Do you know Tourette's?

History and contemporary view of Gilles de la Tourette syndrome

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Abstract

Gilles de la Tourette's syndrome (GTS) is a developmental neuropsychiatric disorder. GTS pathognomonic symptom is a tic - a sudden, purposeless movement or vocalization. Tics can be simple or manifest as complex series of movements or whole sentences. Tics are rarely isolated. They usually present in bouts, series of repetitions, which may last for several seconds.

GTS was formerly thought to be a rare disorder. However, prevalence studies consistently show rates of 0.3 to 1.0% in children and adolescents. Usually symptoms diminish before adulthood, but most patients still have at least some symptoms as grown-ups.

Co-morbidity is a rule - 80% to 90% of GTS patients have at least one other neuropsychiatric disorder, OCD and ADHD being the most common.

Treatment is aimed at reducing tic frequency and severity and the related impairment and distress. Several pharmacologic and psychological treatment options are available. Treatment of tics is not always necessary, and often co-morbid disorders are the focus of treatment.

GTS is a relatively common disorder and, due to high psychiatric co-morbidity, psychiatrists are bound to meet patients with tic symptoms. Recognizing tics as part of the patient's symptomatology helps in forming the therapeutic alliance and finding the correct combination of pharmacologic and psychological treatments.

Introduction

Tourette's syndrome is a developmental, neuropsychiatric disorder characterized by tics: repetitive, sudden, purposeless movements or vocalizations. The syndrome was first systematically presented by the French neurologist Georges Albert Edouard Brutus Gilles de la Tourette (1857-1904), in 1885. He called it "maladie de tics", tic disorder.

Georges Gilles de la Tourette was described during his school years as "having no discipline" and "... a difficult character with unpredictable mood swings" (Walusinski & Bogousslavsky, 2011). After studying medicine for two years he enrolled in the Pitié-Salpetrière Hospital in Paris, and soon became one of Jean-Martin Charcot's favourite pupils. It was Charcot who later named the new disorder "Syndrome Gilles de la Tourette", in honour of one of his brightest students. For convenience, the abbreviated "Tourette's syndrome" is often used, although the correct term includes the whole surname, Gilles de la Tourette. Based on this, I will use the abbreviation GTS in this article.

Actually, Tourette was not the first to describe this tic disorder. In 1873, Armand Trousseau published a case series of five patients with "non-painful tics" (Rickards et al. 2010). Trousseau differentiated between motor and vocal tics and also speculated on the obvious heritability of the tic disorder he described. Tourette was aware of Trousseau's findings - in his 1885 article he mentions Trousseau twice, quite critically, dismissing Trousseau's article on the basis of the case series being too small to draw firm scientific conclusions. After that Tourette goes on to describe his own case series of nine patients. In defence of Tourette it must be said that he was more meticulous and systematic in describing the patients.

Tourette was a very prolific writer and interested in various subjects, for example hysteria and hypnosis (or mesmerism, as it was called then). He revered his teacher and was fascinated by Charcot's experiments with hypnosis. However, Tourette is remembered for GTS. Thus it is rather surprising that Tourette himself returned to the subject only once after his original paper, in an article published in 1899.

Tourette died in 1904 after an epileptic convulsion. His last years were ridden with illness, the symptoms of which had manifested years earlier. In 1900, a local newspaper described the famed neuropathologist as being in his office "completely

naked, flailing wildly in front of a scared patient, who was crouching behind furniture" (Walusinski & Bogousslavsky, 2011). After the incident Tourette apparently stopped his private practice. Tourette's wife took care of him during his last years, which were spent in a mental institute in Lausanne, Switzerland.

Diagnosis

Diagnosis of GTS is based on typical history and clinical picture. Laboratory and imaging studies are sometimes needed for exclusion of other possible causes. The pathognomonic symptom of GTS is a tic, which is a repetitive, sudden, purposeless movement or vocalization. A tic is not completely involuntary, and a patient may be able to suppress it, at least for a short while.

A tic is usually preceded by premonitory urge, which could be described as an itching feeling, often felt in the muscle involved, and relieved by doing the tic. Suppressing the tic for extended periods of time increases the subject's inner tension until he feels compelled to do the tic, after which the tension is released. These somatosensory symptoms are sometimes referred to as sensory tics.

In contrast to obsessions and compulsions, which the patient usually feels as alien, tics are often experienced as ego-syntonic, both intentional and under conscious control. In obsessive-compulsive disorder, compulsions are performed to relieve anxiety caused by obsessions. Both obsessions and the related anxiety are lacking in GTS.

Current diagnostic criteria for GTS, both ICD-10 and DSM-5 are presented in Table 1. DSM-5-criteria are the latest and should be preferred, but as shown in Table 1, the differences are minimal. ICD-10 includes the frequency of symptoms criterion, which has been omitted from DSM-5. The DSM-5 only requires that symptoms have been present for at least a year. This is based on the fact that patients may experience periods of fewer, or even no tics, even though they are not "cured" of GTS. Rather the natural course of GTS may be episodic in some patients (see Course, below).

A notable exception to psychiatric diagnoses in general is the lack of the "impairment" criterion. This reflects the fact that clinicians often see patients fulfilling the diagnostic criteria for GTS (having clear tics etc.), except that the symptoms do not cause them subjective or objective harm or impairment. The requirement for impairment has never been in the ICD-10, and it was dropped from DSM from the Fourth edition, text revision (DSM-IV-TR) onwards.

Table 1. Diagnostic criteria of GTS.

ICD-10
(International Classification of Diseases, 10th revision)

F95.2 Combined vocal and multiple motor tic disorder
[de la Tourette's syndrome]
A. Multiple motor tics and one or more vocal tics that have been present at some time during the disorder, but not necessarily concurrently.
B. The frequency of tics must be many times a day, nearly every day for more that one year, with no period of remission during that year lasting longer than two months.
C. Onset before 18 years of age.

DSM-5
(Diagnostic and Statistical Manual of Mental Disorders, 5th edition)

307.23 Tourette's disorder
A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
B. The tics may wax and wane in frequency but have persisted for more than 1 year since first tic onset.
C. Onset is before age 18 years.
D. The disturbance is not attributable to the physiological effects of a substance (e.g., cocaine) or another medical condition (e.g., Huntington's disease, postviral encephalitis).

Diagnostic assessment includes evaluation of the nature, frequency and severity of tics. In addition, the age at onset and tic history should be recorded. The possible psychosocial burden (occupational, academic and/or interpersonal) caused by tics should be evaluated (Cohen et al., 2013). The assessment should always include a thorough psychiatric evaluation because of the high co-morbidity of GTS with other neuropsychiatric disorders. Neurological and medical examination may be necessary and should be done especially if the clinical picture seems to be atypical.

Co-morbidity

Psychiatric co-morbidity is extremely common in patients with GTS, as up to 88% of the patients have at least one other neuropsychiatric disorder (Freeman et al., 2000), the most common being ADHD (50-60%), followed by OCD (25-50%). Mood disorders are also more frequent in patients with GTS, with 13% of GTS patients attending specialist clinics also having major depression (Robertson 2006).

Recognizing co-morbid disorders is of high importance, as they influence the clinical picture and course of GTS. Patients with co-morbid disorders have worse psychosocial outcomes, and co-morbidity has been linked to increased hospitalisations and even suicide. Co-morbid disorders may also modulate drug response.

Course

Typically, tics begin at a mean age of 5 to 6 years, although the age at onset may vary from 2 years up to 21 years. Motor tics usually manifest earlier, with vocal tics following one to two years after that. With age, tics, both motor and vocal, usually get more complex. In addition, awareness of the premonitory urge usually increases as subjects get older.

Tics often follow a waxing and waning course and depending on the severity of the symptoms, there may be almost "tic-free" periods interspersed between episodes of symptom exacerbation.

Tics are commonly at their worst during childhood, the "peak age" usually being 10 to 12 years. After that the symptoms usually get better. Despite this, 80% to 90% of children and adolescents with GTS still have tics in adulthood. However, the tics are often quite mild and actually it is typical that the person is not aware of the symptoms.

Prognosis of GTS in children and adolescents is thus quite favourable. Only a minority of patients experience tics in adulthood. However, this subgroup also includes those patients with the most severe and debilitating symptoms (Bloch & Leckman, 2009).

Treatment

Both pharmacological and non-pharmacological treatments have been investigated as potential treatments for GTS. Drug treatment of GTS has long relied on clinical experience, single-case reports or published case series. There has been a relative lack of randomized controlled trials (RCT), especially RCT with modern, rigorous methods. Even though high-level studies of different compounds compared to placebo have been increasingly published during recent years, the database is still rather small. In addition, sequential drug trials are lacking, so there are no evidence-based data on what to do if the first drug fails.

This is not the only problem with drug treatment of GTS. A possible mistake is to forget the waxing and waning course of tics, both when starting a new drug, and when assessing the drug response. In addition, many external factors (insomnia, work stress etc.) may influence the clinical presentation of GTS, and thus should be accounted for in the assessment.

Treatments are aimed at diminishing the frequency and/or severity of the tics. However, not all GTS patients need, or want treatment for their tics. Drug treatment for GTS should be considered when tics cause subjective discomfort (pain or injury), social isolation, emotional problems, or marked functional interference for the patients. This decision is based on individual, thorough evaluation of the impairment. In many patients the severity of tics is not in itself necessarily correlated with the impairment. Even mild tics may cause marked impairment, depending on the environment. One example could be a GTS patient working in customer service.

In the long run, many GTS patients discontinue drug treatment, usually because of side effects. In clinical practice, it is common that the focus of the treatment is not tics, but co-morbid disorders, which usually are the main cause of functional impairment.

Drug treatments

Previous research on the pathophysiology of GTS concentrated mainly on the dopaminergic pathways. This was based on the clinical finding that antipsychotic drugs, affecting the dopamine system, were effective in reducing tics. First reports of haloperidol treatment were published in the 1960s (Rickards et al., 1997, Shapiro & Shapiro 1968).

Antipsychotic drugs, blocking mainly the dopamine-2-receptors, are still the mainstay of treatment, even though increasing evidence also points to imbalance in other neurotransmitters, especially the serotonergic and glutamatergic systems.

Haloperidol and pimozide are the most used typical antipsychotics for the treatment of GTS. They are also the most studied and seem to have the best evidence of efficacy (Roessner et al., 2011). Of these drugs, pimozide may be a bit more efficacious and better tolerated. Haloperidol is currently the only drug indicated for GTS. To use pimozide, a special permission from the Medicines Agency is needed.

Of the newer, atypical antipsychotics, the best evidence base so far is for risperidone, which seems to be especially efficacious in patients with co-morbid OCD. Both ziprasidone and aripiprazole have shown promising results in the treatment of tics. Some evidence also exists for quetiapine and olanzapine. Clozapine, which lacks dopamine-2 antagonism, has not been effective in the treatment of GTS, and may even exacerbate tics.

Clonidine, an α-2-receptor agonist has been used for the treatment of GTS for decades. In randomized controlled trials, it reduces tics more than placebo. Clonidine decreases activity of the central nervous system and has also been shown effective in reducing hyperactive and impulsive symptoms of ADHD. Clonidine could be regarded as the first choice when a GTS patient has co-morbid ADHD. Clonidine is antihypertensive, so blood pressure should be monitored during the treatment and drug started and tapered off slowly.

When comparing efficacy, taking into consideration side effects, it seems that risperidone has the most favourable profile. It is not surprising that in the European experts' recommendations, risperidone is rated in first place (Roessner et al., 2011), followed by clonidine, aripiprazole and pimozide.

Psychotherapies

Habit reversal training (HTR) is the most extensively studied therapy for GTS. It consists of awareness training, followed by competing response training. HRT is usually a short therapy, with 10 to 14 weekly sessions. Several randomized controlled trials show a tic reduction of 20-40%, which is maintained in 3 to 6 months follow-up (Verdellen et al., 2011).

Exposure and response prevention and cognitive-behavioural treatment have also had a favourable effect on tics in controlled trials. Self-monitoring, relaxation training and contingency management have been studied in open trials, and some patients may benefit from them. Psychoeducation is, of course, necessary for all patients.

Other treatments

Botulinum toxin injection is a possible treatment option for simple motor tics (Marras et al., 2001), but vocal tics have also been treated by injecting botulinum toxin to vocal cords. In one study, 93% of patients improved, with 50% being tic free after the injection (Porta et al., 2004).

Deep brain stimulation (DBS) is a reversible neurosurgical procedure involving implanting of bilateral electrodes to stimulate selected brain areas. DBS is used for treatment-resistant Parkinson's disease, and it has been increasingly used experimentally for psychiatric indications, like OCD and treatment-resistant depression. For GTS, DBS is still a very experimental treatment. There are still many open questions regarding patient choice and electrode treatment (Porta et al., 2009).

Conclusions

GTS is a neuropsychiatric disorder, which was once thought to be very rare. This seems not to be true - prevalence figures of 0.3-1.0% have been presented. Generally, long-term outcomes for pure GTS are good. However, GTS is highly co-morbid with other neuropsychiatric disorders, and patients usually seek treatment for these co-morbid problems. Every psychiatrist is prone to meet GTS patients sooner or later, and should be aware of the basic assessment and treatment guidelines of GTS.

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