



**Tourette  
Association**  
of America

Awareness. Research. Support.

Research  
and  
Medical  
Programs



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Research  
Progress  
Report  

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2015-2016

# 1<sup>ST</sup> WORLD CONGRESS ON TOURETTE SYNDROME & TIC DISORDERS

JUNE 24–26, 2015  
LONDON, UK

The 1st World Congress on Tourette Syndrome & Tic Disorders was held in London, UK on June 24 through June 26, 2015. Sponsored by the Tourette Association of America in collaboration with The European Society for the Study of Tourette Syndrome (ESSTS) and Tourettes Action UK, the overarching theme of the Congress was “New Frontiers in Research, Treatment, and Global Collaboration.”

More than 430 research scientists, physicians, neurosurgeons, psychologists, social workers and other experts from 38 countries and six continents gathered for the international meeting to present and discuss research in all areas, including drug development, genetics, comorbid conditions, surgical therapies and behavioral treatments for children and adults living with Tourette Syndrome and Tic Disorders. This unprecedented global assembly marked the first time a collective forum of such size and significance was ever convened to explore means of improving the lives of people affected by these neurodevelopmental conditions.

and 161 posters with important discoveries and developments that have the potential to change our understanding of these conditions.

“The 1st World Congress on Tourette Syndrome and Tic Disorders saw the largest gathering and networking of clinicians, scientists and other experts in the history of these conditions,” said Kevin McNaught, Ph.D., Executive Vice President, Research and Medical Programs, Tourette Association of America. “Notably, discoveries and development in most—if not all—areas of study were presented and discussed among researchers from the 38 countries represented at the Congress. We hope that this global collaboration and momentum will grow in the years ahead as we seek to increase understanding and develop effective treatments for Tourette and related conditions.”

Research topics ranged from investigations of the therapeutic use of cannabis to control Tourette and Tic Disorder symptoms, to analysis and new data exploring a variety of deep brain stimulation therapies, to new developments in Tourette Syndrome genetics and a host of other topics.

“The Congress allowed for a meaningful and dynamic discourse on novel treatments and therapies that will pave the way for ideas and strategies for years to come,” said Marc Scullin, M.A., Tourette Association of America, one of the Congress organizers.

Looking to capitalize on the spirit of collaboration that the World Congress has fostered among Tourette professionals worldwide, the Tourette Association of America has already started planning The 2nd World Congress on Tourette Syndrome and Tic Disorders. Stay tuned for more details!

To view photos and a video montage from the 1st World Congress on Tourette Syndrome & Tic Disorders, please visit [www.touretteworldcongress.org](http://www.touretteworldcongress.org).



Leading experts in the field made history as they laid the foundation for a new global workforce focused on Tourette and Tic Disorders research, presenting 185 scientific abstracts

## Tourette Association of America and the American Academy of Neurology Offer New Clinical Research Training Fellowship in 2016



The Tourette Association of America has partnered with the American Academy of Neurology and the American Brain Foundation to sponsor a two-year fellowship for clinical research and training in Tourette Syndrome. This is the Tourette Association’s first collaboration with the AAN, and the Clinical Research Training Fellowship in Tourette Syndrome is also the AAN’s first fellowship specifically focused on Tourette Syndrome and related disorders. The partnering organizations will commit funding for two years, including tuition to support formal education in clinical research methodology at the applicant’s institution. The recipient will be announced in April at the 2016 AAN Annual Meeting in Vancouver, BC, Canada.

## Tourette Association's Centers of Excellence Program Gains Momentum

In the first full year since designations were announced, the Tourette Association's Centers of Excellence (CofE) have been busy, with several sites launching their own websites and others hosting successful trainings and community events. "We have had a tremendous response to the CofE designation," said Heather Simpson, MOT, OTR/L, coordinator for the South East Regional Consortium, which is comprised of 5 institutions throughout the SE United States (pictured). Heather added, "The most exciting opportunity that the CofE designation has provided us is the ability to engage in cross center studies." The SE Consortium has started a Tourette database initiative that includes all 5 institutions working in a coordinated research effort. In addition to facilitating research efforts, the CofE designation has also helped sites provide



elite clinical care. "The CofE designation has allowed our site to create a specialized multidisciplinary team focused on providing comprehensive and integrated care to individuals and families with TS," said Dr. Michael Himle, Director of the CofE at The University of Utah. As a direct result of these activities, Dr. Himle's CBIT program has more than doubled the number of families entering his program over the past 6 months. Dr. Himle continued, "The CofE designation has helped us shine a light on the phenomenal Tourette clinical care and research available in Utah." In year two of the program, the Center of Excellence sites will continue to set the pace for Tourette care and practice by providing the highest levels of clinical care, research, training, and community outreach.



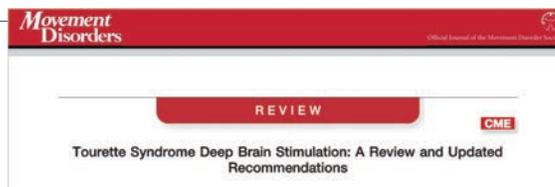
## CBIT Continues to Reach a Wider Audience Through Translation & Technology

In the past year, Dr. Douglas Wood's team has published several papers using the database created as part of the Tourette Association and NIH funded CBIT project. These papers have yielded interesting findings in the areas of premonitory urges in adults<sup>i</sup>, premonitory urges and anxiety<sup>ii</sup>, caregiver strain<sup>iii</sup>, and environmental reactions in relation to tics<sup>iv</sup>. The information in the database has also been used to demonstrate that behavior therapy does not increase tics that are not targeted for treatment<sup>v</sup>. The CBIT manual has now been officially translated into two languages (Korean and Norwegian), and a recently published paper demonstrated the effectiveness of CBIT in Japan<sup>vi</sup>. Drs. Woods and Himle recently partnered with Dr. Suzanne Mouton-Odum from PsycTech to develop an online self-help version of CBIT. The website, [www.tichelper.com](http://www.tichelper.com) has been developed and is now being tested. In addition, the Tourette Association continues to make CBIT more widely available through our conducting of the Behavior Therapy Training Institute Program and ongoing 12-year partnership with the CDC.

<sup>i</sup> Reese et al. (2014). *Behavior Therapy*, 45: 177-86, <sup>ii</sup> Rozenman et al. (2015). *Children's Health Care*, 44: 235-48  
<sup>iii</sup> Ramanujam et al. (2015). *Children's Health Care*, 44: 249-63, <sup>iv</sup> Capriotti et al. (2015). *Children's Health Care*, 44: 205-20,  
<sup>v</sup> McGuire et al (2015). *Behavior Research and Therapy*, 70: 56-63, <sup>vi</sup> Nonaka et al. (2105). *Children's Health Care*, 44: 293-306

## International Deep Brain Stimulation Registry Publishes New Guidelines and Plans a 1 Year Outcome Paper

The Tourette Association of America International Deep Brain Stimulation (DBS) Registry recently published a paper with updated guidelines and recommendations for DBS as a treatment for Tourette<sup>i</sup>. The registry currently has 157 registered patients and at the World Congress in London, the DBS investigators began planning an image registration initiative to identify DBS lead locations within the cohort. The groups are hoping to compile a significant set of lead localization images for the implanted patients, which will help determine (along with already-registered active electrodes and parameters) whether or not they are activating consistent volumes of tissue across



targets and to hopefully correlate the outcomes. During the World Congress, the investigators also decided to examine the economic impact of the DBS intervention for Tourette Syndrome. Each DBS registry principal investigator who attended the World Congress will pursue the input of a health economist at their respective institutions and will work toward a consensus on what information would be meaningful to collect in the database. The group plans to begin work immediately on a paper regarding the 1-year outcomes across multiple targets for all Tourette Syndrome patients registered in the database.

<sup>i</sup> Schrock et al. (2015). *Movement Disorders*, 30: 448-71

# Tourette Association Funds 8 New Grants to Study Tourette Syndrome

## Striatal Circuit Mechanisms for Tourette Syndrome



**Kristen Ade, Ph.D.**

*Duke University Medical Center, Durham, NC*

**\$40,000**

Approximately one half of patients with TS are also diagnosed with obsessive compulsive disorder (OCD). The high degree of overlap between these two psychiatric disorders suggests that they may arise from similar dysfunction in the brain, and a number of studies indicate that dysfunction within a region called the striatum may underlie both TS and OCD. Using a novel method to evaluate neural activity, I previously found abnormalities in striatal activity in a mouse model of OCD. In this study, I will investigate whether OCD-like behaviors and similar striatal circuit abnormalities are observed in a mouse model of TS interactions of the Histamine and Dopamine systems in Tourette Syndrome.

## Behavioral and Physiological Phenotypes Induced by an Early Loss of Striatal Cholinergic Interneurons: Proving Face Validity for a Novel Mouse Model of Tourette Syndrome



**Juan E. Belforte, Ph.D.**

*University of Buenos Aires School of Medicine,*

*Buenos Aires, Argentina*

**\$120,000**

The basal ganglia are a group of subcortical nuclei that control several aspects of voluntary movement and the striatum is their primary region receiving information to be processed. The activity of neurons in the striatum is controlled by cells called interneurons. Postmortem studies from Tourette Syndrome patients showed that one particular kind, the striatal cholinergic interneuron, is reduced in these patients. However, it is still unknown if the loss of cholinergic cells is responsible for Tourette's symptoms. We will mimic this cell loss in rodents and explore whether the emerging behavioral symptoms are compatible with the ones of Tourette Syndrome.

## Network Architecture of the Brain in Tourette Syndrome and its Phenotypic Subgroups



**Deanna J. Greene, Ph.D.**

*Washington University School of Medicine, Saint Louis, MO*

**\$150,000**

Tourette Syndrome (TS) is a complex, heterogeneous neuropsychiatric disorder for which the underlying brain mechanisms are not well understood. We aim to take a comprehensive approach, investigating the structure and function of the whole brain, to better this understanding. We will use sophisticated classification methods to identify brain network function and structure, measured with MRI, that distinguishes children with and without TS. We will also use graph theory methods to identify subgroups of TS based on whole brain MRI data. The results from this project have the potential to pinpoint new brain markers of TS and help understand its heterogeneity.

## Expedited Therapeutic Outcomes with Habit Reversal Training for Youth with Chronic Tic Disorders



**Joseph F. McGuire, Ph.D.**

*University of California Los Angeles, Los Angeles, CA*

**\$40,000**

Behavioral interventions, such as the Comprehensive Behavioral Intervention for Tics (CBIT) reduce the severity of tics. While many people who receive CBIT experience some benefit, only about half experience a clinically meaningful response. Recent research has identified several medications (called cognitive enhancers) that may increase the learning that occurs during treatments like CBIT to produce greater and/or accelerated improvement in symptoms. This study seeks to examine if one of these medications (called d-cycloserine, DCS) can accelerate improvements for children receiving behavior therapy.

## Determining the Long-Term Effects of Comprehensive Behavioral Intervention for Tics: A Nine Year Follow-up of Original Child CBIT Study Participants



**John Piacentini, Ph.D.**

*University of California Los Angeles, Los Angeles, CA*

**\$150,000**

The Tourette Association Behavioral Sciences Consortium showed that the Comprehensive Behavioral Intervention for Tics (CBIT) is a safe and effective treatment for tics. CBIT is now a front-line and widely-used treatment for tics. Although research shows that CBIT continues to help 6 months after successful treatment and may also help to reduce anxiety, social difficulties, and stress on families, questions remain regarding the long-term benefits of this treatment. This study will contact the original child CBIT study participants, most of whom are now adults, to assess their current tics, related problems and overall functioning.

## Somatic Attention and Inhibiting Response to Urges in Tourette Syndrome



**Cheryl A. Richards, Ph.D.**

*Washington University School of Medicine, Saint Louis, MO*

**\$150,000**

The underlying causes of tics are still unknown. We will examine to what extent somatic attention, such as focusing on physical sensations, and motor inhibition failure contribute to tics. We will study two groups of people: people with TS and people who do not have TS. We expect that people with TS will exhibit more brain activity when focusing on spontaneous physical sensations compared to the other subjects. We also expect that activity in certain brain regions will be associated with successful tic suppression by people with TS and successful eye blink suppression by people in both groups.

## A Double-Blind, Randomized, Placebo-Controlled Crossover Pilot Trial of Medical Cannabis in Adults with Tourette Syndrome



**Paul Sandor, M.D.**

*Toronto Western Hospital, Toronto, Canada*

**\$75,000**

For many individuals with Tourette Syndrome (TS), available medications do not help with their symptoms, or cause significant side effects. There is some evidence that inhaled cannabis can be helpful and well-tolerated in adults with TS, but this has not been well studied. Our goal is to carry out a study of vaporized cannabis for tics in adults with TS. We will compare three different types of medical cannabis in terms of how much they help tics, and how much they cause side effects.

## Prevalence of TD and Tics among a Community-Recruited Sample of Adults from Haiti



**Catherine Striley, Ph.D.**

*University of Florida College of Medicine, Gainesville, FL*

**\$150,000**

Community Health Workers will go door-to-door in Carrefour, Haiti to look for symptoms of Tourette Syndrome (TS) and chronic tic disorder (CTD) in adults, aged 18 to 65, using a study-specific video screener. Participants will be videotaped while taking the computerized assessment and these videos will be sent to specialists in the US to confirm current symptoms. Results will help determine the true prevalence in this population and whether or not current estimates of prevalence are the result of biased diagnosis and reduced access to treatment, or if they reflect a real difference in prevalence in populations of African descent.

## Tourette Association Research Grant and Fellowship Program

The Tourette Association accepts research grant proposals from researchers in basic and clinical studies on all aspects of Tourette Syndrome.

For more information visit [www.tourette.org/Research/research\\_resgrantawards.html](http://www.tourette.org/Research/research_resgrantawards.html)

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Your kind and generous gifts in support of our cutting-edge research programs and dedicated world-class scientists are sincerely appreciated. They help us meet our mission of making life better for all people affected by Tourette and Tic Disorders through research. To make a donation, please go to <http://tourette.org/researchgift.html>

# Tourette Association Grant Updates

## Izhar Bar-Gad, Ph.D.

Bar-Ilan University, Ramat-Gan, Israel

*Interaction of the Dopaminergic and GABAergic Systems in the Formation of Tics*

This project focused on the modulation of tic expression following changes of neurotransmitter input to an area associated with tic formation. We discovered that phasic (transient) changes in the input led to the formation of individual tics time-locked to the event. The input to the damaged area determined only the timing of the tic and not the shape of its expression. These findings support a clear dissociation between the neuronal mechanism determining the timing of the tic ('when') and the body part expressing the tic ('where'). The results from this study have been presented as lectures at the Gordon Research Council Basil Ganglia Conference in Ventura, California in February 2014 and the European Society for the Study of Tourette Syndrome conference in Paris, France in April 2014.

## Marco Bortolato, M.D., Ph.D.

University of Kansas, Lawrence, KS

*Role of 5-alpha Reductase 2 and Androgens in Tourette Syndrome*

The goal of these studies is to verify whether the severity of TS symptoms can be influenced by the interaction of the gene SRD5A2 (which encodes for the enzyme 5-alpha reductase 2) and early environmental stress. Data were obtained from 374 TS patients, and are being currently analyzed. In separate studies, we are testing whether the therapeutic effects of finasteride (a 5-alpha reductase inhibitor) in male TS patients may reflect changes in plasma steroid concentrations. Notably, recent data from animal models suggest that the mechanisms of finasteride are based on the reduction of allopregnanolone, a key regulator of stress response; thus, we are currently testing whether the severity of TS symptoms correlates with allopregnanolone levels in plasma.

## Luciana Frick, Ph.D.

Yale University, New Haven, CT

*Histamine Regulation of Brain-immune Interactions in an Animal Model of Tourette Syndrome*

We investigated immune system abnormalities in Tourette Syndrome, using an animal model. Specifically, we investigated neuroimmune cells in the brain, called microglia, in mice that recapitulate a rare genetic cause of Tourette Syndrome. These mice are deficient in the neurotransmitter and immune signaling molecule histamine; this deficiency leads microglia to be hyper-reactive to inflammatory challenges. This suggests that individuals with a genetic susceptibility may respond abnormally to infections, which may contribute to the development of tics. Histamine modulating drugs modulate microglial function and may be able to counteract this process.

## Zixiu Xiang, Ph.D.

Vanderbilt University, Nashville, TN

*M4 PAMs as Potential Therapeutic Agents in Treatment of Tourette Syndrome*

Tourette Syndrome (TS) involves dysfunction of multiple neurotransmitter systems in the brain, including excessive striatal dopamine release, decreased striatal cholinergic function and increased glutamatergic transmission from the cortex and thalamus to the striatum. Using electrophysiological and electrochemical approaches in conjunction with optogenetic tools, transgenic mice and a series of novel compounds that are highly selective for subtype 4 muscarinic acetylcholine receptors (M4 mAChRs), we found that activation of M4 mAChRs reduces dopamine release and glutamatergic transmission in the striatum. These findings suggest that the M4 mAChR could be a novel therapeutic target for the treatment of TS.

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