia: What are the successes? What can we do better? Jankovic  
The intent is not to provide clinical education regarding treatment of dystonia, but rather to summarize them and focus instead on future needs. Ideally, this presentation might cover physiotherapy, oral medications, Botulinum toxin, and surgery. We hope to have a brief overview of each, and their limitations. This presentation sets the stage for further scientific investigations so new therapies can be developed, and more details for each therapy will be covered in the last session on Experimental Therapies.

#### 10:00 Coffee Break

#### Late breaking news

Chairs: Albanese, Relja

The TBA talks are designed to accommodate new findings, important findings not otherwise covered in the program, as well as an opportunity for junior presenters to have the platform. Topics will be chosen from posters submitted, and reviewed by a central committee.

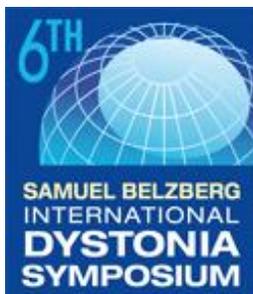
10:30 TBA (chosen from posters submitted)

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#### Point of View: Dystonia and tremor



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There is ongoing debate about relationships between tremor and dystonia. Some view this association as an entity called “dystonic tremor”. Others view it as two separate disorders. The goal is to present both perspectives.

- |       |  |        |
|-------|--|--------|
| 10:50 | Dystonia plus tremor = a discrete entity known as dystonic tremor        | Fasano |
| 11:00 | Dystonia plus tremor = two separate but frequently overlapping disorders | Pandey |
| 11:10 | Discussion   |        |

## Hot topics: The science of phenotyping

The intent is to cover some disorders at the borderlands of dystonia. The issue of pseudodystonia was not addressed by the 2013 consensus group, and remains uncertain. Several opinion-based articles have appeared, but there is no real agreement on what this term means. The paroxysmal dyskinesias traditionally have been considered a subtype of dystonia, because dystonia is often the main problem. However, some have suggested that they are distinct disorders unrelated to dystonia. The intent of this presentation is to address potential relationships between the paroxysmal dyskinesias with the dystonias.

- |       |  |        |
|-------|--|--------|
| 11:20 | Pseudodystonia: How does it differ from “real” dystonia?             | Lynch  |
| 11:30 | Paroxysmal dyskinesias: A subtype of dystonia or a different entity? | Galosi |
| 11:40 | Discussion   |        |

## Chair’s summary & discussion with audience

**Jinnah, Tijssen, Albanese, Relja**

- |       |  |
|-------|--|
| 11:50 | Chair’s summary of the morning session |
| 12:00 | Open discussion of morning session     |

## 12:30 Lunch Break & Poster Session (provided for all delegates)

All posters viewable for entire meeting: 1<sup>st</sup> third to present today from 13:30-14:30

## II.SPECIAL TOPICS IN DYSTONIA

**Chairs: Bressman, Carecchio**

### Understanding mechanisms through the science of phenotyping

- |       |  |         |
|-------|--|---------|
| 14:30 | Task-specific dystonias: What do they tell us about the etiology of dystonia?<br>While some of the clinical phenomenology and epidemiology may be summarized by way of introduction for participants not familiar with this topic, the main intent of this presentation is to focus on what this group of disorders tells us about etiology and environmental contributions to dystonia.   | Hallett |
| 14:50 | Sex differences across the dystonias: How can we begin to delineate mechanisms?<br>While a brief summary of sex differences may be warranted for participants not familiar with this topic, the intent of this presentation is to focus should be on biological mechanisms. Since there are limited data on the biological basis for sex differences, it may be necessary to cover basic mechanisms that are known from other related disorders. | Hess    |
| 15:10 | Autoimmune mechanisms in dystonia: What can they tell us about etiology in dystonia?<br>A number of autoimmune mechanisms have now been described for dystonia. The intent of this presentation is to provide a brief summary of known causes, as well as their biological basis.  | Balint  |
| 15:30 | Dystonia in pediatrics: What can we learn from inherited metabolic disorders?<br>The intent of this presentation is to provide examples from inherited metabolic disorders that may provide clues towards biological mechanisms that are more broadly relevant. The goal is not to provide a catalog of the many different disorders, but to highlight those that tell us about biological mechanisms.   | Leuzzi  |

## 15:50 Coffee Break

## Point of View: Functional (psychogenic) dystonia

**Chairs: Espay, Sharma**



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There are multiple papers on the imaging and physiological characteristics of psychogenic dystonia. Some of these imply this is an organically determined neurological disorder. The converse opinion is that the “biological” measures are a consequence, not a cause of dystonia. The goal of these presentations is to present both perspectives.

- 16:20 Functional dystonia: A manifestation of neurological disease Aybek  
16:30 Functional dystonia: A manifestation of psychiatric illness Carson  
16:40 Discussion

**Point of View: Non-motor features of dystonia**

While a brief summary of non-motor features may be warranted as introduction for participants not familiar with this topic, the main intent is to focus on scientific relevance and biological basis. Some evidence suggests that non-motor features reflect shared biological mechanisms

with dystonia, while other evidence implies it is a reaction to a chronic stigmatizing disorder. The goal of these presentations is to cover both perspectives.

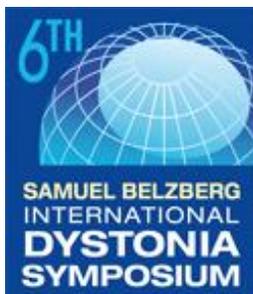
- 16:50 Non-motor features of dystonia: Shared biological substrates with motor features Peall  
17:00 Non-motor features of dystonia: An expected side effect of a chronic disorder Martino  
17:10 Discussion

**Chair's summary & discussion with audience**

**Bressman, Carecchio, Espay, Sharma**

- 17:20 Chair's summary of the afternoon session  
17:30 Open discussion of afternoon session

**19:00 WELCOME RECEPTION**



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**Day 2: Friday, 2 June 2023**

**III. ANATOMICAL BASIS FOR DYSTONIA**

**Chairs: Simonyan, Mink**

**What areas of the nervous system are responsible for dystonia?**

- 8:00 Organization of normal movement: cortex, basal ganglia and cerebellum Rothwell  
 The intent of this presentation is to provide an introductory framework for motor control in general, in a way that both clinicians and scientists can appreciate. Specifically, what does each of these regions do, and how are they integrated? We hope this presentation can set the stage for subsequent presentations in which the proposed substrates for dystonia can be addressed.
- 8:20 Structural imaging of dystonia: Modern lesion network mapping M Fox  
 The intent of this presentation is to provide both historical and new evidence regarding the anatomical substrates for dystonia. We hope to have some brief synthesis of prior structural studies, for example VBM, as well as more recent evidence from recent studies of lesion network mapping.
- 8:40 Functional imaging of dystonia: Common themes or too much heterogeneity? Stoessl  
 The intent of this presentation is to provide a synthesis of the many and often conflicting fMRI-based studies. The goal is not a "literature review" but a synthesis with new ways to think about where this field is now, and where it needs to go.
- 9:00 Anatomical basis for dystonia: What can we learn from animal studies? Sillitoe  
 The intent of this presentation is to focus on what has been learned about the anatomical basis of dystonia from animal models. We hope to provide a balanced overview of prior work, as well as more recent work, without too much focus on a single experimental approach.
- 9:20 New imaging methods: How can they be applied in dystonia? Perlmutter  
 The intent of this presentation is to focus on novel imaging methods such as novel PET ligands and targets (molecular imaging), high-Tesla MRI studies, iron imaging, artificial intelligence and DystoniaNet, and others.

**10:00 Coffee Break**

**Late breaking news**

**Chairs: Lin, Vidailhet**

- 10:30 TBA (chosen from posters submitted)  
 10:35 TBA (chosen from posters submitted)  
 10:40 TBA (chosen from posters submitted)  
 10:45 TBA (chosen from posters submitted)

**Point of view: Developmental or degenerative?**

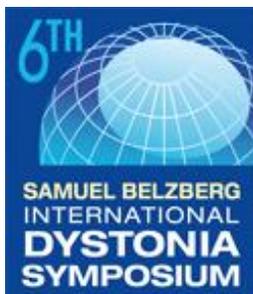
Many papers and reviews state that dystonia is a developmental disorder. Others imply dystonia is a neurodegenerative disorders. The goal of these presentations is to present both perspectives, each of which may apply in different circumstances.

- 10:50 Dystonia is a developmental disorder Dauer  
 11:00 Dystonia is a degenerative disorder Kaji  
 11:10 Discussion

**Point of view: Integrative models**

Early studies of cervical dystonia emphasized a basal ganglia origin, while more recent studies have emphasized the cerebellum. The intent of these presentations is to emphasize the network model, focusing on different proposed networks.

- 11:20 Cervical dystonia is caused by a defect in the neural integrator for head control Shaikh  
 11:30 Cervical dystonia is caused by a defect in the network for attentional orienting Fearon  
 11:40 Discussion



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**Chair's summary & discussion with audience** **Lin, Mink, Simonyan, Vidailhet**  
 11:50 Chair's summary of the morning session  
 12:00 Open discussion of morning session

**12:30 Lunch Break & Poster Session (provided for all delegates)**

All posters viewable for entire meeting: 2<sup>nd</sup> third to present today from 13:30-14:30

**IV. PHYSIOLOGICAL BASIS FOR DYSTONIA Chairs: Standaert, Hallett**

**Functional changes in neural activity**  
 14:30 Physiological changes in human dystonia: Where are we now? Chen  
 For many years, human physiological studies using indirect methods have emphasized three problems: imbalance in inhibition/excitability, sensorimotor integration, and maladaptive plasticity. The relevance of some of these problems has been questioned in recent studies, because they may be non-specific findings in many movement disorders. The intent of this presentation is to provide an update, and address whether these problems are causal, consequential, or epiphenomenal.

14:50 Deep brain stimulation in humans: What can we learn about etiology? Kuhn  
 While some brief summary of methods and clinical outcomes may be useful for participants unfamiliar with this topic, the major intent is to focus mostly on what this method has taught us about the underlying biology of dystonia.

15:10 Physiological basis for dystonia: What can we learn from animal studies? Pisani  
 The intent of this presentation is to summarize physiological studies from animal models of dystonia, and how they might relate to human dystonia.

15:30 Cerebellar stimulation for dystonia? Lozano  
 The main target of DBS for dystonia has been the basal ganglia or related subthalamic or thalamic regions, and this will be covered in another lecture. The main goal of this presentation is to address whether other targets, such as the cerebellum, should also be considered.

**15:50 Coffee Break**

**Point of view: Sensorimotor integration** **Chairs: Berardelli, Roze**  
 There has been a lot of work on abnormal sensory thresholds across many types of dystonia. The intent of these presentations is to address the significance of these findings for the biology of dystonia.

16:20 Abnormal sensory processes are a fundamental defect underlying dystonia Tinazzi

16:30 Abnormal sensory processes are a non-specific consequence of the disorder Conte

16:40 Discussion

**Point of view: Maladaptive plasticity**

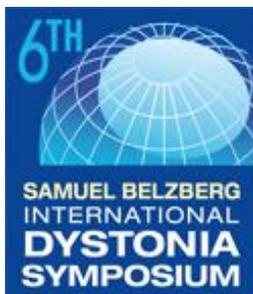
There has been a lot of discussion about plasticity in dystonia, both from human and animal studies. However, its causal role in dystonia has never been established, and it is not specific to dystonia. The findings reported may be a fundamental defect underlying dystonia, or a consequence of dystonia. The goal of these presentations is to present both perspectives.

16:50 Abnormal plasticity is the fundamental defect underlying dystonia Quartarone

17:00 Abnormal plasticity is a non-specific consequence of many movement disorders Sadnicka

17:10 Discussion

**Chair's summary & discussion with audience** **Berardelli, Hallett, Roze, Standaert**  
 17:20 Chair's summary  
 17:30 Open discussion of afternoon session



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**Day 3: Saturday, 3 June 2023**

**V. MOLECULAR MECHANISMS**

**Chairs: Calakos, Klein**

**Dystonia genes: A growing list**

- 8:00 Overview of dystonia genetics Zech  
 The intent of this presentation is to provide a summary of old and new genes that may cause dystonia.
- 8:20 Dystonias with partial penetrance: What are the biological mechanisms? Ip  
 Many forms of dystonia are known or suspected to be partially penetrant. The goal of this presentation is to summarize this phenomenon, and provide information regarding potential biological causes.
- 8:40 Induced pluripotent stem cells: Novel technologies and application to dystonia Bragg  
 Induced pluripotent stem cells have been widely exploited for a number of disorders, but they are just beginning to be used for dystonia. The goal of this presentation is to describe this approach, and provide some examples of its use in dystonia.
- 9:00 Shared biological pathways in dystonia: One or many paths to novel therapeutics? Mencacci  
 There are many causes for dystonia, and some of these causes appear to share similar mechanisms. The intent of this presentation is to explain why the identification of these mechanisms is important, and to summarize some of these shared mechanisms. The presentation should not be limited to only newly discovered genes, but rather a synthesis of the best documented shared pathways.
- 9:20 Novel ways to exploit existing resources Teller  
 There are several large collaborative efforts in North America, Europe and Asia. All of them have research resources that are shared, such as clinical data, DNA samples, brain bank specimens, cell banks, etc... The intent of this presentation is to advertise some of these resources to accelerate dystonia research.

**10:00 Coffee Break**

**Late breaking news**

**Chairs: Lohmann, Ozelius**

- 10:30 TBA (chosen from posters submitted)  
 10:35 TBA (chosen from posters submitted)  
 10:40 TBA (chosen from posters submitted)  
 10:45 TBA (chosen from posters submitted)

**Point of view: What is a “dystonia gene”?**

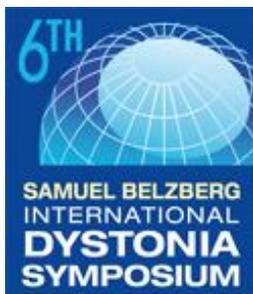
The nomenclature for inherited dystonias has changed over the years, with several approaches currently being used in the literature. Some of this uses a plan based on DYT numbering, some uses a plan based on DYT combined with gene name, and some relies only on the gene name. The intent of these presentations is to summarize the various perspectives for those not familiar with them.

- 10:50 The list of “DYT” genes Marras  
 11:00 The list of “other” genes Lohmann  
 11:10 Discussion

**Point and counterpoint: Rare monogenic dystonias vs common idiopathic dystonias**

One of the major reasons for the enthusiasm for finding new genes is the claim that lessons learned are relevant to more common adult-onset focal dystonias, both biologically and clinically. One of the major reasons that many clinicians do not follow genetic discoveries is because they are not relevant to the vast majority of the more common dystonias they see, and their biology seems different. The goal of these presentations is to summarize both perspectives.

- 11:20 Monogenic dystonias: shared mechanisms with common idiopathic dystonias Calakos



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- 11:30 Monogenic dystonias: mechanisms distinct from more common idiopathic dystonias Erro  
 11:40 Discussion
- Chair's summary & discussion with the audience Calakos, Klein, Lohmann, Ozelius**
- 11:50 Chairs summary  
 12:00 Open discussion of morning session
- 12:30 Lunch Break & Poster Session (lunch provided for all delegates)**  
 All posters viewable for entire meeting: 3<sup>rd</sup> third to present today from 13:00-14:00

**VI. EXPERIMENTAL THERAPEUTICS**

**Chairs: S. Fox, Dressler**

- Novel therapeutics on the horizon**
- 14:30 Novel experimental oral therapeutics: What are the targets? Jinnah  
 While a brief summary of oral agents for dystonia may be needed by way of introduction, the main goal of this presentation is to focus on oral agents under development. These may include information from recent trials published: levetiracetam, perampanel, escitalopram, and actyl hexapeptide 8. It may also include oral agents under investigation: ampicillin, diplagurant, sodium oxybate.
- 14:50 Botulinum toxin therapy: What are the new trends? Comella  
 While some introductory material regarding common uses of BoNT may be useful for those not familiar with it, the main focus here is to focus on the limitations of BoNT, and modifications to traditional strategies that can improve outcomes. This may include changes in dosing intervals, traditional patterns of treatment, and/or longer-acting formulations current in development.
- 15:10 Surgical therapies: What's next? Moro  
 While some introduction to the topic of surgical therapy in dystonia may be warranted, the main focus is to address strategies recently published or under development such as adaptive DBS, directional stimulation, new targets, better understanding of the network changes induced by DBS, re-emergence of lesion therapy, and others.
- 15:30 Clinical trials: What are the obstacles to testing new options? Pirio Richardson  
 With several new potential treatment options being tested or considered, the issue of optimal trial design has been increasingly important. While some introduction to traditional outcome measures is warranted, the main intent of this presentation is to focus on novel or better outcomes recently published or under development. These may include new or revised scales, objective measures (sensors, video-based measures, etc...), and patient-reported outcomes.
- 15:50 Coffee Break**
- Hot topics: Some recent successes Chairs: LeDoux, Rosales**
- 16:20 Physical and occupational therapy in dystonia: Tijssen  
 Physical and occupational therapy is an important topic for patients, yet the most rigorous trials have failed to show consistent benefits. The intent of this presentation is to address studies that have been reported, and perhaps what might need to be done to determine the role of these options as treatments for dystonia.
- 16:40 Inherited dystonias with targeted therapies Meneret  
 There has been enormous progress in the development of novel treatments for several rare inherited disorders, often because understanding the underlying mechanism has pointed to obvious therapeutic interventions. While a short summary of some treatable inherited disorders may be warranted to introduce this topic to those who are not familiar with it, the main intent of this presentation is to describe some of the more recently discovered treatments, and even some treatments in development.



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- 17:00 PKAN: One enzyme defect, multiple targets Pérez Dueñas  
This rare inherited disorder has been the target of 3 recent clinical trials, each using a different strategy for treatment. More treatments are in development. The intent of this presentation is to describe these developments as a potential model for other dystonic disorders.
- Chair's summary & audience discussion** **Pisani, Dressler, Perlmutter, LeDoux**
- 17:20 Chairs summary of the session
- 17:30 Audience Discussion
- 18:00 CONFERENCE CONCLUDES**