

# PROGRESS IN SCIENTIFIC AND MEDICAL RESEARCH

45 YEARS OF DISCOVERY  
2017 PROGRESS REPORT



Tourette Association of America

Awareness. Research. Support.

[tourette.org](http://tourette.org)

## 45 YEARS OF DEDICATED SERVICE

The Tourette Association of America was founded in 1972 with the aim of improving the lives of all people affected by Tourette Syndrome (TS) and Tic Disorders. The TAA invests in research which may lead to tomorrow's breakthroughs in diagnosis and treatment. Our research programs are central to the mission of improving the lives of those impacted by Tourette and Tic Disorders.

## SUCCESSES: TREATMENTS, CARE, RESEARCH

To date, the TAA has awarded over **\$21 million** to nearly 450 projects across **16 countries**. Every \$1 of TAA grant funding has helped investigators obtain approximately \$10 in grant funding from the National Institutes of Health (NIH), leveraging TAA's initial seed investments toward larger research impact.

Together we:

- Facilitated the first FDA approval of a drug for Tourette in over 30 years (Abilify) [aripiprazole].
- Discovered a new class of drug, ecopipam, effectively reduces tics, with little adverse effects in children and adults.
- Developed and clinically demonstrated that Comprehensive Behavioral Intervention for Tics (CBIT), a medication-free behavioral therapy, is as effective as drugs in some individuals.
- Showed Deep Brain Stimulation (DBS) can effectively treat severe Tourette Syndrome and developed guidelines for its clinical use in scientific and medical journals.
- Helped to identify genes and genetic variations (eg. CNTNAP2, SLITRK, HDC, NRXN1 and CNTN6) that cause rare forms of Tourette Syndrome, increase the risk of developing the disorder, and link Tourette Syndrome with other conditions like Obsessive Compulsive Disorder.
- Established a wide range of research resources that facilitate global collaboration and accelerate research including Brain Bank, Gene Sample Collections, International Consortium on Genetics, Neuroimaging Consortium, International Deep Brain Stimulation Registry and Behavioral Sciences Consortium.
- Funded and supported ongoing development of novel and promising treatment approaches, such as medical cannabis, dental orthotic devices and home-based behavior therapies, some of which already have obtained US patent protection and Federal business grants to support commercialization and development.

## PROGRESS IN AWARENESS, SUPPORT AND RESEARCH

For over a decade, the TAA has partnered with the CDC (Centers for Disease Control and Prevention) to produce educational materials and facilitate programming to educators, schools, patients and medical professionals. Our program with the CDC has delivered over **1,000** free educational opportunities (in person and online) to nearly **350,000** care providers, school personnel, families, individuals and members of the general public.

## RESEARCH HIGHLIGHTS

**TAA researchers discover new genes for the disorder, providing clues to underlying brain mechanisms.**

In breaking research published this spring, researchers from two major genetics consortia identified new gene abnormalities linked to Tourette Syndrome. In one study, led by Drs. Jeremiah Scharf at Massachusetts General Hospital for Children, Giovanni Coppola at the University of California Los Angeles, and Carol Mathews at the University of Florida, deletions of a gene called NRXN1

and duplications of a different gene named CNTN6 were shown to substantially increase the risk of developing Tourette in some individuals. The Tourette Association of America International Consortium for Genetics (TAAICG) and its collaborators studied genetic material from over 2,400 individuals with Tourette Syndrome and 4,100 without to determine that individuals with Tourette were up to 20 times more likely to have abnormalities in these 2 genes.

In a second study, led by Doctors Matthew State at the University of California San Francisco and Jay Tischfield of Rutgers University, 325 Tourette disorder parent-child groups from the Tourette International Collaborative Genetics cohort and a replication sample of 186 parent-child groups from the TAAICG identified four additional possible risk genes: WWCT, CELSR3, NIPBL, and FN1. **The new genes identified from both of these studies are thought to play unique roles in brain development and brain communication processes, opening up countless new avenues for experimental research targeted toward new treatments. Both of these studies were published in the prestigious scientific journal Neuron.**

### **Brain Structure Changes Identified in Children with Tourette Syndrome**

In a collaborative multicenter study published in the journal Molecular Psychiatry this summer, Drs. Bradley Schlaggar and Kevin Black from Washington University School of Medicine used structural magnetic resonance imaging (MRI) to compare 103 children and adolescents with Tourette Syndrome to a well-matched group of 103 children without tics. Kids with Tourette Syndrome demonstrated lower white matter volume in the orbital and medial prefrontal cortex brain regions, and increased grey matter volume in other specific areas of the brain, namely the posterior thalamus, hypothalamus and midbrain. These brain regions are involved in various processes, including awareness of internal body sensations, which is important given the occurrence of premonitory sensations that precede tics in many patients.

*“Our study is the tip of the iceberg in understanding the complex biological mechanisms underlying this disorder. With recent advancements in genetic research, we are at the cusp of identifying many genes involved in Tourette Syndrome”*

Jeremiah Scharf, M.D., Ph.D., Assistant Professor of neurology and psychiatry at Harvard Medical School and Massachusetts General Hospital, Boston, and co-corresponding author of the study.

### **Michael Ullman, PhD, Georgetown University, Washington DC**



Recent evidence suggests that children with TS may show enhanced procedural memory performance. Procedural memory, which underlies numerous motor and cognitive skills, such as driving and grammar, is rooted in certain brain circuits affected in TS. In this project, Dr. Ullman and team will comprehensively examine procedural memory, the brain, and clinical correlates in children with Tourette Syndrome. Understanding the mechanisms underlying this enhanced memory could result in the development of novel therapies targeting these pathways.

### **Hannah Reese, PhD, Bowdoin College, Brunswick, ME**



Psychosocial treatments for Tic Disorders have substantially improved in recent years. However, a significant number of individuals either do not respond to the current treatments, find them unacceptable, or cannot access them. Initial pilot data suggest that a mindfulness-based intervention may be beneficial for adults with tic disorders. In the present study, Dr. Reese and team aim to further develop this mindfulness-based intervention, adapt it to be delivered online to enhance accessibility, and conduct a single-blind randomized controlled trial comparing it to online group psychoeducation, relaxation, and supportive therapy.

### **Joseph McGuire, PhD, University of California Los Angeles, Los Angeles, CA**

*\* Funded in partnership with the American Brain Foundation and the American Academy of Neurology*



While behavior therapy significantly reduces tic severity, neurocognitive functioning (e.g., difficulty paying attention, inhibiting responses, remembering instructions, etc.) may impact the magnitude of benefit obtained from behavior therapy. This project will identify the neurocognitive profile of youth who do and do not respond to behavior therapy and will explore changes in brain structure following behavior therapy. This information will be used to revise current treatments and identify augmentative strategies to help patients with Tourette Syndrome obtain further benefit from behavior therapy.

### **Flint Espil, PhD, Stanford University, Stanford, CA**

*\* Funded in partnership with the American Brain Foundation and the American Academy of Neurology*



Persistent Tic Disorders, including Tourette's Disorder, may occur because of problems in an area of the brain called the prefrontal cortex. A recent study found that some areas of the prefrontal cortex were not as active in those with tics when compared to people without tics, and lower activity predicted poor response to treatment. The goal of this study is to examine whether the same areas of the prefrontal cortex are underactive in youth (ages 10-17) with Persistent Tic Disorders, and whether this also predicts whether or not they will respond to therapy for their tics.

## Medical Cannabis as a treatment for TS and other neurological conditions.

There is increasing interest in medical cannabis (marijuana) as a potential treatment for tics and other symptoms in Tourette Syndrome. Over the past 6 years, the TAA has funded 5 grants to scientists from Israel, Canada and the US to investigate the potential of medical cannabis and novel drug candidates targeting medical cannabis pathways. As a result of our funding, research examining the therapeutic potential of targeting the endocannabinoid system has demonstrated positive laboratory results and achieved US patent protection. Currently, the TAA is working to facilitate careful and rigorous laboratory and clinical exploration in this area and tackling unique challenges such as variability in manufacturing and regulatory issues.

## Deep Brain Stimulation – A promising neurosurgical treatment.

Deep Brain Stimulation or “DBS” is a procedure that utilizes an implantable electrode to alter the activity of brain circuitry. The procedure is FDA approved for Parkinson’s disease, essential tremor, dystonia and OCD, and currently utilized for patients who have not responded to standard medical or behavioral therapy. To investigate the potential for DBS to benefit Tourette Syndrome patients, the TAA sponsored the development of a registry, led by Dr. Michael Okun from the University of Florida and co-sponsored by Medtronic.

## NEWLY FUNDED GRANTS TO STUDY TOURETTE SYNDROME

The TAA’s newest grant awardees are tackling ways to improve treatment for Tourette Syndrome by testing brain surgical methods, mindfulness strategies, and methods to improve the success of behavioral interventions and enhance our structural understanding of brain changes that occur in the condition.

### Kevin McCairn, PhD, Kyoto University, Japan

(In collaboration with Mayo Clinic Department of Neurosurgery)



One of the least understood symptoms of Tourette Syndrome is the emergence of involuntary vocalizations such as throat clearing, coughing, grunting, or barking in more mild cases or obscene language or other contextually inappropriate phrases in more complex cases. Previous work supported by the TAA has identified a network in the brain, a region associated with emotional processing called the limbic system, which when made over excited, induces vocal tics. In this upcoming study, Dr. McCairn and team will investigate how brain chemicals are changed during the change from a normal state to one where vocal tics express themselves, and how intervention with brain surgical methods, namely Deep Brain Stimulation (DBS), may help alleviate these symptoms. Planning for this study is currently underway.

## Centers of Excellence Locations

The Tourette Association of America's Center of Excellence (CofE) program aims to improve the quality of life of people with Tourette Syndrome and other Tic Disorders by promoting the highest level of care, research, education & training, and advocacy & awareness for these conditions.

Baylor College of Medicine  
Houston, TX  
(713) 798-2273

Children's Mercy Hospital  
Kansas City, MO  
(816) 346-1384

Johns Hopkins Hospital  
Baltimore, MD  
(410) 955-4259

Massachusetts General  
Hospital  
Boston, MA  
(617) 726-5532

University of California,  
Los Angeles  
Los Angeles, CA  
(310) 825-0122

University of Utah  
Salt Lake City, UT  
(801) 585-7575

Yale Child Study Center  
New Haven, CT  
(203) 785-5880

New York State  
Consortium:  
Weill Cornell Medical College  
New York, NY  
(212) 821-0789

University of Rochester  
Medical Center  
Rochester, NY  
(585) 275-2808

Icahn School of Medicine  
at Mount Sinai  
New York, NY  
(212) 659-1660

South East Regional  
Consortium:

Emory University School  
of Medicine  
Atlanta, GA  
(404) 778-3444

University of Alabama  
at Birmingham  
Birmingham, AL  
(205) 638-6820

University of Florida  
Gainesville, FL  
(352) 294-5400

Palmetto Health -  
USC Medical Group  
Columbia, SC  
(803) 434-7961

University of South Florida  
St. Petersburg, FL  
(727) 767-8230

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