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Progress in research on Tourette syndrome

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ABSTRACT

Tourette syndrome (TS) is a heritable neuropsychiatric disorder commonly complicated by obsessions and compulsions, but defined by frequent unwanted movements (motor tics) and vocalizations (phonic tics) that develop in childhood or adolescence. In recent years, research on TS has progressed rapidly on several fronts. Inspired by the Fifth International Scientific Symposium on Tourette Syndrome, the articles in this special issue review advances in the phenomenology, epidemiology, genetics, pathophysiology, and treatment of TS.

1. Introduction

Tourette syndrome (TS) is defined by chronic, but variable, unwanted movements (motor tics) and sounds (phonic tics) that develop spontaneously in childhood or adolescence. However, this relatively simple definition neither conveys the breadth of clinical symptoms and disability that TS can produce in patients nor explains the fascination TS has evoked in physicians, scientists, and the general public.

Research on TS has grown increasingly rapidly over the past several decades (see Fig. 1). The Tourette Syndrome Association, which provided much of the preliminary funding for these initiatives, has helped disseminate research advances by hosting five International Scientific Symposia on Tourette Syndrome. The most recent such symposium took place on June 12–13, 2009, in New York City. Over 250 experts and delegates from 17 countries attended the meeting, which included 24 plenary lectures, 7 round table discussions and 57 poster presentations.

Several notable studies were presented for the first time at the Fifth Symposium. To give only two examples, Dr. Larry Scahill discussed results of a very large study of the prevalence of medically diagnosed Tourette syndrome in the United States, published only a few days earlier by the U.S. Centers for Disease Control and Prevention (CDC) (Scahill, Bitsko, & Visser, 2009). Dr. Doug Woods reported for the first time the results of a randomized controlled trial of a behavioral treatment for tics called CBIT (Comprehensive Behavioral Intervention for Tics); the results generated substantial enthusiasm and discussion and were subsequently published in JAMA (Piacentini et al., 2010). Abstracts and video clips from plenary lectures are available online (http://www.tsa-usa.org/Z_IntSciSymp5/IntlSciSymposTS5_contents.html), as are poster abstracts (http://www.tsa-usa.org/aResearch/images/5thIntlSciSympPosterAbstracts.pdf).

This introductory article will point out highlights of the work presented at the Symposium and introduce the remaining articles, in which speakers from the Symposium provide updated summaries of research in their respective areas of TS expertise. Together, the articles in this special issue comprise a solid introduction to the current state of research on TS. Eddy and Cavanna (2014) first discuss the phenomenological, genetic and other features that link

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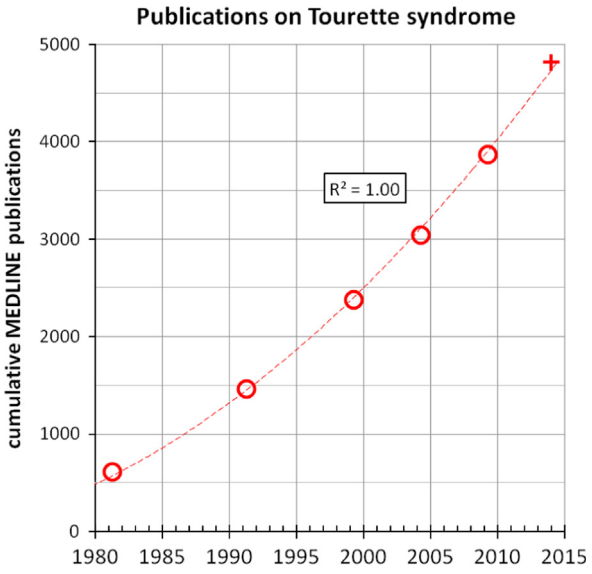

Fig. 1. Cumulative number of published articles on Tourette syndrome and other tic disorders as of the dates of each of the five International Scientific Symposia on Tourette Syndrome (circles) and 28 Feb 2014. The dashed line is the best-fit quadratic curve to these 6 data points ($r > 0.999$). PubMed was searched for ("Tic Disorders"[MeSH] OR Tourette), limited to the relevant publication date ranges.

Table 1
Paradigm shift in TS treatment suggested by the success of CBIT (table from John C. Piacentini, Ph.D.).

Old paradigm	New paradigm
Ignore your tics	Become more aware of your tics
Tics can't be controlled	Learn to manage tics
Don't punish	Reward efforts to manage tics
Don't try to suppress tics	Use behavioral strategies
Tics and urges to tic get worse when you suppress	Tics and urges improve with behavioral treatment
Suppressing one tic makes new tics develop	New tics don't develop from behavioral treatment

TS and obsessive–compulsive disorder, followed by a review of the phenomenology of tic disorders by Leckman, King, and Bloch (2014).

2. TS research highlights

The known heritability of TS provides tantalizing potential for progress in understanding its causes and pathophysiology (Deng, Gao, & Jankovic, 2012). At the Symposium, Dr. Nelson Freimer reviewed the current state of genetics research in TS, including results from multisite collaborative studies of sib pairs and large multigenerational families, which together involved DNA from over 2000 individuals (Tourette Syndrome Association International Consortium for Genetics, 2007). A locus on the short arm of chromosome 2 was most robustly linked to susceptibility to TS. Genome-wide association studies were being analyzed, with preliminary evidence for several strong signals that were being followed up for specificity. Combined studies with OCD symptoms in TS probands and vice versa were promising leads. Some of the studies discussed have published results since the meeting (Crane et al., 2011; Knight et al., 2010; Olfson et al., 2011). Dr. Jim Hudziak reported on a genetic study of a large sample of children (30,000+). This study showed strong evidence for high heritability of tics (explaining 69–78% of the variance), with environmental effects limited to those unique to each individual rather than those environmental effects shared by family members. In this issue, Dr. David Pauls and colleagues update the status of the search for the genes responsible for the high heritability of TS (Pauls et al., 2014).

Other presentations focused on the physiology of tic disorders, a topic reviewed comprehensively elsewhere (Leckman, Vaccarino, Kalanithi, & Rothenberger, 2006; Albin, 2006; Plessen, Bansal, & Peterson, 2009; Leckman, Bloch, Smith, Larabi, & Hampson, 2010; Singer, Jankovic, Mink, & Gilbert, 2010; Jankovic & Kurlan, 2011). Dr. Suzanne Haber discussed research on the anatomy of the basal ganglia, focusing on how the organization of its connections with the cortex of the brain may underlie the development of both normal and abnormal movements. Dr. Flora Vaccarino discussed her exciting research findings on the substantial (~50%) loss of certain interneurons in the striatum in postmortem brain samples from people who had TS during life. Dr. Joshua Berke discussed his research into the function of these interneurons and their response to behavioral tasks and drugs that affect dopaminergic neurotransmission. Dr. Bradley Schlaggar discussed important results from his laboratory's brain imaging studies in TS, which show a difference in TS in the patterns of simultaneous, spontaneous fluctuations in the activity of different regions of the brain (functional connectivity). In this issue Church and Schlaggar, 2014, place that work in context of other neuroimaging findings; see also (Greene, Black, & Schlaggar, 2013). Presentations by Drs. Barak Caine and Joseph Garner discussed potential translational science approaches using animal models to understand the cause and physiology of tics or to rapidly screen potential new treatments.

Another Symposium session focused on public health and the connections between science, patients and the public. Dr. Larry Scahill presented data from the CDC epidemiological study mentioned above (Scahill et al., 2009); for this issue, he and his colleagues summarize recent studies on the prevalence of TS (Scahill, Specht, & Bradbury, 2014). Dr. John Walkup reported on information on "real-life" TS treatment from two large samples, one from Medicaid and one from private insurers (Olfson et al., 2011). The results suggest that many children with tics do not get medical attention, and that those who do present to clinicians have substantial comorbidity. Dr. Anne-Liis von Knorring reported on comorbid symptoms in tic patients from community samples. In clinical samples, biases were suspected to have inflated the rate of comorbid psychological symptoms. However, even in her community samples of TS or chronic motor/vocal tic disorder, almost all children (92%) had at least one psychiatric diagnosis in addition to the chronic tic disorder. Dr. Doug Woods presented results of a survey of 741 adults with tics or parents of children with tic disorders. The survey revealed that treatment actually being received does not reflect current standards of care. For instance, haloperidol was the most common treatment for adults, and although habit reversal (HRT) or CBIT is well proven to be effective, almost no patients had been treated with it; in fact, in terms of number of patients treated, HRT/CBIT came in 6th place, after 5 unproven psychotherapies including relaxation. This finding probably reflects in part a need to better inform physicians of the treatment's efficacy, but other possible explanations include a shortage of trained HRT/CBIT therapists and the fact that clinical trials participants do not represent the full range of patients seen in clinical settings (e.g. research studies require a patient and parent who can comply with the treatment protocol).

A session on neuroimmunology provoked vigorous debate. Speakers included Drs. Tanya Murphy, Michael Schwartz, Gavin Giovannoni, Roger Kurlan, and James Leckman. Although new data continue to raise interesting questions about the association of