

# D-DAYs 2018

AND 25<sup>TH</sup>  
ANNIVERSARY  
OF DYSTONIA  
EUROPE

## ABSTRACT BOOK



DYSTONIA  
EUROPE



Belgische Vereniging  
voor Dystoniepatiënten vzw



**Dystonia Europe would like to thank the following for their involvement in making this conference possible:**

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Frans & Martine Vanderstraeten

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Maja Relja, Croatia  
Patrick Santens, Belgium  
Alexander Schmidt, Germany  
Donna Walsh, Ireland  
Marie Vidailhet, France

Brussels, April 2018

Dear Participant,

Welcome to Brussels for the Dystonia Europe 25<sup>th</sup> Anniversary Conference & our Annual European Dystonia Days - D-DAYS 2018!

On behalf of Dystonia Europe and in collaboration with the Belgian Dystonia Association, we are delighted to welcome you to Brussels.

During these days we will celebrate twenty-five years of achievement across the world of dystonia and the hope this brings for the future - tremendous advances in medical and scientific understanding of the illness, in public awareness, and in diagnosis and treatment. We are very grateful to all the speakers and chairs who have joined us to share their expertise within dystonia.

As well as learning more about dystonia we also hope that you will enjoy meeting old friends, and connect with new ones, and above all, have a pleasant weekend here in Brussels.

We also take the opportunity to thank our sponsors for making this very special event possible. Dystonia Europe is very grateful for your support and we are glad that so many of you are showing direct interest in our work by being represented here.

We thank you all for joining us here in Brussels for our 25<sup>th</sup> Anniversary Celebration and we wish you an enjoyable, interactive and fruitful conference and:

**Happy 25<sup>th</sup> Anniversary for Dystonia Europe!**

Warm regards

Handwritten signature of Merete H. Avery in black ink.

**Merete Avery**  
President  
Dystonia Europe

Handwritten signature of Frans Vanderstraeten in black ink.

**Frans Vanderstraeten**  
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**Prof. Marwan Hariz**

Queen Square,  
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**Dr. Laura Cif**

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VIB Group Leader  
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## DEEP BRAIN STIMULATION (DBS) FOR DYSTONIA: FROM REFERRAL TO OUTCOME.

The journey of people with dystonia from diagnosis to referral for deep brain stimulation (DBS) and then to outcome is long and sometimes tortuous. To start with, there is often a rather long journey from symptom appearance to receiving the correct diagnosis in the first place: insidious onset of non-specific symptoms and physicians' lack of awareness about dystonia may contribute to a delay in getting the proper diagnosis. Then, after years of medical trials, surgery may be considered for some patients. The referral to surgery may be at the initiative of the treating physician or at the initiative of the patient. Conflicting attitudes towards DBS may play a role in decisions on referral or not for DBS, or postponing surgery.

Referral is usually to a DBS team which consists as a minimum of a movement disorders neurologist and a functional neurosurgeon, but often the team includes also a DBS nurse and a neuropsychologist.

Eventually the DBS team will meet the patient to evaluate the type of dystonia, its various symptoms and their suitability for surgery, and what to expect from DBS. Symptoms severity and functional impairment are rated on validated scales, including video-filming of the patient for future follow up. Usually an MRI of the brain (and when appropriate the spine) is performed and a neuropsychological test battery is administered. If all the tests indicate reasonable chances for improvement from DBS, a new encounter between the DBS team and the patient and his/her family is planned in order to explain in details the surgery and what to expect from it. This process from first referral to final decision on surgery, and then to admission

and surgery itself, may take several months depending on the waiting list of a particular DBS centre.

Surgery is usually done in general anaesthesia. The preferable brain target in which to implant the electrodes is the globus pallidus internus (GPi). GPi DBS for dystonia is considered a safe and established procedure, but its success rate depends on the type of dystonia, on accuracy of electrode location, and of course on the quality of postoperative programming and follow up.

DBS is a life-long treatment for dystonia aiming at symptomatic relief, and requiring life-long follow-up of the patient. Based on 20 years of experience of managing DBS for dystonia, the authors conclude that there is only exceptionally "final" or "definite" outcome.

Initially, the DBS parameters have to be titrated to address the symptoms and minimize side effects. The full effect of DBS on dystonia may take weeks to months to be fully apparent. DBS requires regular checks, and sometimes repeated adjustment of stimulation parameters over the years, especially in children. The battery needs to be replaced before it is completely empty. Even when using rechargeable stimulators, these need regular checks and maintenance.

In summary, the outcome of DBS for dystonia depends on diagnostic and selection skills, surgical skills and management skills.

In general, outcome of DBS is better in patients with primary than secondary dystonia, better in mobile than fixed dystonic postures, better early than late in the course of the disease.

## RECENT DEVELOPMENTS IN RESEARCH

Basic research aims to explain why dystonia develops with the expectation that this 'fundamental' information is the pipeline to new therapies.

Basic research in dystonia often focuses on inherited forms of the disease where researchers work to define a cascade leading from a cause (genetic mutation) to symptoms.

This talk will showcase highlights from dystonia basic research over the last five years.

These include work with genetically modified mice that point to developmental windows and certain brain areas as important in disease development. There are also studies implicating glial cell defects in forms of the disease, and

new information about the molecules and signals that become disturbed in dystonia that might turn out to be therapeutic targets.



**Dr. Jean-Pierre Bleton**

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## DYSTONIA IN ACTION

Cervical dystonia (CD) is the main form of focal dystonia occurring in adulthood that manifests itself in involuntary contractions of some of the cervical muscles, and which results in abnormal postures and / or movements of the head. The recommended and widely used treatment is the injections of botulinum neurotoxin A or B (BoNT) into dystonic (hyperactive) muscles. BoNT helps to reduce severity of spasms of the dystonic muscles by means of therapeutic (neuro-chemical) paresis. Physiotherapy or rehabilitation is considered to be a valuable complementary therapy (Delnooz 2009). Up till now, there are no available guidelines or consensus unanimously accepted to determine the modalities of this rehabilitation. (de Pauw, 2014). Nevertheless, the main contribution of rehabilitation seems to be the activation of the anti-dystonic corrective muscles, whose function is inhibited (Mezaki, 2007).

The usual way of practicing rehabilitation consists of weekly or bi-weekly sessions in hands-on and face-to-face physiotherapy sessions. It appears, in the light of studies on rehabilitation for paretic upper limb after cerebrovascular accidents (Cunningham, 2016) and impaired balance in the Parkinson's disease (Jöbges, 2004), that the effects of rehabilitation are dependent on the amount of daily exercises and the regularity of the practice over a period of time of several weeks (dose-effect correlation). Unfortunately, the items of duration and amount of daily exercises are poorly documented for CD.

Regarding CD, as Pr Marie Vidailhet wrote in 2014: " The real challenge consists of favourably modifying the patient's motor pattern, by "reprogramming" inappropriate involuntary movements, and by the use of multiple learning, sensory perception, neuronal plasticity and compensation processes". It is now well known

that under the effect of motor learning and training, the somatotopic organization of the primary motor cortex (M1) can be radically transformed. (Jeannerod, 2006). Our team has shown in a study on dystonic patients suffering from writer's cramp that tailored rehabilitation leads to significant clinical increase and, in the cortex controlling the dystonic hand, "super normal" reorganization of the finger maps (Bleton, 2011).

Although, environmental and psychosocial factors could drastically influence the quality of exercises practiced at home and scientific literature does not provide conclusive evidence, it seems useful to recommend relatively intensive self-rehabilitation in long-term ailments such as CD.

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**Prof. Marjan Jahanshahi**

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## LIVING WELL WITH DYSTONIA

Dystonia is a chronic disorder that can have a negative impact on the daily activities and quality of life of people with the illness. Some people with dystonia may experience depression and anxiety. Research evidence suggests that factors such as the individual's attitude to the illness, coping style, and social support are important in determining how people adjust to a chronic illness such as dystonia. Based on this research evidence, I will present some

common sense approaches that people with dystonia can use for self-management of their illness. By using these strategies and ensuring that the process of adaption is continuous and ongoing, people with dystonia can live well with the illness.



**Dr. Bruno Bergmans, MD, PhD**

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## WHAT CAUSES DYSTONIA?

Unfortunately in many patients we don't know what is the cause of their dystonia. In that case, we label the dystonia as "idiopathic".

In rare instances the cause of the dystonia can be a genetic mutation. Scientific advances make that more and more dystonia genes are known. Three genes are more common. DYT1 which typically causes a childhood-onset torsion dystonia, but the phenotypic spectrum is wide. DYT6 is another dystonia gene that is more encountered in the adult population. DYT11 or mutations in the epsilon-sarcoglycan gene are the typical cause of myoclonus-dystonia, a rare form of familial dystonia presenting with a mixture of myoclonic and dystonic features. The exact function of many dystonia genes is unknown, but increasing scientific insights are clarifying step by step bits and pieces of the story.

A wide spectrum of neurological diseases can be associated with dystonia/dystonic features, either caused by the disease itself, or by a side-effect of medication (like dystonic dyskinesias in Parkinson's disease patients).

Quite commonly, dystonia can be a side-effect of specific medication intake. Neuroleptics typically can cause dystonia, either acute or after a delay. When the dystonia only occurs, some time (and this can be many years) after the initiation of the treatment with the neuroleptic, we call it a tardive dystonia. These dystonias can be very troublesome. They can affect different body parts.

A specific subset of dystonias (task-specific dystonias, dystonias that only occur when the patient undertakes a specific task, like writing, playing a musical instrument,...) is thought to arise from a disturbance in sensory mechanisms.



**Joost van den Dool**

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## LONG-TERM SPECIALIZED PHYSICAL THERAPY IN CERVICAL DYSTONIA: OUTCOMES OF A SINGLE BLIND RANDOMIZED CONTROLLED TRIAL

**Background:** Cervical dystonia (CD) is a neurological movement disorder characterized by involuntary muscle contractions causing abnormal postures and/or twisting movements of the head and neck. The main treatment option is botulinum toxin (BoNT) injections in affected muscles to improve head postures and reduce pain. However, BoNT treatment is often unsatisfactory: many patients maintain difficulties performing daily tasks. In addition to BoNT treatment, patients are often referred for physical therapy (PT), but there is little evidence regarding the long-term effectiveness.

**Objective:** To evaluate the effectiveness of a specialized PT (SPT) program on disability in CD compared to regular PT (RPT).

**Methods:** 96 patients with primary CD and stable on BoNT treatment for one year were randomized to receive SPT or RPT. The primary outcome was disability assessed with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS). Secondary outcomes were, pain, anxiety, depression, quality of life and total costs over 12 months. Data was collected at baseline, six and 12 months. A mixed between-within subjects ANOVA was used to test changes over time and group differences.

**Results:** Both groups showed significant improvements on the TWSTRS disability scale over time ( $p=0.00$ ). No significant between group differences were found ( $p=0.28$ ). Secondary outcomes showed significant better

improvements in the SPT group on the SF-36 General Health perceptions ( $p=0.04$ ) and self-perceived improvement ( $p=0.03$ ). Better improvements on anxiety were seen in the RPT group ( $p=0.05$ ). Total costs were lower for SPT compared to RPT after 12 months (-147 euro (CI 95% -343 to 150)).

**Conclusion:** PT in general improves disability in CD but SPT is not more effective on the TWSTRS disability scale. However, patient perceived effects and general health perception were more effective and treatment costs were lower in the SPT group. With a lack of structured PT interventions for CD, lower costs and comparable effects, we recommend implementation of the SPT program in CD.



**Prof. Alexander Schmidt, MD, MA<sup>1,2</sup>**

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## MUSIC AND DYSTONIA

Musician's dystonia (MD), a task-specific form of isolated focal dystonia, presents with loss of voluntary motor control of extensively trained movements when a musician is playing his or her instrument. The frequency is estimated at about 1-2% among professional musicians; the disorder is highly disabling and in many cases terminates performance careers.

The pathophysiology of MD remains largely elusive. The disorder has been associated with intensive training regimes and other

environmental risk factors and thus long been regarded as solely environmentally acquired. However, neurogenetic research within the past decade identified a genetic contribution to MD and the first molecular genetic risk factors of the disease. The therapy of MD is limited, therefore prevention plays an important role.

Within the lecture recent aspects of the pathophysiology, therapy and prevention of MD will be presented and discussed to improve the understanding of this complex disease.



**Prof. Elegast Montbaliu**

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## COMPUTER ACCESS FOR CHILDREN WITH SEVERE GENERALIZED DYSTONIA.

Dystonia is the dominant movement disorder in dyskinetic cerebral palsy. Dystonia is generalized over all body regions (arms, legs, trunk, neck, mouth, and eyes), with higher severity in the upper limbs than in the lower limbs, and substantially increase with activity. Dystonia has a major effect on the daily activity, quality of life, and societal participation of individuals with DCP. Dystonia particularly affects posture, mobility, hand and oral-motor function, and—to a lesser extent—non-verbal communication. The medical management options are not

appropriate as standalone treatment. Combinations with rehabilitation approaches carried out by physiotherapists, occupational therapists, and speech and language therapists are key components of the management of dystonia. Current practice is mainly based on clinical expertise. This expertise is usually offered by dedicated multidisciplinary rehabilitation teams designing individualized management programs that begin as early as possible in the

life of the patient. In a 21st century, computer access is obvious but for children with severe generalized dystonia is experienced as a window to the world and achieved with different practical tools.



**Prof. Dr. Patrick Santens**

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## THE HISTORY OF DYSTONIA

Dystonia is not a recent phenomenon. Pieces of art, dating back to the ancient world, already picture images of people affected by abnormal postures characteristic for dystonic movements. However, with the exception of "torticollis", which first appeared in late medieval literature, there was no unifying terminology until the beginning of the twentieth century when Oppenheim described "dystonia musculorum deformans". The use of photography and cinematography and the increasing efforts for a systematic description of clinical phenomenology contributed to the interest in abnormal movements but especially the rise and fall of psychoanalysis blurred the concept of dystonia during most of the twentieth century. In the 1980's increasing

evidence from neurophysiology finally put an end to an ongoing debate on the organic nature of dystonic movements. This boosted the search for treatments that improve the quality of life of people with dystonia. Nevertheless, notwithstanding these centuries of history, continuing efforts are necessary to increase awareness and recognition of the burden for those affected.



**Donna Walsh**

Executive Director,  
EFNA



**Frédéric Destrebecq**

Executive Director,  
EBC

## POSITIVE PARTNERSHIPS FOR BRAIN & NEUROLOGY IN EUROPE WITH EFNA & EBC

In this presentation, delegates will hear about the work of the European Federation of Neurological Associations [EFNA] and the European Brain Council [EBC].

- EFNA is an umbrella of pan-European, disease-specific, neurology patient groups - including Dystonia Europe.
- EBC is a multi-stakeholder organisation whose mission is to promote brain research and brain health in Europe.

The presentation will focus on the synergies between both organisations; exploring examples of best practice multi-stakeholder partnership

- with the patient perspective at the centre - across a number of flagship projects.

This will include profiling of EFNA's Training Initiatives for Neurology Advocates and the EBC's Value of Treatment project, as well as other initiatives and spin-off activities where Dystonia has featured or will feature in future.

There will also be time for an interactive Q&A and feedback from delegates which can be used EFNA and EBC to inform their approaches to patient advocacy, engagement and empowerment.



**Prof. Maja Relja**

Referral Centre for Movement Disorders and Neurodegeneration, Department of Neurology, Clinical Medical Centre, Medical School University of Zagreb, Croatia

## TRAINING OF FAMILY DOCTORS COULD IMPROVE DYSTONIA MANAGEMENT: CROATIAN EXPERIENCE

**Introduction:** Although an under-diagnosed condition, dystonia syndromes (DS) represent the third most common disorder in movement disorder centers. DS is difficult to recognize due to its large phenomenological complexity. We have shown lack of specific training in dystonia by general neurologist (GNs), family doctors (GP) as well as other allied health professionals in the study performed by European network for the study of DS (Valadas et al. Eur J Neurol 2016).

**Objectives:** To improve diagnosis and management of DS in Croatia by specific training in dystonia.

**Design/Methods:** A questionnaire was developed and sent to dystonia patients in Croatia and close neighbors part of eastern Slovenia during year 2010. and 2015. (5years after specific training of residents, GNs and GP was introduced in postgraduate medical education. Training courses, training schools and focused symposia were introduced twice a year to facilitate training in dystonia). The questionnaire was composed of 30 questions divided into three parts (part I. general questions as name, age, etc; part II. specific questions as disease duration, type of DS, time to correct diagnosis, who made correct diagnosis, experience with first visit to GP etc; part III. Availability of therapy, type of therapy, therapy side effects etc.).

**Results and Discussion:** Total questionnaires processed: 467 in 2010. and 367 in 2015. All regions of the country appeared to be well

represented in the respondent sample. In both 2010 and 2015, women outnumbered men by about 3 to 1, and about three-quarters of the sample were aged over 50 while cervical dystonia was the most common type of DS (62% of cases). Generalised dystonia was found in 8% of cases. Botulinum toxin type-A was used 80% of patients. In year 2010, only 27% said they had obtained a correct diagnosis promptly within one year of first DS symptoms, for 19% of respondents, diagnosis had taken at 3-5 years, and in 14% of patients longer than 10 years. In only 12% of cases had respondents' GPs recognised the symptoms and referred to an appropriate specialist, while in 31% of cases GP did not recognised DS and did not referred patients to a specialist. In year 2015, (5year of continuous dystonia education for GNs, GP) significantly higher number of responders (35%) had obtained a correct diagnosis within one year of first DS symptoms while only 7% waited for over 10 years. In 35% of responders GP recognised the symptoms and referred to an appropriate specialist while 20% was not diagnosed and did not referred patients to a specialist

**Conclusions:** Collaboration in specific training for residents, GNs, GP could represent the basis for improving all aspects of dystonia management especially diagnosis and therapy.



**Alistair Newton**

Founder & Past President DE St Andrews, UK

## DYSTONIA EUROPE – HOW AND WHY IT ALL STARTED 25 YEARS AGO

The journey of Dystonia Europe started in 1992, one year before the official founding in Spoleto, June 1993.

Just like an international express train, the route we have followed since then has taken us through many countries and cities, over more than 25 years. Brussels in April 2018 will be only our latest stop. Many people have travelled on our 'train' and some of them have been replaced by others along the way. Together, we have achieved many successes and overcome many challenges.

Dystonia was still not well known in 1992 – and dystonia patient advocacy was in its infancy in our continent. Across Europe, only a few patient groups had been formed, and some of them were very new. Some focussed on only one type of dystonia – torticollis, blepharospasm, dysphonia..... International communication and partnership was badly needed.

The Movement Disorder Society (MDS) held its second congress for specialists in Munich in 1992. Workshops for a few delegates from patient organisations took place, as part of a satellite meeting alongside the medical sessions. This was the first time that national dystonia delegates from different European countries had ever met together. From that beginning, funding was obtained for two small planning meetings. The more established national organisations from seven countries (France, Italy, Netherlands, Norway, Spain, Sweden, United Kingdom) were invited to send delegates to discuss the formation of a European Dystonia Federation.

We have come a long way from Munich 1992, and the journey continues...





**Prof. Christine Klein**

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## DYSTRACT – A GERMAN RESEARCH NETWORK

The Dystract Consortium represents a German Research Network within the "Research for Rare" Program of the German Federal Ministry of Education and Research with a focus on dystonia. Dystract combines human clinical, multimodal imaging and electrophysiological, molecular genetic, and experimental cellular and animal research. This includes cutting-edge technologies such as characterization of neurons derived from induced pluripotent stem cells (iPSC) from patients with different genetic and non-genetic forms of dystonia to explore the entire disease pathway of dystonia from the molecular level to brain network abnormalities. Dystract contains the German Dystonia Registry and enrolling patients at multiple sites across Germany, will aid in standardizing the diagnosis and treatment approach to dystonia in Germany and will establish a reference database for all groups involved in dystonia care. Individual subprojects of Dystract include, but are not limited to:

- System physiology of dystonia development in rodent models of DYT1 and DYT12
- Defining motor system endophenotypes in dystonia using a multimodal neurophysiology and structural imaging approach
- Musician's Dystonia as a model for the nature-nurture debate: Classification of endogenous and exogenous trigger factors in musician's dystonia

Individual Dystract projects and first results will be presented in detail at the Dystonia Europe Meeting.

- A randomized, sham controlled trial of pallidal neurostimulation versus botulinum toxin treatment for cervical dystonia (StimTox-CD)
- German Dystonia Registry: Natural History, Epidemiology, Genetics, and Clinical Trial Resource
- Elucidation of novel genetic causes and modifiers for dystonia
- Modeling dystonia in an endogenous human cellular system: Platform and characterization of iPSC derived neurons from patients with monogenic isolated dystonia



**Dirk Dressler, MD, PhD**

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## IS THERE ENOUGH RESEARCH IN BOTULINUM TOXIN THERAPY

Historically, most of the research in botulinum toxin (BT) therapy has come from the clinical BT users, the physicians. This includes the groundbreaking idea, the enormous expansion of its use in hundreds of indications throughout a large number of medical specialties. After more than 20 years this process has now - quite naturally - slowed down. There are still many hidden pearls to be discovered, however, mainly outside of dystonia. Ultrasound-guided application was recently heavily promoted. However, its reasonable use is restricted to few clinical situations. No study so far, has shown superior therapeutic efficacy against electromyography or appropriate clinical application. Over the last 10 years the research and development program of the Movement Disorders Section of Hannover Medical School has focused on translational BT research including BT binding, dose-effect curves, dose-duration curves, drug potency comparisons, immunological investigations and on exploration of new modes of action. Most recently, breakthroughs in clinical BT science have included the introduction of the high dose therapy, the introduction of the short interval therapy, various methods for application pain reduction, the development of treatment guidelines and of dosing table for dystonia.

Research in BT therapy is also performed by BT drug manufacturers. This research has always been limited, though. Many basic BT phenomena such as mode of action, binding, effect duration, immunology and dose-effect curves have not been properly studied. Most of the manufacturers' efforts are still directed towards formal registration studies. Unfortunately, all of the latest registration studies have been outside the field of neurology. Development of BT drug modifications such as liquid preparations, long-duration/short-duration drugs, hybrid BT drugs have not yielded promising results. New competitors in the BT market are providing more or less conventional BT drugs. Currently, BT combined with a special carrier protein is under clinical investigation. Its mechanism of action is not clear. Overall, more and more BT manufacturers from Asia are seeking market access in the lucrative markets of North America and Europe.

For patients the biggest problem is already and will be even more in the future the availability of BT therapy. Lack of special reimbursement codes and dwindling BT prices are blocking the much needed expansion of treatment centers.



## NOTES

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