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A Refresher on Tourette Syndrome

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Tourette Disorder is characterized by a combination of vocal and motor tics that are present for at least one year and not attributable to a substance or other medical condition.

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Abstract

Tourette Syndrome (TS) is recognized as a more common neurodevelopmental disorder than once thought. In this article we present an update on TS including the DSM-5 revised criteria, new findings in the genetics of TS, treatment advances such as new medications for tics and the use of new tools including Cognitive Behavioral Intervention for Tics (CBIT). We also explore supportive services for the ongoing care of patients using nursing education and family therapy.

Introduction

Tourette Syndrome (TS) has been a recognized medical condition for over 125 years and is included in DSM-5 in the first chapter on Neurodevelopmental Disorders.[1] The diagnosis, known as Tourette Disorder, is characterized by a combination of vocal and motor tics that are present for at least one year and "not attributable to a substance or other medical condition."[1] A tic is a "sudden, rapid, recurrent, non-rhythmic motor movement or vocalization".[1,2] The diagnosis in DSM-5 contains only minor changes from DSM-4 TR, which include removal of the word "stereotyped" to describe tics. DSM-4 TR also required that tics not disappear for greater than three months and that statement is no longer included in DSM-5. The condition is often known to wax and wane from early childhood through adolescence, then improves in early adulthood. Some patients continue to suffer from more pronounced tics for much of their life. Though it has been claimed that Mozart had TS, more recent evidence has rebuffed this claim.[2] Historical figures including Samuel Johnson probably would have satisfied diagnostic criteria, however, and Jim Eisenreich, a well known baseball player, uses his TS diagnosis to educate others.

TS Epidemiology

According to the Mental Health Surveillance Among Children study published by the CDC in 2013, the prevalence of TS is 0.35% among children 6 to 17 years of age[3]. The prevalence in boys is twice as high as it is in girls (0.4% versus 0.2%). These are almost certainly underestimates, as TS often presents before the age of six and estimated prevalence rates were derived from parental reports that their child had ever been diagnosed with TS. A meta-analysis of 35 studies found a prevalence of 0.77% overall and, when stratified by gender, a prevalence of 1.06% in

boys and 0.25% in girls.[4] It is worth emphasizing that the prevalence of transient tic disorder in the same study was reported as 2.99%. TS and tic disorders occur at about half the prevalence of depression and the same prevalence as autism and are therefore a common problem in childhood.[3]

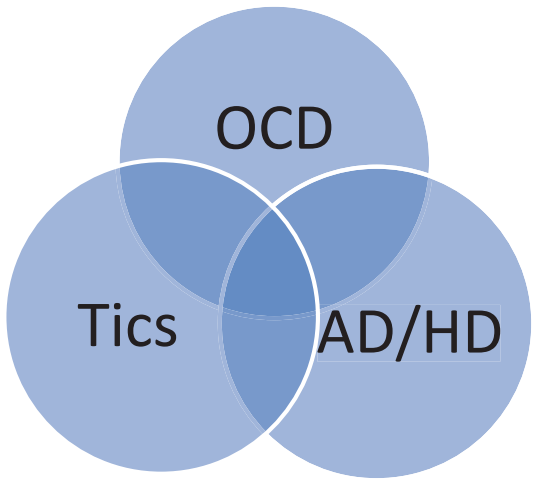
TS Environmental Contributions

There is little doubt that environmental factors contribute to the pathophysiology of TS. In one study of 60 patients with TS, there was a positive correlation between minor stressful events in life and the severity of tics.[3] The role of autoimmune mechanisms remains a topic of considerable debate. Over the last 20 years the existence of entities such as PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection) have been argued. Strictly defined, PANDAS is characterized by an explosion of tics and severe Obsessive-Compulsive Disorder (OCD) behaviors following a streptococcal infection that usually resolves after a few weeks.[5] There is convincing evidence supporting the existence of PANDAS in a minority of TS cases, yet the epidemiological studies remain inconclusive.[6] There is no evidence to support prophylactic treatment with antibiotics at this time for PANDAS and standard treatments are recommended for TS and OCD regardless of etiology.[4]

TS Genetic Contributions

While environmental contributions to the pathophysiology of TS remain debated, the genetic contributions are becoming much better established. The strongest evidence for a genetic basis for TS is gathered from concordance studies among twins and first-degree relatives.[7] For TS, the concordance among monozygotic twins is as high as 56%, while it is 8% for dizygotic twins; first-degree relatives of patients with TS are 10 to 100 times more likely than the general population to develop TS. Yet sorting out the specifics of the genes involved is turning out to be much more complicated than may have been anticipated from these studies. It is now very clear that TS is a polygenetic disease, and multiple genes are contributing to its pathophysiology. Various studies have identified well over a dozen individual genes and chromosomal regions through genome wide analysis and searches for rare copy number variants in patients with TS. An excellent review by Pashou on the genetics of TS contains more detail.[7,8] TS has important genetic etiologies and as the contributions of various genes are elucidated, a new era in terms of its treatment will likely emerge.

Figure 1



Adapted from Jankovich, et. al

Co-Morbidity

Tourette Syndrome is frequently co-morbid with certain psychiatric disorders. The most notable are Attention-Deficit/Hyperactivity Disorder (ADHD) and (OCD).[9,10] See Figure 1. Studies of the rates of co-morbidity have shown widely varying results for both of these disorders with some as high as 80-90% and others as low as 10%.[10,11,12] Recent findings show the lowest co-morbidity rates are seen in the general population, and higher rates of co-morbidity are found when clinically referred patients are surveyed.[13] In addition to OCD and ADHD, rage attacks, sleep disturbances, depression and stuttering were all found at a higher rate in patients with TS than would be expected in the general population.[10] Cognitive deficits have been shown to be more common in TS, especially in the realm of executive functions.[14] Executive functioning is what helps an individual organize, prioritize and plan. In a study by Kurlan et al., aggression was found in 18.5% of patients with tics, and social problems occurred for 24.5 % of patients with tics.[12]

The OCD that accompanies TS appears to have different phenomenology from OCD alone. In the TS patient, touching compulsions and an obsessive need for symmetry are more commonly seen, along with a feeling that sensations need to be "evened up."[4] OCD responds less well to medication when tics are present than when OCD occurs alone.[11] Reasons for the higher rates of co-

morbidity with OCD and ADHD have yet to be clarified. Theories have included some structural areas of the brain that the three have in common including the fronto-striatal cortex as well as similarities in characteristics such as disinhibition.[10]

An individual who has TS, ADHD and OCD may experience unfortunate synergism among the conditions. For example, anxiety associated with an obsession may exacerbate tics and cause the attention span to further deteriorate. It can be challenging at times to discern which condition demands treatment first. Even though TS is known as a neurological disorder, mental health professionals often prove a valuable addition to the treatment team.

Pharmacology

The presence of non-impairing tics, even if qualifying for a TS diagnosis, does not demand treatment with medication or other therapies. Examples of impairment from tics include physical pain, difficulty performing Activities of Daily Living, and ridicule by peers, which can be detrimental to self-esteem. Assessing the level of impairment allows an analysis of the risk benefit ratio regarding the use of medication. Behavioral approaches such as Cognitive Behavior Interventions for Tics (CBIT) and a cautious approach of monitoring without medication are indicated in mild cases.[15] For moderate to severe tics and those that have not responded to CBIT, or when therapy is not an option, medications should be considered (See Table 1).[8]

Randomized, placebo-controlled trials of medications to treat tics show reduction in symptoms from 25-56%.[16] The goal of medication is tic reduction to improve functioning, but eradication of all tics is not typically achieved. It is critical to balance the negative side effects of treatment with the minimal impairment that might be experienced from residual mild tics.[16]

Alpha agonists, although off label for TS, are often used as first line choices for treatment given their lower propensity for side effects.[15] They tend to have a lower response rate at 30-37% than the dopamine antagonists.[8] Clonidine has been used for over 30 years for tics although it has limited empirical support.[17] Guanfacine is thought to be better tolerated but has limited evidence as well. Both can contribute to headaches and somnolence and can lead to rebound hypertension if stopped abruptly. Kapvay® (clonidine) and Intuniv® (guanfacine) are extended release formulations that have received FDA indications for ADHD; however, they have not been studied as treatment for tics.

While the first generation antipsychotics haloperidol and pimozide are FDA approved to treat tics in youth, they are often second and third tier choices, as other options are better tolerated. Pimozide carries a risk of prolonging the QTc more than other antipsychotics used to treat tics, and EKG's are recommended at baseline and with dosage increases.[8] Haloperidol and pimozide can lead to extrapyramidal symptoms as well as drowsiness and carry the risk of tardive dyskinesia.[17] Risperidone has at least four controlled trials demonstrating effectiveness in tic reduction, while studies on aripiprazole are ongoing. Open label studies have shown that aripiprazole and ziprasidone may help and they are used off-label. All antipsychotics are associated with weight gain, but Second Generation Antipsychotics (SGA) are associated with more weight gain in children. Monitoring of fasting glucose and lipids is recommended at baseline, at three months and then annually for the SGAs. The risk of tardive dyskinesia is present with SGAs as well.

Additional options include atomoxetine, a norepinephrine reuptake inhibitor, which is FDA approved to treat ADHD and is showing some early promise to reduce tics.[18] Topiramate also has one study showing impressive tic reduction and is a novel approach when traditional options have failed.[19] Supplements including Vitamin B6 and magnesium have some evidence but are not yet considered standard treatment.

Standard treatments for OCD and ADHD should be considered in the co-morbid patient. For ADHD in the presence of tics, non-stimulants are a logical first choice as stimulants carry warnings about the risk of exacerbating tics. The contraindication of stimulants for those with tics has been brought into question with several studies showing that tics do not always increase with stimulants.[8] Even though OCD may not respond as well to SSRIs when tics are present, the SSRI may still help some and Cognitive Behavior Therapy (CBT) also remains a viable option for these patients.

Comprehensive Behavior Intervention for Tics

Azrin and Nunn first described[15,18,19] Habit Reversal Training (HRT) as an effective intervention for tics in 1973.[20] HRT begins with psychoeducation regarding the neurobiological nature of tics and emphasizes the fact that while tics are not voluntary, it is possible to learn to alter their expression. Primary components of HRT include

Table 1

Medication	Starting dose	Max daily dose	Timing of dose	Suggested Monitoring	Side effects
Guanfacine immediate release	0.5mg	4mg	BID	Vitals at Dr. visits	Sedation
Guanfacine delayed release	1mg	4mg	Daily	Vitals at Dr. visits	Sedation
Clonidine Instant release	0.05mg	4mg	Bid or TID	Vitals at Dr. visits	Sedation
Clonidine delayed release	0.1mg	0.4mg	BID	Vitals at Dr. visits	Sedation
Aripiprazole	2.5mg	15-30mg	Daily	Fasting lipids, Glucose, LFT, Weight	Weight gain, EPS
Risperidone	0.5mg	6mg	BID	Fasting lipids, Glucose, LFT, Prolactin, Weight	Weight gain, EPS
Atomoxetine	18mg	100mg	Daily	LFT if symptomatic	GI Upset
Haloperidol	0.075mg/kg	1.4mg/kg	Daily or BID	ECG	Weight gain, EPS
Pimozide	1mg	10mg	Daily or BID	if >0.05 mg/kg need 2D6 genotyping, ECG	Weight gain, EPS
Topiramate	25mg	200mg	BID	None	Cognitive dulling
Fluphenazine	0.5 mg	3mg	Daily	ECG	Risk of TD
Ziprasidone	20mg w/food	160MG	BID	ECG,fasting lipids,glucose, LFT	Weight gain, EPS

Awareness Training and use of Competing Responses.[20] More recently, Comprehensive Behavioral Intervention for Tics (CBIT), a version of HRT specific to Tourette Disorder, has been developed. CBIT includes Awareness Training and use of Competing Responses, as well as a Function-Based Intervention, which addresses environmental factors influencing tic severity. CBIT is designed to teach its three core components in a series of 8 therapy sessions that occur over a 10-week period.[21]

Awareness Training emphasizes developing insight and awareness of premonitory urges and tic occurrence through self-monitoring. For example, children might practice the tic, or an approximation of the tic, while watching themselves in a mirror and paying attention to the muscles involved. In addition, keeping track of each occurrence of the tic helps to build awareness. For children, low-key prompts from caregivers are an essential part of developing awareness. Competing Responses provide children with alternate behaviors to engage in that are incompatible with the tic. For example, children with a leg lifting tic could be taught to push their feet into the floor rather than lifting their leg, and children with a tic involving head movements might be taught to tighten their neck muscles and hold their heads straight. The purpose of Function-Based Intervention is to identify antecedents and consequences that make tics more likely to happen and that negatively impact the child's functioning. Such factors are identified and then modified in order to reduce the likelihood of future tics and improve the child's ability to function. For example, if a child struggles with academics and experiences worsened tics at homework time, parents might decide to discontinue their homework time, inadvertently reinforcing the tic. CBIT therapists help families address sources of stress and reduce or eliminate secondary gain. If a child is teased by peers, thereby increasing their stress and anxiety, a therapist would help the school educate peers regarding the non-contagious, involuntary, neurological nature of tics, with a goal of reducing or eliminating teasing.

CBIT has been found to yield a significant decrease in tic severity that maintained over time in two randomized, controlled trials.[22] In their 2010 study, Piacentini and colleagues studied 126 children and adolescents with TS and found CBIT produced greater tic reduction than did supportive therapy and education.[22,23] It is important to note that many of these children were already on psychotropic medication and still demonstrated benefit from CBIT.[22] Given the very promising results of recent studies, increasing knowledge of the effectiveness of CBIT and the availability of psychologists and other

mental health providers with training in CBIT has become a primary goal of the National Tourette Syndrome Association.[22]

Supportive Services

The families of children with TS are met with great challenges. These children may display problems with adapting to aspects of the environment, have a higher level of emotional responses, or have a higher level of activity, all the while looking like the little girl or boy that lives next door. "It is therefore imperative to identify methods to deal constructively with those characteristics that make caring for children with TS so difficult."[24] Parents often feel lacking in the ability to educate schools and family members about the disorder and the specific needs of their child, leading to feelings of inadequacy as a parent. Skill sets used with other children do not always seem to have impact on these children. Due to the complexity of the disorder, nursing staff in our Tourette Clinic have been educated about tics, behavioral presentations, interventions and medications used to treat the disorder. The nursing staff can then assist in providing not only advocacy for the patient/family but also an avenue for the parent to be allowed to verbalize thoughts, feelings, and concerns without fear of judgment, thereby potentially providing a sense of validation.

Family therapy is an integral component in providing comprehensive services to families and children affected by TS, especially in the presence of co-morbid disorders. Ross Greene describes the difficulties with adaptation to change in their environments and transitions causing many of these children to have highly explosive, reactive behaviors and that these children "…can lay bare many family issues that might never have risen to the surface had the parents been blessed with a less difficult child."[25]

Conclusion

In the Division of Developmental & Behavioral Sciences at Children's Mercy Hospital, we recognize that patients with TS often need a multidisciplinary approach to treatment. This is especially true with those who suffer from co-morbid OCD and ADHD along with their TS. While we have been treating TS for many years, our newly established TS Clinic will involve psychiatry, neurology, psychology, nursing and family therapists to provide the holistic care needed for these patients.

References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Washington: American Psychiatric Publishing, 2013.
2. Francesco M, Servo S and Cavanna AE. Famous people with Gilles de la Tourette Syndrome. Journal of Psychosomatic Research 2009;67:485-490.
3. Perou R, Bitso BH, and Blumberg SJ. Mental Health Surveillance among Children-United States 2005-2011. Suppl 2, May 17, 2013, Morbidity and Mortality Weekly Report. Surveillance Summaries, 62: 1-35.
4. Knight T, et al. Prevalence of Tic Disorders: Systematic Review and Meta-analysis, Pediatric Neurology, 2012;47:77-90.
5. Murphy TK, Kurlan R and Leckman, J. The immunobiology of Tourette Disorder, Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcus, and related disorders: A way forward. Journal of Child and Adolescent Psychopharmacology, 2010;20: 317-331.
6. Schrag A, et al. Streptococcal infection, Tourette Syndrome and OCD: Is there a connection? Neurology, 2009;73:1256-1263.
7. Paschou P. The genetic basis of Gilles de la Tourette Syndrome. Neuroscience and Biobehavioral Reviews,13;37: 1026-1039.
8. Scahill L, et al. Contemporary assessment and pharmacotherapy of Tourette Syndrome. 2006, The Journal of the American Society for Experimental Neurotheraputics, 2006;3:192-206.
9. Steinberg, T, et al. Life events and Tourette Syndrome. Comprehensive Psychiatry,2013;54: 467-473.
10. Debes NMM. Co-morbid disorders in Tourette Syndrome, Behavioral Neurology, 2013;27: 7-14.
11. March JS. Tics moderate treatment outcome with sertraline but not cognitive behavior therapy in pediatric Obsessive Compulsive Disorder. Biol Psychiatry, 2006;61:344-347.
12. Kurlan R. The behavioral spectrum of tic disorders. Neurology, 2002;59: 414-420.
13. Scharf JM. Prevalence of Tourette Syndrome and chronic tics in the population-based Avon Longitudinal Study of Parents and Children Cohort. JAACAP, 2012;51:192-201.
14. Eddy EM. Executive Functions in uncomplicated Tourette Syndrome. Psychiatry Res, 2012; 200:46-48.
15. Rizzo R, et al. Tourette Syndrome and Co-morbid ADHD: Current Pharmacological Treatment Options. European Journal of Paedatric Neurology, 2013;7:421-428.
16. Dulcan MK. Textbook of Child and Adolescent Psychiatry. Washington: American Psychiatric Press, 2010.
17. Roessner V, et al. Pharmacological treatment of tic disorders and Tourette Syndrome. Neuropharmacology, 2013;68:143-149.
18. Allen AJ, et al. Atomoxetine treatment in children and adolescents with ADHD and Co-Morbid Tic Disorders. Neurology, 2005;65:1941-1949.
19. Jankovic J, Jimenez-Shahed J and Brown LW. A randomised, double-blind, placebo-controlled study of Topiramate in the treatment of Tourette Syndrome. J Neurol Neurosurg Psychiatry, 2010;81:70-73.
20. Azrin NH and Nunn RG. Habit reversal: A method of eliminating nervous habits and tics. Behav Res Ther, 1973;11: 619-628.
21. Woods, DW, Piacentini, JC and Chang, SW. Managing Tourette Syndrome: A Behavioral Intervention for Children and Adults. New York:Oxford University Press, 2008.
22. Scahill L, Woods DW, and Himle MB. Current controversies in the role of behavior therapy in Tourette Syndrome. Movement Disorders, 2013;28:1180-1183.
23. Piacentini, J, Woods, DW and Scahill, L. Behavior therapy for children with Tourette Disorder: A randomized controlled trial. JAMA, 2010;303: 1929-1937.
24. Lee, MY, CHen YC, Wang HS, Chen DR. Parenting stress and related factors in parents of children with Tourette Syndrome. Journal of Nursing Research, 2007;15:165-173.
25. Greene, RW. The Explosive Child: A New Approach for understanding and parenting Easily Frustrated , Chronically inflexible Children. New York: HarperCollins Publishers, Inc, 2001.

Disclosure

None reported. **MM**