

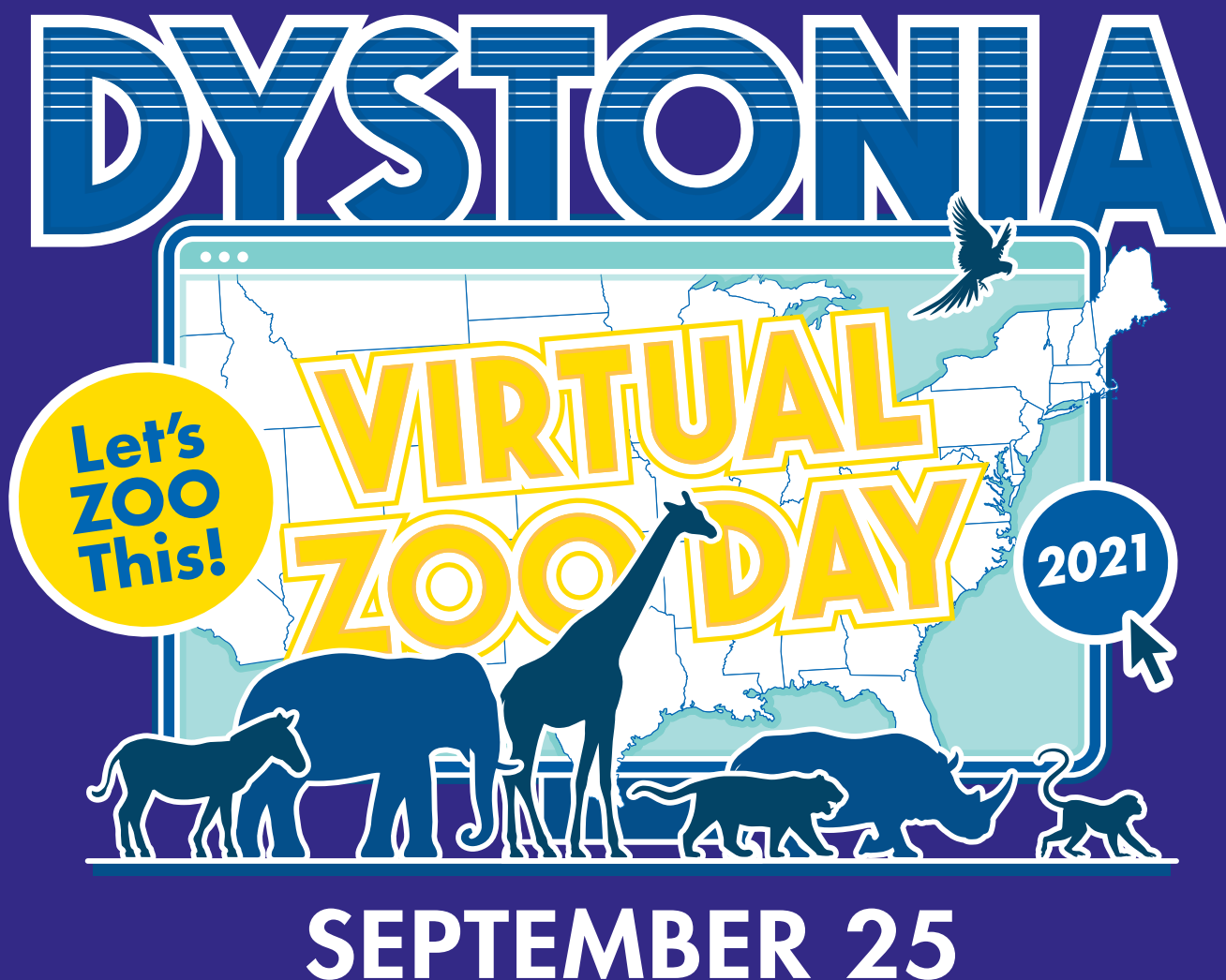


DYSTONIA
MEDICAL
RESEARCH
FOUNDATION

Dystonia Dialogue

NEWSLETTER OF THE DYSTONIA MEDICAL RESEARCH FOUNDATION

Summer 2021 | Volume 44 • No.2



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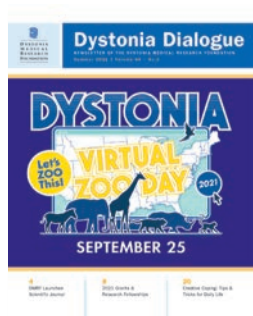
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On the Cover:



On the cover: The dystonia community is uniting for an exciting national day of action to boost dystonia awareness and raise funds for medical research toward a cure. Individuals with all types of dystonia, as well as family members and friends, are invited to take part in Virtual Dystonia Zoo Day to benefit the Dystonia Medical Research Foundation (DMRF). Join us for a live-streamed event

on Saturday, September 25, 2021 and add your voice to this fun and important effort. Learn more on page 12. #letsZOOthis

The Dystonia Dialogue is supported by educational grants from AbbVie Foundation and Revance Therapeutics.

The *Dystonia Dialogue* is the magazine of the Dystonia Medical Research Foundation (DMRF). It is published three times a year to provide information to individuals affected by dystonia, family members, and supporters of the DMRF.

The Dystonia Medical Research Foundation (DMRF) is a non-profit, 501(c)(3) organization founded in 1976. The mission is to advance research for more effective treatments and a cure, to promote awareness and education, and to support the well being of affected individuals and families.

The *Dystonia Dialogue* reports on developments in dystonia research and treatments but does not endorse or recommend any of the therapies discussed. Individuals are urged to consult a physician with questions and concerns about their symptoms and care.

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Foundation Update



Art Kessler
President

The Dystonia Medical Research Foundation (DMRF) was founded out of necessity. Samuel and Frances Belzberg established the DMRF because their child was diagnosed with dystonia and there was nowhere to turn for help. There was essentially no research happening, so they engaged investigators and made it happen. There was no national support for families, so they created the resources they wished were available when their daughter was diagnosed. The spirit of doing what is required continues to infuse the DMRF mission. Where there is a need in the dystonia community—whether in research or patient programs or public policy—the DMRF has never been afraid to step into the gap and create something new.



Janet L. Hieshetter
Executive Director

The DMRF has launched a brand new scientific journal. *Dystonia* is an open access journal dedicated specifically to dystonia research. It is the first publication of its kind, and we could not be more proud. Learn more about this major milestone for the dystonia field on page 4.

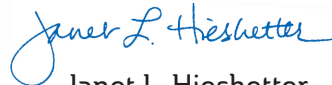
Covid certainly forced DMRF to operate creatively, transforming uncertainty into new opportunity. Virtual Dystonia Zoo Day on September 25, 2021 will build on the immense success of last year's inaugural virtual event to bring the dystonia community together and promote dystonia awareness, all while staying safe during a pandemic. Please consider participating in this year's event, which promises to be bigger and better. Details are available on pages 12–13.

DMRF leadership leans into challenges because we are passionate about finding a cure for dystonia and supporting the well-being of affected individuals and families. 100% of the Board of Directors is personally impacted by dystonia—either themselves or a loved one is diagnosed. We believe in the power of doing what is required. Showing up every day to make the next day better. Please share with us why the work of DMRF is important to YOU. During our 45th year, we are collecting and sharing testimonials to reflect on all that we have accomplished together. Visit: dystonia-foundation.org/45 to share your testimonial.

Thank you for the privilege of being of service to the dystonia community and the incredible opportunity to continually engage the world's most innovative experts in the mission to cure dystonia. Thank you for your support.



Art Kessler
President



Janet L. Hieshetter
Executive Director

STAY IN TOUCH! Sign up for email updates at: dystonia-foundation.org/email

DMRF Launches First Scientific Journal Dedicated to Dystonia

The DMRF has partnered with Frontiers Media to launch *Dystonia*, an open access journal. The journal will bring visibility to the growing dystonia field and highlight advancements in science and clinical practice. This is the first scientific journal exclusively dedicated to dystonia and a major milestone for the dystonia scientific community.

“The field is ready for a journal focused solely on dystonia,” said Co-Editor-in-Chief Aasef Shaikh, MD, PhD, Penni and Stephen Weinberg Chair in Brain Health and Vice Chair for Research in the Department of Neurology at University Hospitals, Cleveland, and Principal Investigator at Daroff-Dell’Osso Ocular Motility Laboratory at Louis Stokes Cleveland VA Medical Center. “There has been a steady increase of publications on dystonia in recent years. Now we have a designated platform to share discoveries and advancements.” Dr. Shaikh serves on the DMRF Medical & Scientific Advisory Council (MSAC) and is a past DMRF Clinical Fellow.



***Dystonia* Co-Editors-in-Chief are Aasef Shaikh, MD, PhD (left) & Roy V. Sillitoe, PhD.**

“Breakthroughs are being made in basic, clinical, and translational research,” explained Co-Editor-in-Chief Roy V. Sillitoe, PhD, Associate Professor of Pathology and Immunology and Neuroscience at Baylor College of Medicine, and Director of Neuropathology Core Laboratory, Jan and Dan Duncan Neurological Research Institute, at Texas Children’s Hospital. “It is an exciting time for the field, and the journal will support the momentum going forward.” Dr. Sillitoe also serves on the MSAC.

Up until this point, dystonia studies have been published in various neurology and neuroscience journals. Since the beginning of 2020 alone, more than 1,600 dystonia papers have been scattered across the medical literature. On average, three new dystonia papers are published every day. *Dystonia* provides a centralized, go-to publication by and for dystonia investigators. It is Gold Open Access, which means the content is available to the medical community and public at no charge to readers.

“DMRF is very proud to be spearheading this major development for the dystonia field,” said DMRF Vice President of Science Richard Lewis, MD. “When there is a need in the dystonia community—whether from patients or researchers—DMRF consistently steps in to address those needs.”

Manuscripts are being accepted now at: frontierspartnerships.org/journals/dystonia. The journal is partially supported by the Joan Miller Young Investigator Fund and Tuft Family Foundation.

Register as a Brain Donor

*Individuals with all types of dystonia are invited to register in advance as a brain donor.
For more information visit: dystonia-foundation.org/brain*



Douglas Kramer Awardees Represent Dystonia Community

The Douglas Kramer Young Advocate Award recognizes exceptional volunteers who are giving voice to dystonia through legislative advocacy. The award was created by the late Florence Kramer, a longtime generous supporter of DMRF. The award is named in memory of her son who had dystonia.

The newest Douglas Kramer Young Advocates were selected just prior to the Covid shutdown, which delayed announcements. The DMRF is proud to finally recognize the 2020/2021 Douglas Kramer Young Advocate Award recipients:

- Kelsey Alford
- Jacquelyn Coello
- Haley Dennis
- Daria Dragicevic
- Maddie Paolero
- Brian Smuda

These outstanding advocates are working with DMRF on legislative and policy matters throughout the year.

For more information about DMRF legislative advocacy activities, visit: dystonia-foundation.org/advocacy

DMRF-Funded Investigators Develop New Approach to Studying Motor Control

DMRF grantee Jesse Goldberg, MD, PhD, Associate Professor and Robert R. Capranica Fellow in the Department of Neurobiology and Behavior at Cornell University, has developed a groundbreaking new approach to studying dystonia and other movement disorders.

The study of dystonia has always required posing fundamental questions about how the human brain controls and coordinates movement. The act of reaching an arm to pick up an object is an incredibly complex neural task—and uncovering precisely what goes wrong in the brain when dystonia interferes with such a task is equally tricky. Much of what is known about human movement control and coordination has come from the study of reaching and grabbing in monkeys, because of the obvious similarities. Lab models such as mice, for example, do not have the anatomy or behavior to replicate human reaching with a limb.

However, Dr. Goldberg and his team discovered that the movements of a mouse's tongue when it licks water from a spout are neurologically comparable to a primate reaching an arm to grab an object. While a hand reach and a mouse lick may not initially appear to have much in common, in both cases the brain must coordinate fine motor adjustments in relation to a specific target. The investigators designed experiments using water spouts fitted with sensors, high-speed cameras, and artificial intelligence applications capable of sifting through millions of image frames to track the mouse tongue movements. Additional techniques allowed the researchers to observe that the licking mice activated the brain's motor cortex in remarkably similar ways to reaching primates. They demonstrated that a single mouse lick is controlled by the brain in a similar way to a human reach. This work opens up new opportunities to study the motor cortex function to understand normal movement as well as the neural basis of movement disorders like dystonia, Parkinson disease, and others. The hope is that this methodology will provide a best-in-class method for closely examining mouse motor control with the right level of precision to clarify behavioral abnormalities in dystonia mouse models, which are critical for strategizing and testing new treatment approaches.

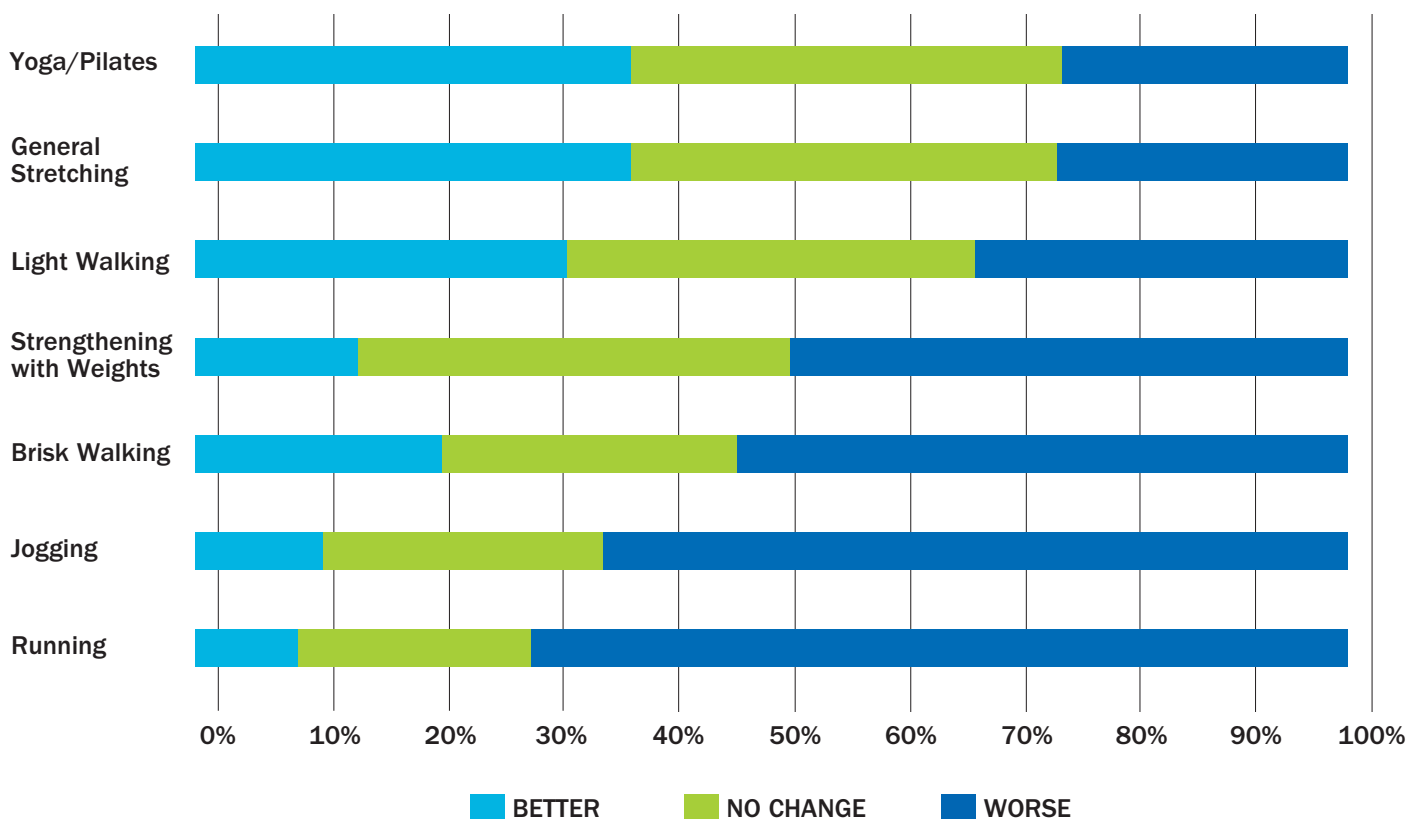
DMRF is proud to have supported Dr. Goldberg's lab in partnership with the Dorothy Feiss Scientific and Medical Research Fund.

Bollu, T., Ito, B.S., Whitehead, S.C. et al. Cortex-dependent corrections as the tongue reaches for and misses targets. Nature (2021).

High Impact Exercise More Likely to Worsen Dystonia

The benefits of exercise and physical activity for neurological disorders is well-known. Individuals with dystonia may experience numerous barriers to healthy levels of exercise, including the fact that physical activity sometimes worsens dystonia symptoms. A team of exercise scientists and physical therapy experts at University of Auckland in New Zealand conducted a survey of 260 dystonia patients about physical activity and barriers to exercise. The survey revealed that lower intensity exercise, such as light walking and general stretching, were among the least aggravating for dystonia symptoms.

This table shows the percentage of survey participants who answered 'better' (bright blue), 'no change' (green), and 'worse' (dark blue) for each activity. The study showed that higher impact exercise tended to worsen dystonia, while low impact exercise may be beneficial, or at least not aggravating, for two-thirds of dystonia patients.



McCambridge A, Meiring RM, Bradnam LV (2019) Physical activity, sedentary behavior, and barriers to exercise in people living with dystonia. *Front Neurol* 10:1121.

Bradnam, L.V., Meiring, R.M., Boyce, M. et al. Neurorehabilitation in dystonia: a holistic perspective. *J Neural Transm* (2020).

For tips on increasing physical activity visit: dystonia-foundation.org/benefits-of-exercise

DMRF Clinical Fellowships Train Young Movement Disorder Specialists

Evaluation by a movement disorder specialist can quicken dystonia diagnosis time, increase treatment options, and maximize benefit from treatment. Many individuals with dystonia must travel significant distance and endure long waits for appointment openings to access a physician with the necessary qualifications to diagnose and treat dystonia. In response to the urgent need for additional clinical experts, the DMRF sponsors one-year clinical fellowships to train second-year fellow physicians in the diagnosis and treatment of movement disorders with special competence in dystonia. The fellowships focus on training in both the clinical evaluation and care of patients and clinical research on dystonia. The training is patient-oriented and includes hands-on experience in clinics as well as participation in professional meetings and workshops.

CONGRATULATIONS TO OUR 2021 DMRF CLINICAL FELLOW AND MENTOR:

Jessica Frey, MD

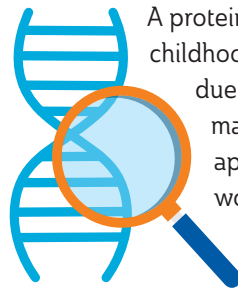
University of Florida

Mentor: Aparna Wagle Shukla, MD

Past DMRF clinical fellows have earned positions in movement disorder programs at prestigious institutions and are meeting the needs of communities previously without movement disorder experts. Clinical fellows remain engaged with the DMRF as reviewers for DMRF educational materials, speakers for educational meetings and webinars, participants at dystonia awareness events, and medical experts for news stories about dystonia.

The Clinical Fellowship Training Program is made possible by support from Ipsen and Merz.

TorsinA Restoration in DYT1 Dystonia Model Identifies a Critical Therapeutic Window



A protein in the brain called TorsinA is known to cause childhood onset dystonia when it cannot function properly due to genetic changes in the DYT1/TOR1A gene. This makes TorsinA a possible target for new treatment approaches. Numerous research teams across the world are investigating whether restoring normal TorsinA function could be an effective strategy to reverse or even prevent dystonia.

One of the most notable aspects of DYT1/TOR1A dystonia is that symptoms typically begin during a very specific age window, approximately 9–12 years of age. Even if a person has the DYT1/TOR1A gene variant, if they reach age 30 without developing symptoms, they almost never develop dystonia. This suggests there is something about the young developing brain that makes it vulnerable to dysfunctional TorsinA.

William Dauer, MD, Director of the Peter O'Donnell Jr. Brain Institute and Professor of Neurology and Neuroscience at UT Southwestern Medical Center, led a study to specifically test whether TorsinA function is uniquely necessary during a critical neurodevelopmental period, and whether genetic rescue is similarly only possible during a specific period of brain development. To rigorously address these questions, he and his team developed a series of experiments in mice. They found that embryonic suppression of TorsinA caused dystonia-like motor symptoms and observable changes in the brain. By contrast, TorsinA suppression in adult mice caused no apparent abnormalities. Furthermore, the ability to correct the TorsinA dysfunction and reduce dystonia symptoms was only possible during specific periods of brain development. Restoring TorsinA expression in young symptomatic mice reversed the abnormal movements and changes in the brain. By contrast, restoring TorsinA expression in adult mice had no effect. These important findings demonstrate that normal TorsinA function is critical to early brain development and suggest that TorsinA-based therapeutics may need to be targeted early in the course of DYT1/TOR1A dystonia.

Dr. Dauer is a past DMRF Stanley Fahn Award recipient and past member of the Medical & Scientific Advisory Council.

Li J, Levin DS, Kim AJ, Pappas SS, Dauer WT. TorsinA restoration in a mouse model identifies a critical therapeutic window for DYT1 dystonia. J Clin Invest. 2021 Mar 15;131(6):e139606.

2021 Grants & Research Fellowships

The ultimate goal of the DMRF's science program is to support the discovery of improved dystonia therapies and a cure. The DMRF is dedicated to stimulating the field of dystonia research and supporting the collaborations and projects necessary to accelerate progress. Currently funded projects are furthering our fundamental understanding of what dystonia is, investigating shared mechanisms among dystonia types, exploring novel new therapeutic approaches, understanding how dystonia-causing mutations ultimately result in symptoms, and uncovering targets for new and improved therapeutics. The DMRF is committed to providing investigators with the grant funding and resources needed to address the most pressing unresolved questions in dystonia research and produce new discoveries.



Congratulations to the newest award recipients, and infinite thanks to DMRF supporters for making this research funding possible.

GRANTS & CONTRACTS

Research grants are available in support of hypothesis-driven research at the genetic, molecular, cellular, systems, or behavioral levels that may lead to a better understanding of the pathophysiology or to new therapies for any or all forms of dystonia. Contracts provide the opportunity to provide research support through the identification of specific, milestone-driven projects conducted by identified investigators.

Genetic Modifiers of Penetrance in DYT1 Dystonia – 2nd Year David Arkadir, MD, PhD

Hadassah Medical Center and Hebrew University of Jerusalem

Some types of dystonia are hereditary, for example, DYT1 dystonia caused by mutation in the TOR1A gene. It is not clear, however, why individuals with the same genetic mutation can develop different severities of symptoms. On the extremes, one individual may experience severe dystonia that starts in childhood and leads to significant motor disability while another individual may be totally asymptomatic and not even aware of having the genetic mutation. Dr. Arkadir and

his team believe that additional genes, yet to be discovered, determine whether an individual carrying a potentially dystonia-causing genetic mutation will develop this movement disorder or not. They attempt to find this gene(s) by comparing the genomes of individuals who have mutation in the TOR1A gene, with or without apparent dystonia symptoms. The goal is to find genes that protect some individuals from developing dystonia, even in the presence of the mutated gene.

Normalizing DYT1 Cholinergic Neurons by CRISPR Disruption of Mutant TOR1A Allele

Xandra Breakefield, PhD

Massachusetts General Hospital

Gene therapy is proving beneficial in an increasing number of neurological diseases. This proposal represents a step in evaluating whether gene therapy could be effective in DYT1 dystonia. Dr. Breakefield has shown that selective disruption of the mutant TOR1A/DYT1 gene can normalize biologic cell functions in patient skin cells. Since dystonia is a neurological disease, the next step is to evaluate whether this approach

can normalize function in TOR1A/DYT1 neurons (brain cells). Collaborating with Dr. D. Christopher Bragg and Dr. Nutan Sharma the investigators have access to stem cells from DYT1 patients, which can be turned into neurons. If successful in rescuing neurons, the lab will work with Dr. David Standaert to translate the technology into a mouse model which would provide some of the data needed for the Food & Drug Administration to allow a clinical trial. Ultimately, Dr. Breakefield envisions a clinical trial in which children carrying the mutant TOR1A/DYT1 gene and manifesting symptoms at an early age are administered gene therapy in a single dose. This could be done at the same time as deep brain stimulation (DBS), with the intent to eventually turn off the DBS device to assess if it remains needed. The ultimate goal of this effort is the development of better therapies for DYT1 dystonia.

A Next Generation Sensing Neural Interface Study for Adaptive DBS in Dystonia

Simon Little, MBBS, MRCP, PhD

University of California, San Francisco

In addition to being a treatment, deep brain stimulation (DBS) is helping researchers understand how dystonia affects the brain. Recent work has shown that brain signals in dystonia are different from individuals without dystonia or with other neurological disorders. This has revealed a pattern of activity in the deep parts of the brain that repeats around five times per second in people with dystonia and is linked to muscle activity. However, investigators don't yet know the significance of this signal and whether it causes muscles to contract or is simply a marker that they have done so. Also, if it is a cause of dystonia, it isn't yet known how this interferes with the healthy sensory messages that come into the brain or the movement signals that leave the brain. To answer these questions, Dr. Little and team will use new sensing-enabled DBS devices which can record brain signals as well as provide stimulation therapy. They have implanted this device in a small group of dystonia patients and found that the dystonia signals are present in all patients recorded so far. Next they plan to investigate how this signal relates to muscle activity and sensory processing. They will also test this new type of adaptive stimulation to see if it may be more effective and cause fewer side effects than standard continuous DBS. This study will further understanding of how brain signaling goes wrong in dystonia, knowledge which could potentially lead to the design of new and improved therapies.

The Role of Cholinergic Neurons in Isolated Focal Cervical Dystonia – 2nd Year

Scott Norris, MD

Washington University School of Medicine

Cervical dystonia produces excessive involuntary muscle contractions in the neck. These muscle contractions result in uncomfortable, awkward, and sometimes painful positions of the head, neck, and shoulders. This research project focuses on improving understanding of the brain's role in cervical dystonia, specifically directed toward improved treatment. The investigators use state-of-the-art brain imaging techniques, positron emission tomography (PET) and magnetic resonance imaging (MRI), to observe the working brain. PET allows researchers to observe chemical messengers (neurotransmitters) in the brain—in this case, acetylcholine. MRI allows researchers to observe how one region of the brain communicates with other brain regions. Combining PET and MRI techniques provides a powerful opportunity to determine how altered chemical messenger levels may influence the way brain regions communicate in cervical dystonia by comparing brain activity of patients with cervical dystonia and control volunteers without cervical dystonia. Acetylcholine is a neurotransmitter of interest because some dystonia patients improve when taking medications that alter levels of acetylcholine. The researchers suspect that brain regions that use acetylcholine are damaged in patients with cervical dystonia and therefore the communication between brain regions that rely on acetylcholine is disrupted. If they find that acetylcholine affects how brain regions communicate in cervical dystonia, future research can attempt to correct the communication problem with new medication or brain stimulation therapies.

Role of Cerebellar Network Excitability and Plasticity in the Pathophysiology of Dystonia

Antonio Pisani, MD

University of Pavia

Dr. Pisani and his team are studying brain circuits in two types of genetic dystonia: DYT1 dystonia, which is the most common inherited form, and DYT25 dystonia which is rarer. They are testing the idea that loss of these genes leads to changes in brain plasticity, which is how the brain learns motor tasks and adapts to new environments. They believe that abnormal plasticity is a shared factor responsible for abnormal movements observed in patients. They study two animal models, one with the DYT1/TOR1A gene mutation and

the other with loss of DYT25/GNAO1. By conducting studies on brain circuits in these models, they hope to learn about the effects of the loss of these genes on brain plasticity. One of the features of abnormal movements in dystonia is that once the symptoms develop, they can be difficult to treat and may become permanent. This is a kind of dysfunctional plasticity. Therefore, if investigators can understand the mechanisms and control the abnormal plasticity, they might be able to ‘undo’ the changes in the brain that cause these movements, leading to better treatments.

Targeting the cAMP Pathway in the Striatum to Treat Dystonia

Emmanuel Roze, MD

Paris Brain Institute

The striatum is a deep structure in the brain that plays a critical role in the control of movements. cAMP is a molecule that regulates many cell functions, including those in neurons (brain cells). The cAMP signaling pathway controls processes important for the function of neurons in the striatum and the control of movements. (A signaling pathway is the string of communication among a group of molecules to complete a specific task in the cell.) Various genes that encode proteins involved in this cAMP pathway can cause dystonia when mutated, particularly GNAL and ADCY5. Mutations of GNAL lead to *reduced* cAMP production while mutations of ADCY5 lead to *increased* cAMP production. To better understand how disruptions in the cAMP pathway produce dystonia, the investigators will attempt to characterize movement dysfunction and striatal biochemical abnormalities of genetic mouse models. To investigate the cAMP pathway as a target to treat dystonia, they will ‘correct’ the abnormal cAMP pathway in the mouse models using drugs and investigate whether treatment improves the biochemical abnormalities and movement dysfunction. Finally, they will evaluate the effect of caffeine in ADCY5-related dystonia patients which is suspected to reduce excess of cAMP production and has been found to be helpful in some patients. To this end, they will use questionnaires and a randomized, controlled clinical trial with a single dose of caffeine.

Connie and Jim Brown Early Stage Investigator Award Cerebellar Repetitive Transcranial Magnetic Stimulation in Monogenic Myoclonus-Dystonia

Anne Weissbach, MD

University of Lübeck

Myoclonus-dystonia (M-D) is a neurological movement disorder often characterized by a combination of generalized

myoclonic jerks, dystonia, and psychiatric disorders. Mutations in the SGCE and VPS16 genes have been identified as genetic causes of the disease. Both genes are important for the function of an area of the brain called the cerebellum. These investigators and others have demonstrated that individuals with M-D have deficits of cerebellar mediated learning. How cerebellar malfunction in these patients affects the cortex of the brain, particularly regions important for motor control is of particular interest. Dr. Weissbach is leading the first study to investigate potential symptom reduction and neurophysiological changes in M-D patients before and after repetitive non-invasive transcranial magnetic stimulation (rTMS). The study aims to identify the clinical cerebellar deficit, identify abnormalities of cerebellar function and its interaction with the cortex of the brain as well as examine the reversibility of these abnormalities through the application of cerebellar rTMS. These findings will foster development of new treatment strategies.

RESEARCH FELLOWSHIPS

Over the years, DMRF has created funding awards to support young investigators at different stages in their scientific training. Postdoctoral fellowship awards support outstanding young scientists who have earned a doctoral degree and have embarked on a period of mentored research. DMRF is supporting postdoctoral fellows who are working to fundamentally improve our understanding of brain dysfunction and molecular mechanisms underlying dystonia.

Investigating Abnormal Neurodevelopment in a Novel in vivo Model of Inherited Dystonia

Simon Lowe, PhD

University College London Institute of Neurology

While researchers have uncovered a number of genetic mutations that cause dystonia, and it is well-known that dystonia affects certain areas of the brain, not enough is known about the mechanisms that ultimately cause the movement dysfunction. Some disease-causing mutations act *acutely*, which means they cause a disorder by directly altering the function of the brain, affecting its ability to perform tasks. Other mutations act *developmentally*, which means they alter the way the brain develops, causing lasting alterations in the way the brain works. Knowing which is happening is key to understanding and treating a disorder. Dr. Lowe is investigating a form of dystonia caused by a single mutation in the gene KCNMA1, which has a number of important roles in neurons (brain cells). Dr. Lowe and his team developed the first

animal model of this disorder in the fruit fly. Using advanced genetic techniques he is able to turn the mutation ‘on’ and ‘off’ at different stages of the flies’ lifecycle. Preliminary data show that turning the mutation on in the adult fly has no effect, but turning the mutation on and then back off again during its development causes severe, lasting movement defects in the adult fly. These defects very much resemble the movement dysfunction seen in humans. This is a clear demonstration that the mutation causes movement dysfunction in the fly by altering nervous system development. Dr. Lowe aims to confirm this and delineate the key developmental stage with additional experiments, and then ask the question *how* this mutation affects development. The investigation intends to provide mechanistic insights into a specific form of inherited dystonia and answer key questions about *when* and *how* dystonia occurs that may be the same in other forms of dystonia.

Neural Signals in the Cerebellar Nuclei Gate the Manifestation of Dystonia-like Symptoms

Meike van der Heijden, PhD

Baylor College of Medicine

The wide range of underlying causes for dystonia has made it difficult to develop one-size-fits-all treatment. Development of a treatment that would be broadly effective across the dystonias would be highly beneficial. Recent studies have suggested that the cerebellum may be a central node in a brain network that triggers dystonia in humans and mouse models. One specific area of the cerebellum, the cerebellar nuclei, sends neural signals to other regions of the brain and spinal cord that are involved in motor control. Imaging studies in dystonia patients and electrical recordings in dystonia mouse models have shown that these neuronal signals are different from people without symptoms and control mice, respectively. Interestingly, therapeutic stimulation of the cerebellar nuclei using deep brain stimulation (DBS) alleviates symptoms in some people with acquired dystonia and in a mouse model with severe dystonia. Dr. van der Heijden hypothesizes that the cerebellar nuclei act as a fulcrum in the

expression of dystonia symptoms. On the one hand, abnormal neuronal signals in the cerebellar nuclei can cause dystonia-associated symptoms. On the other hand, stimulating these nuclei with DBS can alleviate dystonia-associated symptoms. However, to fully understand how to best optimize DBS treatment, it is necessary know precisely what the balanced state neuronal signaling is in the cerebellar nuclei, and in what direction these communication signals are skewed in mouse models of dystonia. To answer this question, the investigators are recording brain activity profiles in multiple mouse models of dystonia with different severities of dystonia-associated symptoms. They use mathematical computations to determine what aspect of the neural signals are abnormal and cause dystonia-associated movement impairments. They hope to find precisely how cerebellar signals contribute to dystonias with different causes. This knowledge will be an important step for optimizing cerebellar DBS to become a first-line treatment for patients with dystonia.

DYSTONIA COALITION CAREER DEVELOPMENT AWARDS

The DMRF is proud to support two Dystonia Coalition Career Development Awards. The goal of the Career Development Program is to facilitate career development for junior investigators interested in clinical and translational research relating to dystonia, or to provide a mechanism for more senior investigators from other fields to get involved in dystonia research. More information about the Dystonia Coalition is available at: rarediseasesnetwork.org/cms/dystonia

Non-invasive Neuromodulation to Study Long-term Plasticity Mechanisms in Task-specific Dystonia

Noreen Bukhari-Parlakturk, MD, PhD

Duke University School of Medicine

Immune Mechanisms in Cervical Dystonia

Laura Scorr, MD

Emory University School of Medicine

DMRF Merchandise to Promote Awareness

Have you checked out the DMRF online store lately? You'll find many practical items to promote dystonia awareness: face masks, tote bags, pop sockets, pins, key chains, and more. For details and to order visit: dystonia-foundation.org/merch



DYSTONIA

SATURDAY

Let's
ZOO
This!

VIRTUAL
ZOO DAY

2021



LOCATION

THIS IS AN ONLINE EVENT.

dystonia-foundation.org/letszoothis

PROGRAM FOR THE DAY

The livestream program will include live zoo keeper chat, stories from the dystonia community, craft demonstration, and more.

On a single day, DMRF supporters across the country will take action to boost dystonia awareness and raise funds for medical research toward a cure. Your support will ensure DMRF continues to advance urgently-needed dystonia research and offer programs for affected individuals and families.

All team donations are eligible to be matched!
Your team may be flock, a pride, or a herd.
Even a lone wolf can be a team.

NATIONAL SPONSORS



THERAPEUTICS



HOW TO PARTICIPATE

- 1 Visit dystonia-foundation.org/letszoothis for complete event details.
- 2 Sign up to join us September 25, 2021.
- 3 Start your team. You can start your team with just one person.
- 4 Order your official Virtual Dystonia Zoo Day t-shirt.
- 5 Invite family members and friends to participate.

TICKET OPTIONS

- Virtual Event Ticket - Free
- Activity Kit - \$10
- Virtual Dystonia Zoo Day T-shirt - \$10 (includes ticket)
- Family Pack - \$50 (includes 4 shirts, activity kit, and ticket)
- Team Pack - \$250 (includes 25 shirts, activity kit, and ticket)

WHO'S ON YOUR TEAM?

All team donations are eligible to be matched:

- Teams that recruit 10 people (free or paid registrations) will qualify for a \$100 match.
- Teams that recruit 25 paid registrations or raise \$250 will receive personalized team t-shirts and have all funds matched.
- Teams that recruit 50 paid registrations or raise \$500 will receive team shirts, team bonus, and have all funds matched.
- Teams that recruit 100 paid registrations or raise \$1,000 will receive shirts, team bonus, and be able to share a recorded message during Virtual Dystonia Zoo Day, plus have all funds matched.

IMPORTANT DATES

- **August 15** – Deadline to receive personalized team t-shirts and activity kits for teams of 25+
- **September 1** – Deadline for shirt orders in time to ship for event

Shipping is available to US addresses only.



TEAM HIGHLIGHT

"Liam's Unshakeable Ninjas," named in honor of eight year old Liam Johnson, is already one of the largest and highest earning Virtual Dystonia Zoo Day teams. The Johnson family started the team at the 2019 Pittsburgh Dystonia Zoo Walk, shortly after Liam was diagnosed.

Promote dystonia awareness on social media by sharing pics wearing your event shirt and enjoying the activity kits!

#LetsZOOthis





Building a Support System

Living well with dystonia often requires complex treatment plans, ongoing medical appointments, and careful self-monitoring of symptoms and response to treatment. Having a multi-level support system can help you feel and function at your personal best. Social support in particular can have dramatic and positive effects on quality of life.

A multi-level support system is a collection of people, organizations, and resources available to support daily living and overall well-being. These can include:

- Medical Experts
- Co-Workers & Career Mentors
- Recreational Interests
- Wellness Practices
- Community Resources
- Family & Friends
- Peer Support
- Spiritual Support
- Mental Health Professionals
- Complementary Therapies

Keep Your Friends Close

Consider creating a go-to list of people and organizations you can count on. Have their contact information readily available in your phone or address book so you can reach out when you need to.

- | | |
|--|---|
| <input checked="" type="checkbox"/> Family members | <input checked="" type="checkbox"/> Friends |
| <input checked="" type="checkbox"/> Doctors and medical professionals | <input checked="" type="checkbox"/> Spiritual advisor |
| <input checked="" type="checkbox"/> Mental health support | <input checked="" type="checkbox"/> Crisis resources |
| <input checked="" type="checkbox"/> Dystonia Medical Research Foundation | |

For more information about DMRF support resources, visit these links:
dystonia-foundation.org/support-groups
dystonia-foundation.org/mental-health

FINANCIAL SUPPORT

Did you know that Americans with disabilities live in poverty at more than twice the rate of people without disabilities? Sixty-five percent of adults with disabilities participate in at least one safety net or income support program. These resources may help fortify financial security:

Pharmaceutical Assistance

Drug manufacturers often offer financial assistance programs to help individuals who meet specific criteria afford treatment. This includes the companies that manufacture botulinum neurotoxins, one of the most common dystonia treatments. Information about these programs is available at: dystonia-foundation.org/botulinum-toxin-injections

Employment Resources

The Job Accommodation Network (JAN) offers guidance on workplace accommodations and job protections for employees with disabilities, including dystonia. Go to: askjan.org and search 'dystonia.'

JAN can also direct you to state vocational rehabilitation agencies that help individuals with disabilities obtain and/or maintain employment.

Disability Benefits

The US Social Security Disability Insurance (SSDI) and Supplemental Security Income (SSI) programs provide assistance to people with disabilities. Information about eligibility and the application process is available at: ssa.gov/benefits/disability

DMRF offers a fact sheet of Frequently Asked Questions about Social Security Disability Benefits at: dystonia-foundation.org/print

Local Resources

States and municipalities may offer assistance programs for local residents. Contact your state Department of Human Services Department to make sure you are not missing out on programs for which you may be eligible.

People on the Move

The DMRF is grateful for the partners and volunteers across the country working to improve dystonia awareness and support medical research. Every effort makes a difference!



Amanda Lockhead of Nashua, New Hampshire was crushed when the pandemic prevented her from organizing her annual event to raise dystonia awareness and research funds. She re-invented her event as March to End Dystonia. For every \$5 donated to the DMRF, Amanda is walking a mile. She has since walked 150 miles, sometimes covering up to 10 miles in a day. Her goal is 500 miles. Information about March to End Dystonia is available at: dystonia-foundation.org/friends/amanda-lockhead

THANK YOU Social Media Fundraisers

Thank you to everyone who generously collects donations to benefit DMRF on social media. Media platforms like Facebook and Instagram provide DMRF with limited information about these fundraisers, and we wish to acknowledge all of our supporters.

To collect donations for DMRF through Facebook's fundraiser tools, go to: facebook.com/fundraisers to get started.

Learn how to use Instagram donation stickers at: help.instagram.com

Be sure to notify DMRF of your social media fundraiser to be eligible for the match. Tag or DM us on Facebook or Instagram (@dystoniamrf), or send a message via: dystonia-foundation.org/contact



Support for Support Leaders

In April DMRF hosted a Virtual Leadership Conference for support group leaders and online moderators. The program included presentations on topics to help support leaders in their roles and break out discussion groups. DMRF gratefully acknowledges Ipsen Biopharmaceuticals and Supernus Pharmaceuticals for support of this program.

Pet Palooza Raises Dystonia Awareness & Research Funds



In February, the first-ever Dystonia Pet Palooza brought animal lovers together to raise awareness while celebrating the special bond between people and pets.

Congratulation and many thanks to DMRF supporter **Terri Chapman**. Her dog **Sydney** was the top earning pet, raising over \$3,000!

These top dogs raised more than \$500:

- Bentley – Denise Gaskell
- Friday – Evelyn Amerio
- Molly - Emily McNaughton
- Pyewackett - Lynn Ostermann
- Snoopy – Virginia Bryan
- Violet – Dee Linde

The DMRF express deep gratitude to all the generous people and creatures who participated in this important and fun campaign.

How Do Botulinum Neurotoxin Injections Work?

Mechanism of Action is Key to Versatile Treatment

Botulinum neurotoxin (BNT) injections are a common dystonia treatment. The approval of Botox® (OnabotulinumtoxinA) by the Food & Drug Administration (FDA) for cervical dystonia in 1989 was a game-changer for patients and clinicians alike. Since that time, several BNT products have been approved by the FDA for cervical dystonia and blepharospasm. Physicians are allowed to use BNT ‘off label’ for additional dystonias.

Dystonia, spasticity, migraine, chronic pain, and overactive bladder are examples of the medical conditions now treated on or off label with specific BNT products. It is being studied for use in wound healing and depression. Its use for cosmetic purposes to reduce the appearance of wrinkles made ‘Botox®’ a household name.

How can a therapy be effective for so many different conditions? The way BNT works is key to its usefulness in specialties as diverse as neurology, urology, and dermatology. BNT is injected into muscle. It blocks signals from the nerves that make the muscle contract. When the signals are blocked, muscle contractions are reduced and the muscle relaxes. The injections are repeated every three to six months.

Mitchell Brin, MD, FAAN, FANA, FAHS, Senior Vice President of Research & Development and Chief Scientific Officer for Botox® & Neurotoxins at Allergan, an AbbVie Company, explained, “When you think about situations where a motor nerve is connected to muscle, such that dampening the effect of the motor nerve can possibly treat the disease manifestations, then you can begin to explore what other potential uses there are for the toxin. We’ve also identified that it can help with disorders of excessive secretion like hyperhidrosis [excessive sweating], and that was originally an observation that came out of the movement disorder community. As long as you can inject the toxin into the relevant target tissue, it may have an effect, and then you can titrate it with the goal of achieving the desired result while minimizing side effects.”

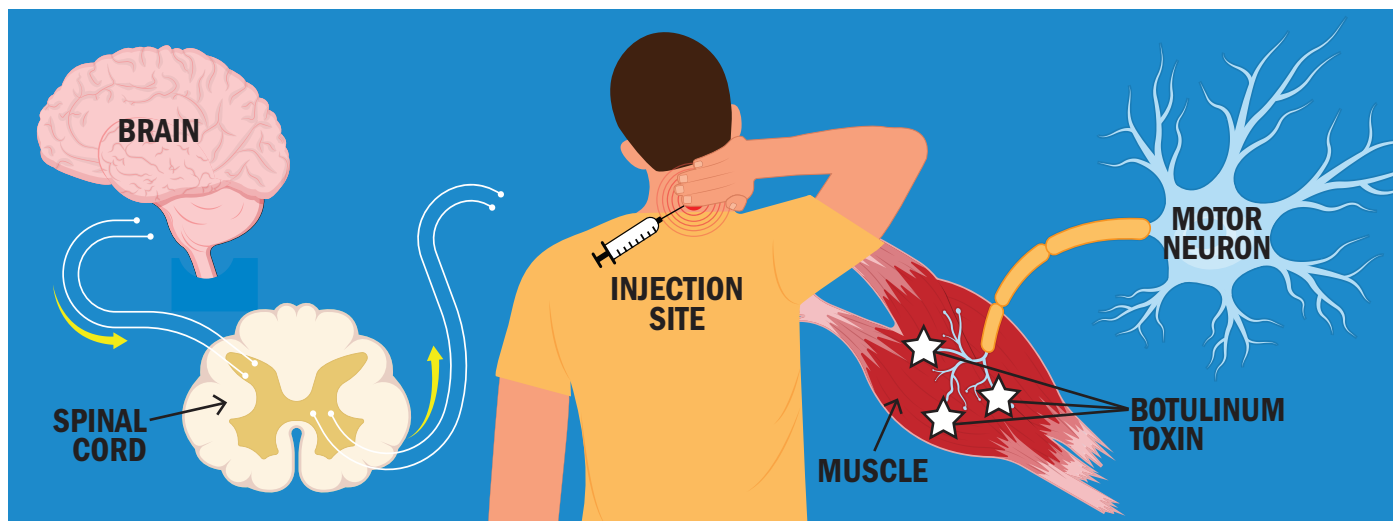
Every time a pharmaceutical company seeks approval of a new indication for an already-approved medication,

About Botulinum Neurotoxin Injections

- BNT is a biological product, not a chemical drug.
- The effects of the injections are temporary, which allows treatment to be adjusted to the unique needs of each patient.
- BNT products are uniquely FDA-approved for specific indications described in the packaging insert.
- Physicians may use BNT ‘off label’ for additional purposes they deem medically appropriate.
- BNT may be used to treat dystonia along with oral medications, physical therapy, and/or additional methods.

the FDA requires an extensive application often equal to the original approval application. Controlled clinical trials must demonstrate the drug is safe and beneficial. Dr. Brin said, “It’s really a community effort from the perspective that it’s the pharmaceutical company that is identifying indications to go through the regulatory pathway, and it is the company, learning directly from the doctors on the front lines, to identify the appropriate treatment plan to be used in human clinical research. Going through the regulatory pathway to get an approval that can be on label, then training physicians how to use it and what the science is behind it—that is in essence how you make it available for patients. And that’s the goal, to help patients.”

More information about BNT therapy can be found at: dystonia-foundation.org/facts-botulinum-neurotoxin



The brain communicates with muscles by sending signals along the spinal cord and nerves. In dystonia, these signals instruct the muscles to contract excessively, which results in involuntary movements and postures. BNT blocks the signals from nerves within the muscles from causing the muscle fibers to contract. The muscle contractions lessen, causing the muscle to relax.

“The injections have allowed me to get a heel strike and help me get a proper heel-toe movement as I walk forward. They also help keep my foot from turning in and rolling over. The injections have given me the ability to walk and do regular activities without support. I just have to pace myself because as I tire, it becomes more of a struggle to get the proper foot placement.”

DMRF Board Member Donna Driscoll is diagnosed with focal leg dystonia. She has been getting BNT injections off label in her calf and foot for more than a decade.

“When I got diagnosed I had a severe tremor with a mean head pull to the right. I thought life was over. I wanted to hide from the world. With botulinum toxin injections I no longer tremor, I’m able to work, play with my son, and function. Without the injections I wouldn’t have any of that.”

DMRF member Joshua Duran is diagnosed with cervical dystonia and has been treated with BNT for 10 years.

Botulinum Neurotoxin Products Available in US

Brand Name	Medical Name	Manufacturer	FDA Approval
Botox®	OnabotulinumtoxinA	Allergan, an AbbVie Company	1989
Dysport®	AbobotulinumtoxinA	Ipsen	2009
Myobloc®	RimabotulinumtoxinB	Supernus	2000
Xeomin®	IncobotulinumtoxinA	Merz	2010

Accelerating Advancements in Deep Brain Stimulation

New Technology & Decades of Clinical Experience Continue to Shape Innovative Therapy

Svetlana Miocinovic, MD, PhD is Assistant Professor in the Department of Neurology, Movement Disorders Section, at Emory University School of Medicine. Her research focus is on the electrophysiology of human motor circuits and the development of device-based therapies. Her clinical focus is using deep brain stimulation (DBS) to treat movement disorders.

As an expert in DBS for dystonia and other movement disorders, she recently shared her insights into advancements happening in DBS and the future of this ever-evolving therapy.

DD: How did you get interested in movement disorders and DBS?

SM: I was always interested in neuroscience, so neurology was an obvious choice. In addition to being a practicing physician, I wanted to do research to help unravel mysteries of the brain, so I entered a joint MD/PhD program. Working on engineering research projects during my PhD introduced me to deep brain stimulation. During neurology residency, I learned about the clinical aspects of movement disorders. They continued to capture my interest and I enjoyed interacting with patients dealing with these conditions, so I decided to become a movement disorders specialist with additional focus on DBS.

DD: How did Covid-19 affect the DBS program in your clinic and your approach to caring for patients?

SM: When the Covid pandemic forced us to shut down our clinic, I was very worried what would happen with our DBS patients and how we would be able to continue caring for them. I immediately reached out to neurologists and neurosurgeons at my institution and several other large DBS centers, and together we devised recommendations for DBS



Dr. Miocinovic is a past DMRF Clinical Fellow and co-mentored a recent DMRF Clinical Fellow.

device management during a pandemic which we published early on to help other clinicians struggling with the same issues. This process helped me deal with my own personal and professional stress brought on by the pandemic, but also made me realize that we have the knowledge and tools to provide necessary care even in difficult times.

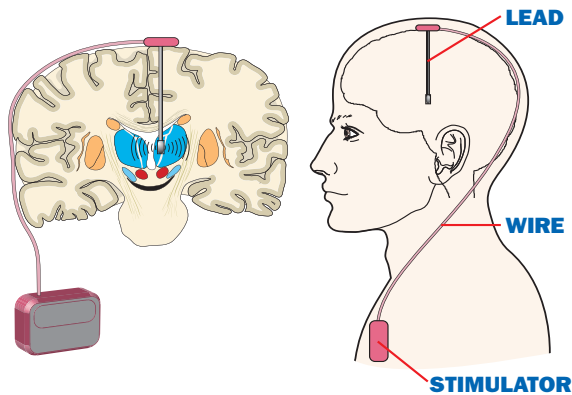
DD: How do you explain to your patients how we believe DBS reduces dystonia symptoms?

SM: In movement disorders including dystonia, the motor symptoms seem to be caused by increased synchronization between brain areas. Normally, brain

regions work independently to perform specific movements or process sensory information, but in dystonia they are excessively synchronized, or 'coupled'. For example, moving the hand can cause involuntary movement in the whole arm. DBS provides a steady pacing signal to the central motor brain regions, which reduces this abnormal coupling and allows independent function in the connected areas.

DD: What are some of the advancements happening in DBS?

SM: There have been several exciting new developments in DBS in recent years. We now have rechargeable batteries that last 15 years. This is especially important for people with dystonia who may require implants at a young age, and this avoids numerous battery changes. Another development is



What is Deep Brain Stimulation?

Deep brain stimulation (DBS) is a surgical treatment that uses an implanted medical device to treat dystonia and other neurological disorders. Once reserved for only severe cases of generalized dystonia, DBS is being used to treat a greater variety of dystonia patients than ever before. The use of DBS is evolving as research progresses. The movement disorders field now has more than two decades of experience and data regarding the long-term safety and efficacy of DBS.

For more information, including a recording of a recent DMRF webinar entitled “Deep Brain Stimulation from the Patient Perspective,” visit: dystonia-foundation.org/deep-brain-stimulation

segmented (or directional) electrodes which provide more flexibility to shape the electric field. Traditional electrodes are ring shaped so the electric field spreads equally in all directions, but with segmented electrodes we can steer stimulation toward the target areas and away from regions causing unwanted side effects. The latest commercially available development are ‘sensing’ stimulators that can record brain function in addition to providing stimulation. This will hopefully soon lead to new adaptive stimulators.

DD: What are you personally most excited about in terms of the future of DBS?

SM: I am excited about the development of adaptive DBS which are ‘smart’ stimulators that, in addition to providing stimulation, can record brain activity and self-adjust to provide optimal benefit. This may mean increasing stimulation

when symptoms are present and reducing stimulation when they are not as pronounced, for example during sleep. Research is ongoing to understand how brain activity relates to dystonic symptoms and which signals are going to be the most useful to serve as feedback to the DBS device. This approach should reduce time needed to find optimal stimulation settings, reduce side effects, and prolong battery life. I am also interested in personalizing DBS for people with dystonia. We can do this by understanding how different types of dystonia—based on both clinical symptoms and genetic features—respond to DBS and which brain targets and stimulation settings are the most effective for an individual, or if other non-DBS treatment options may be better.

DD: If a person with dystonia is discussing the possibility of DBS with their medical team, what is an important question for them to be sure to ask their neurologist and/or neurosurgeon?

SM: Different types of dystonia can respond differently to DBS so it is important to understand the expected outcome for their specific condition in terms of both the therapeutic benefit and potential side effects. There are also different brain targets to treat dystonia and different surgical approaches (e.g. having parts of the procedure done while awake or asleep) so it is important to understand the available options.

DD: What has the support of DMRF meant over the course of your career so far?

SM: DMRF support came at a critical point in my career, and I am so grateful for the support then and ongoing support now. When I completed my clinical training, I knew I wanted to get back into research and pursue a combined career as a physician-scientist, but it had been several years since I spent time in the lab. DMRF funding allowed me to spend two years as a postdoctoral research fellow during which time I learned about clinical DBS research, built expertise in management of dystonia, and secured funding to start my own laboratory.

New Deep Brain Stimulation Resource



The DMRF has created a private peer support group on Facebook for individuals who have undergone, are in the process, or are considering DBS for dystonia.

Dystonia & Deep Brain Stimulation

Moderators: Dee Linde & Andi Elliott

facebook.com/groups/dbs.dmrp

Creative Coping: Tips & Tricks for Daily Life

AT A GLANCE

- Living with dystonia often requires creative adaptations.
- Self-made strategies compensate for treatment limitations
- Many adaptations take advantage of ‘sensory tricks.’

Medical treatment for dystonia is available, but effectiveness varies. Few treatments, on their own, provide 100% relief. Living well with dystonia often requires adaptations invented by those experiencing the disorder firsthand.

An international team of clinicians recently published examples of the “self-concocted, curious, and creative” ways in which movement disorder patients manage symptoms. The clinicians noted how important these coping techniques are to improved quality of life. In many ways, these homegrown strategies compensate for less-than-ideal medical treatment.

Among the most resourceful tricks, a patient with severe speech impairment due to neurodegeneration with brain iron accumulation tattooed a keyboard on their forearm to aid communication. While such an approach may initially appear extreme, it is a brilliant self-made solution to a problem medicine could not heal—and without cumbersome equipment or expensive technology.

Most of the innovative patients highlighted in the paper were individuals with dystonia. An individual with spine arching found that wearing a shape-wear ‘corset’ made it easier to stand.



Individuals with movement disorders invent brilliant ways to cope with every day challenges.

A woman with cervical dystonia, a focal dystonia that affects neck muscles, demonstrated that wearing a loose scarf around the neck helped straighten her head. A woman with retrocollis, which tipped her head back, was able to look forward by wearing a backpack that provided light support to the back of the head.

DMRF support groups and online support forums are important spaces for individuals to share these coping adaptations.

Sharon Gibson found that false eyelashes help relieve blepharospasm, a focal dystonia that causes involuntary eye closure. Sharon’s daughter Karen Gibson said, “It’s not 100% effective but they help, and there seems to be a residual effect for a few hours after removing them.” Sharon is diagnosed with progressive supranuclear palsy,



which causes a range of neurological and movement symptoms.

DMRF Support Leader and author Tom Seaman, who is affected by cervical dystonia, used his massage chair to support his head while seated at a table doing a jigsaw puzzle. “My neck and back were really hurting from all the looking down, so I decided to be creative to finish off adding the last few pieces. And it worked!” he said. Tom also uses the massage chair to read.

Many of these adaptations take advantage of a well-known phenomenon in dystonia called ‘sensory tricks’ or ‘alleviating maneuvers.’ A sensory trick is a gesture or action that temporarily reduces dystonia symptoms, often in a way that would not intuitively seem to help. The effects can last from a few seconds to several minutes or longer. A classic example is that an individual

with cervical dystonia may temporarily reduce dystonia and correct head posture by placing a hand under the chin. A light touch is enough to relax the muscles. The hand is not forcibly trying to overpower the involuntary movements.

In some cases, individuals can elicit the same response by thinking about doing a sensory trick or imagining the sensory trick in their mind. Some individuals have tricks that involve more forcible stimulus such as pressing on a body part.

Sensory tricks vary a great deal, even among people with the same type of dystonia. Some individuals with dystonia do not experience beneficial sensory tricks.

How or why sensory tricks occur is not well understood. Research suggests that sensory tricks 'normalize' the dystonic brain by re-balancing how the brain coordinates the functions required for smooth, coordinated movements. Understanding the neurophysiology of sensory tricks could be critical to developing new treatment strategies.

Mulroy E, Ganos C, Latorre A, Terkelsen AJ, Balint B, Agarwal PA, Batla A, Bhatia KP. Self-concocted, curious and creative coping strategies in movement disorders. Parkinsonism Relat Disord. 2021 Feb; 83:140-143.

SENSORY TRICKS BY DYSTONIA TYPE

Here are noted examples of sensory tricks, not an exhaustive list.

Cervical Dystonia

- Touching specific parts of the face, cheek, temple, nose, behind the ear, back of the head, back of the neck
- Raising the arm and holding finger near the sensory trick spot without touching face
- Visual focus on a specific target, focusing on a stationary object while walking
- Looking in the mirror
- Resting the back of the head or neck
- Resting the back or shoulder
- Bending forward
- Wearing a collar or scarf
- Leaning elbows on armrest
- Yawning

Blepharospasm

- Tight goggles or glasses
- Lundie Loop attachments on glasses
- Touching or pulling on eyelids
- Tape on eyebrows
- Touching specific parts of forehead, nose, side of eyelids, chin
- Pushing back head
- Massaging cheek bones, eyelid, forehead
- Closing the jaw, chewing gum
- Covering the eyes
- Picking teeth
- Wearing a cap or turban

Blepharospasm + Oromandibular Dystonia (Meige Syndrome)

- Talking, singing/ humming
- Pulling on upper eyelid
- Pinching back of neck
- Yawning
- Belching
- Sucking in or blowing air
- Drinking cold beverage

Lower Cranial Dystonia/ Oromandibular Dystonia

- Toothpick in mouth
- Holding object clenched in teeth
- Dental splint
- Touching lip
- Touching lower face
- Touching tongue to top of mouth
- Biting lips
- Swallowing
- Tilting head forward
- Chewing gum
- Sucking, whistling, kissing
- Pen/cigarette/tongue depressor in mouth
- Biting food or plastic between back teeth, dental prosthetic
- Singing, talking
- Thinking about talking
- Playing instrument with larger mouthpieces
- 5 minute ice massage of facial muscles

Laryngeal Dystonia/ Spasmodic Dysphonia

- Smiling
- Grimacing
- Laughing
- Speaking over loud background noise

Focal Hand Dystonia/ Writer's Cramp

- 5 minute hand immersion in cold water
- Adjusting pen grip, writing with closed fist
- Using pens of different sizes
- Writing on chalk board
- Painting
- Touching specific part of 'normal' hand to the dystonic hand

Runner's Dystonia

- Holding hands above head
- Running in clockwise direction
- Mentally imagining running in clockwise direction

Truncal Dystonia/ Camptocormia

- Low-slung back pack
- Using walker with wheels
- Pressing back against wall

DYT1 Dystonia

- Piano playing

From Ramos VF, Karp BI, Hallett M. Tricks in dystonia: ordering the complexity. J Neurol Neurosurg Psychiatry. 2014 Sep; 85(9):987-93.

DYSTONIA



In May, DMRF hosted a research update webinar for members and donors. The program featured a live question and answer session with Scientific Director Joel S. Perlmutter, MD of Washington University in St Louis and fellow dystonia experts Aasef Shaikh, MD, PhD of Case Western University and Ellen Hess, PhD of Emory University School of Medicine.

A recording of the webinar, entitled “Dystonia Research Extra Access,” is available at: dystonia-foundation.org/research-webinar-2021

Due to the volume of questions received, the panel was not able to respond to every submission during the program. Below are responses to questions from viewers that were not answered during the webinar.

Q: Is there a biomarker for dystonia?

A: A biomarker is a specific, objective characteristic of a disease or medical condition that can be measured or observed to make a diagnosis. Body temperature and blood pressure are examples of biomarkers. Antibodies in blood are biomarkers. There is no biomarker for dystonia at this time. Dystonia is a clinical diagnosis, meaning diagnosis depends on a physician’s ability to observe the symptoms and obtain a thorough patient history. Medical tests may be ordered to rule out other conditions or disorders. There are research efforts underway to detect and measure neurological biomarkers in dystonia.

Q: Is there any evidence of vaccines triggering a dystonia gene?

A: There is no evidence to suggest vaccinations cause dystonia. Movement disorder experts have examined this issue closely. As with any medical procedure, the DMRF encourages individuals to discuss the benefits and risks of vaccinations with their doctors.

Q: Serotonergic drugs make me more spastic. How do physicians treat depression in a case like this?

A: Selective serotonin-reuptake inhibitors (SSRIs) are a category of antidepressant drugs. Use of SSRIs has been associated with the development of movement disorders, either as a result of the drug or worsening of an underlying condition. Dopamine antagonist drugs (neuroleptics) have also been associated with causing or worsening movement disorders. An alternative class of antidepressants might be used, such as serotonin and norepinephrine reuptake inhibitors (SNRI), perhaps in combination with additional treatment approaches. These may include lifestyle adjustments, self-help activities, cognitive behavioral therapy, other types of counseling, and/or a range of intensive psychological and psychiatric therapies. Untreated depression can have serious health consequences, so it is essential to talk to your doctor or mental health professional when experiencing symptoms of depression or if there is a history of depression.

Q: How often does dystonia that begins in one part of the body spread to other areas of the body?

A: Dystonia symptoms typically begin in one part of the body and may spread to other body areas. This is seen most dramatically in childhood onset dystonias, which may ultimately affect many parts of the body and particularly limbs. Symptom spread is a possibility in adults, but less so. In adults, research has shown that where the symptoms begin strongly predicts both the risk of spread and the body areas to which symptoms spread. For example, patients with blepharospasm experience spread more frequently than those with cervical, hand, or laryngeal dystonia/spasmodic dysphonia. A more detailed examination of what is known about dystonia progression can be found at: dystonia-foundation.org/natural-history-symptom-spread

Spasmodic Dysphonia

Spasmodic dysphonia (SD), also known as laryngeal dystonia, is a focal, task-specific dystonia. SD is a neurological disorder featuring involuntary contractions of the vocal cord muscles.

The involuntary muscle contractions typically occur during speech and affect voice quality. SD does not usually interfere with crying, laughter, shouting, singing, or whispering.

There are two major types of SD: **Adductor** and **Abductor**.

Adductor SD accounts for 80% of cases. This type results in muscles spasms that close the vocal cord muscles too tightly, cutting off the voice.

Abductor SD is less common. This type results in the vocal cord muscles not closing properly, causing a breathy voice.

Some individuals experience both types of SD.

Approximately 30% of people with SD also have voice tremor, which affects the pitch and loudness of the voice.

SD typically develops gradually during middle age.

Most cases of SD are sporadic, without any family history of SD or other types of dystonia.

About 20% of individuals with SD have symptoms of other focal dystonias, for example focal hand dystonia or cervical dystonia, which affects the neck muscles.

SD is sometimes seen in individuals with generalized dystonia, which affects muscles throughout the body and limbs.

A number of medical specialists may diagnose and treat SD including speech-language pathologists, laryngologists, otolaryngologists (ear-nose-throat specialists), and movement disorder neurologists.

The primary treatment for SD is regular botulinum neurotoxin injections, often with voice therapy.

Additional treatment options may include surgical interventions such as selective laryngeal adductor denervation-reinnervation (SLAD-R) for select patients.

Treatments under investigation for SD include oral medications, implantable devices to stimulate vocal cord muscles, and deep brain stimulation.

Individuals with SD experience high rates of social anxiety disorder. Treatment for social anxiety disorder may include cognitive behavioral therapy, oral medications, or both.

Additional information and resources are available at: dystonia-foundation.org/spasmodic-dysphonia



Common Symptoms of Spasmodic Dysphonia

- Patterned breaks or 'gaps' in voice
- A strangled, choking quality to the voice
- Voice sounds breathy, whispery
- Tremoring voice
- Breathless voice spasms
- Inconsistent pitch and volume to voice
- Speaking requires physical effort
- Symptoms do not occur during emotional vocal expressions such as laughter, crying, or yelling

Dystonia Dialogue

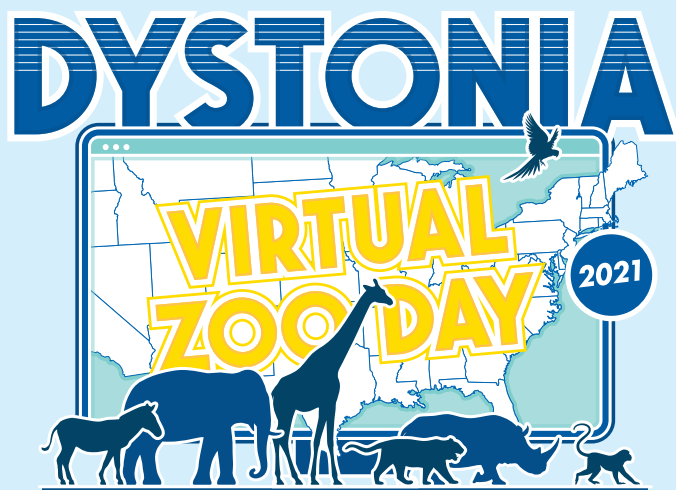
Dystonia Medical Research Foundation

One East Wacker Drive • Suite 1730

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WEB <https://dystonia-foundation.org>



SATURDAY, SEPTEMBER 25
dystonia-foundation.org/letszoothis

On a single day, DMRF supporters across the country will take action to boost dystonia awareness and raise funds for medical research toward a cure.

Anyone and everyone can participate in this fun, free event. All team donations are eligible to be matched. Your team may be flock, a pride, or a herd. Even a lone wolf can be a team.

See inside for details. #LetsZOOthis!

