Contrasting features between Tourette syndrome and secondary tic disorders

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Abstract

Tics are rapid, recurrent, non-rhythmic movements or emitted sounds. Tics are the hallmark of Tourette syndrome (TS); however, a number of other disorders may be associated with tics, so-called secondary tic disorders (STD). We assessed clinical history and performed blinded evaluations of video-recordings from patients with TS and STD in order to identify features that may differentiate tics associated with TS vs STD. There were 156 patients with TS and 38 with STD, 21 of whom had functional (psychogenic) tics. Patients with TS were more frequently male and had a younger age at onset. Tics in TS tend to involve muscles in the cranial-cervical area more often and have greater severity and complexity than those in patients with STD. Similar findings were observed when contrasting patients with TS with patients with functional tics only. Simple phonic tics showed the greatest diagnostic accuracy for TS, compared with STD, but marked overlap in the types of tics and comorbidities was observed between patients with TS and STD. Patients with TS were more likely males, had a younger age at onset, phonic tics and motor tics affecting predominantly the head and neck area, and had a greater complexity and severity of tics than those with STD. When these features are absent a consideration should be given to the possibility of a tic disorder other than TS.

Introduction

Tics are sudden, rapid, recurrent, non-rhythmic purposeless movements or emitted sounds. Tourette syndrome (TS), a childhood onset neuro-behavioral disorder, is the most common diagnosis in patients with motor and phonic tics (Johnson et al. 2022). However, some patients may present with a tic disorder that does not fulfill the diagnostic criteria for TS or have a clear temporal relationship with a traumatic brain injury, drug exposure, encephalitis, or an autoimmune or a degenerative disorder, so called secondary tic disorders (STD) (Johnson et al. 2022). An increasingly recognized observation is that a large proportion of patients with tics have a functional (previously known as psychogenic) etiology (Baizabal-Carvallo and Jankovic 2014). This became especially relevant during the COVID-19 pandemic (Hull et al. 2021; Pringsheim et al. 2021). Patients with STD are categorized in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5), as "Other Specified Tic Disorders" (American Psychiatric Association 2013). Similar to TS-related tics, STD cause distress or impairment in social, educational/occupational or other vital area functioning, according to the DSM-5 criteria.

Patients with TS have been studied in large cohorts, they have a mean age at onset of 6.4 years, with a clear male predominance over females: 3–4:1 (Freeman et al. 2000). Patients with TS develop simple and complex motor and phonic tics in a rostro-caudal sequence, usually preceded by a premonitory sensation from which awareness increases with age (Kwak et al. 2003). About 90% of TS patients report an associated neuropsychiatric comorbidity, mostly attention-deficit/hyperactivity disorder (ADHD) in 60% of cases and obsessive–compulsive disorder (OCD) in a quarter of cases (Freeman et al. 2000). On the other hand, patients

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with STD are usually described in single case reports or small case series without direct comparison with TS-related tics. An older age at onset (after 18 year of age), lack of family history of tics, absence of premonitory sensations, lack of the typical neuropsychiatric comorbidities observed in TS and temporal or comorbid association with a brain insult or another neurological disorder suggests a STD. In this study, we aimed to contrast the clinical features of tics in the setting of TS vs STD in order to gain insights into clinical phenomenology and diagnostic clues between both groups of disorders.

Materials and methods

Video-recordings of consecutive patients with tics were assessed during a 3-year period at the Parkinson's Disease Center and Movement Disorders Clinic, Baylor College of Medicine, Houston, Texas. The video rater was blinded to the etiologic diagnosis in the subjects. The evaluator was a movement disorders specialist with expertise in TS. All patients were recorded from 10 to 15 min to capture their tics. We then reviewed medical records and classified the patients as TS or STD according to the DSM-5 (American Psychiatric Association 2013). The diagnosis of STD was also supported by a clear temporal association with the offending event or a clear pathophysiological association with another disorder, for example tics in the context of Sydenham's chorea or Huntington's disease. A functional etiology was diagnosed according to the Fahn and Williams criteria, which require, in addition to other features such as sudden onset and distractibility, that the observed movements are incongruent or inconsistent with typical organic movement disorders (Fahn and Williams 1998). Depending on the presence of the various clinical features patients were assigned to one of four categories of increasing diagnostic certainty: possible, probable, clinically established and documented. Accordingly, patients with functional tics were diagnosed with a clinically established functional neurological disorder. After reviewing clinical history and video-recordings, we eliminated 14 patients, due to uncertainty about comorbid TS (n = 6), no tics were observed on video-recordings (n = 6), or patients had another movement disorder, rather than tics (n = 2).

We assessed the type of tics (motor or phonic), their phenomenology (simple or complex), and distribution of tics (Johnson et al. 2022). The latter was performed with a semi-quantitative scale, assigning 1 point to each affected body part (face, neck, phonic, arms, trunk/abdomen and legs) with a score range of 1–6 points, after adding the points from every body part where tics were observed in the recordings or reported by the patient. The severity of tics was rated based on review of video-recordings and classified into six

categories, analogous to other studies, based on the Global Severity Rating and Rush Video-Based Tic Rating Scales as previously described (Goetz et al. 1999). The following categories were included: 0: None; 1: very mild (tics rarely observed on video); 2: mild (tics are noticeable but not disruptive); 3: medium (tics are frequent but mildly disruptive); 4: marked (tics are severe and disruptive); 5: severe (tics are very severe and disruptive); 6: very severe (tics are extremely disruptive). Comorbid (ADHD) and obsessive–compulsive disorder (OCD) were diagnosed based on review of the medical records according to the DSM-5 criteria (American Psychiatric Association 2013). We evaluated the diagnostic performance of variables showing statistically significance between groups.

Patients or a close family member provided written informed consent for videotaping and publishing in a scientific journal approved by the Baylor College of Medicine Institutional Review Board for Human Research and Sante Research Board.

Statistics

We summarized data in percentages, means and standard deviations. The chi-square (χ^2) and the Fisher's exact tests were performed to compare proportions between groups. Odds ratios (OR) and confidence intervals (CI) at 95% were used to assess risk for variables of interest. The t test for independent samples test was used to compare means between groups. We calculated sensitivity and specificity for variables showing statistically significance difference between patients with TS and STD. The Youden's J statistics ($J = $ sensitivity $+$ specificity $- 1$) was used to assess the performance of a diagnostic variable. All statistic evaluations were carried out by means of SPSS version 22; a P value < 0.05 was considered significant.

Results

TS vs non-TS

There were 156 patients with TS and 38 patients with STD. Presumed etiologies of tics in the STD group are presented in Table 1. Patients with TS were more commonly male (78.2 vs. 57.8%, $P = 0.010$) and significantly younger at age of onset and evaluation ($P < 0.001$). Patients with TS showed a broader body distribution of tics compared with STD patients with more affected body parts for the former group ($P = 0.003$).

A caudocephalic anatomic distribution gradient was observed in patients with both TS and STD. However, some cranial tics were statistically significantly more common in patients with TS, such as excessive eye-blinking, eye-rolling

Table 1 Diagnosis for patients with secondary tic disorder

Diagnosis	N (%)
Functional tics	21 (55.26)
Post-traumatic	3 (7.89)
Drug-induced	3 (7.89)
Sydenham disease	2 (5.26)
Huntington disease	2 (5.26)
Basal ganglia calcification	2 (5.26)
Down syndrome	2 (5.26)
Other	
Chromosome 15 duplication	1 (2.63)
Antiphospholipid syndrome	1 (2.63)
Stroke	1 (2.63)
Unclear	1 (2.63)

tics, jaw tics; head jerks were also more common in patients with TS (Table 2). Patients with TS showed greater overall severity of tics and a significantly higher frequency of simple phonic tics and complex motor and phonic tics (Table 2). Patients with TS also had a greater frequency of comorbid ADHD and OCD.

TS vs. functional tics

Most patients with STD (n = 21, 55.26%) were diagnosed with a functional tic. Premonitory sensation was reported in 4 (19%) patients with functional tics and 1 patient with post-stroke tics. When TS was compared with functional tics only, patients with TS were more frequently males ($P = 0.010$), had a younger age at onset and evaluation ($P < 0.001$), had a greater frequency of facial tics ($P = 0.018$), including eye-blinking ($P = 0.002$) and jaw

Table 2 Summary of contrasting clinical features between patients with TS and STD

	TS n = 156, (%)	STD n = 38, (%)	Functional tics N = 21, (%)	TS vs. STD (OR, 95% CI)	TS vs. functional tics (OR, 95% CI)	TS vs. STD (P value)	TS vs. functional tics (P value)
Sex (male)	122 (78.2)	22 (57.8)	11 (52.3)	2.61 (1.23–5.51)	3.26 (1.28–8.32)	0.010	0.010
Age at evaluation (y)	19.39 ± 12.46	32.47 ± 15.67	35.71 ± 15.96	–	–	< 0.001	< 0.001
Age at onset (y)	9.20 ± 8.46	28.58 ± 15.23	31.62 ± 15.25	–	–	< 0.001	< 0.001
Tic distribution							
Eyes blinking	99 (63.46)	8 (21)	6 (28.57)	4.61 (2.23–9.53)	3.64 (1.48–8.94)	< 0.001	0.002
Eye rolling	42 (26.92)	3 (7.89)	3 (14.28)	3.52 (1.13–10.9)	2.04 (0.63–6.62)	0.013	0.212
Grimacing	63 (40.38)	9 (23.68)	4 (19.04)	1.90 (0.95–3.78)	2.59 (0.91–7.36)	0.056	0.058
OM	41 (26.28)	1 (2.63)	0	10.29 (1.45–72.8)	–	0.001	0.004
Face	142 (91.02)	28 (73.68)	15 (71.42)	2.53 (1.41–4.52)	3.14 (1.37–7.16)	0.010	0.018
Neck	98 (62.82)	16 (42.10)	10 (47.61)	1.95 (1.10–3.48)	1.72 (0.77–3.83)	0.020	0.180
Shoulder	76 (48.71)	17 (44.73)	8 (38)	1.14 (0.64–2.02)	1.47 (0.64–3.36)	0.660	0.360
Arms	72 (46.15)	13 (34.21)	6 (28.57)	1.5 (0.82–2.75)	1.97 (0.80–4.84)	0.183	0.128
Trunk	55 (35.25)	10 (26.31)	5 (23.8)	1.41 (0.73–2.72)	1.64 (0.63–4.26)	0.295	0.298
Legs	46 (29.48)	9 (23.68)	2 (9.52)	1.27 (0.64–2.51)	3.53 (0.85–14.6)	0.477	0.053
No. of affected body parts	3.08 ± 1.56	2.34 ± 1.27	2.05 ± 1.61	–	–	0.003	0.001
Tic features							
Severity	3.20 ± 1.21	2.76 ± 1.12	2.76 ± 1.13	–	–	0.033	0.096
SIB	24 (15.38)	2 (5.26)	0	2–78 (0.71–10.9)	–	–	0.082
Tic complexity and category							
Simple motor tics	155 (99.35)	38 (100)	21 (100)	–[a]	–[a]	1.000	1.000
Complex motor tics	80 (51.28)	4 (10.52)	2 (9.52)	6.49 (2.39–17.6)	8.2 (1.96–34.15)	< 0.001	< 0.001
Simple phonic tics	119 (76.28)	5 (13.15)	3 (14.28)	11.69 (4.78–28.6)	13.3 (4.08–43.3)	< 0.001	< 0.001
Complex phonic tics	21 (13.46)	0	0	–[a]	–[a]	0.017	**0.141**
Neuropsychiatry comorbidities							
ADHD	68 (43.58)	5 (13.15)	3 (14.28)	3.98 (1.62–9.74)	4.02 (1.23–13.1)	0.001	0.010
OCD	89 (57.05)	7 (18.42)	5 (23.8)	4.47 (2.07–9.66)	3.76 (1.44–9.81)	< 0.001	0.003

ADHD attention-deficit/hyperactivity disorder, *OCD* obsessive–compulsive disorder, *SIB* Self-injurious behavior, *TS* Tourette syndrome

[a]Risk estimation was not computed for TS

tics ($P = 0.004$); however, facial grimacing and eye-rolling did not show statistically significant differences. Although patients with TS had a greater number of affected body parts, no differences in severity was observed ($P = 0.096$). Complex motor and simple phonic tics were more common in patients with TS ($P < 0.001$, for both variables); but complex phonic tics were equally observed between groups. Comorbid ADHD and OCD were statistically more common in patients with TS ($P = 0.010$ and 0.003, respectively) (Table 2).

Diagnostic performance

After testing sensitivity, specificity and diagnostic performance (J value) of contrasting features between TS and STD or functional tics; simple phonic tics showed the highest diagnostic accuracy to differentiate between TS and STD or TS and functional tics ($J = 0.62$ and 0.61, respectively). Complex tics had the highest sensitivity for the diagnosis of TS (0.95); whereas oromandibular tics had the greatest specificity (0.97) for the diagnosis of TS when compared with STD (Table 3).

Table 3 Summary of diagnostic performance for TS of studied variables

Clinical feature	Sensitivity	Specificity	J value
TS vs. STD			
Simple phonic tics	0.76	0.86	0.62
Eye-blinking tics	0.63	0.78	0.41
OCD	0.58	0.81	0.39
ADHD	0.43	0.86	0.29
Complex tics	0.95	0.30	0.25
Affected body parts ≥ 3	0.57	0.68	0.25
OM tics	0.26	0.97	0.23
Neck tics	0.62	0.57	0.19
Eye-rolling	0.26	0.92	0.18
Facial tics	0.40	0.76	0.16
TS vs functional tics			
Simple phonic tics	0.76	0.85	0.61
Complex tics	0.51	0.90	0.41
OCD	0.58	0.76	0.34
Eye-blinking tics	0.63	0.71	0.34
Affected body parts ≥ 3	0.57	0.76	0.33
ADHD	0.43	0.85	0.28
OM tics	0.26	1.00	0.26

ADHD attention-deficit/hyperactivity disorder, *OCD* obsessive–compulsive disorder, *OM* oromandibular

Discussion

In this study, we found that patients with TS have a distinct motor/phonic tic syndrome compared with patients with STD. Patients with TS were more frequently male and had a younger age at onset. Furthermore, tics in TS tend to involve muscles in the cranial-cervical area more frequently and have greater severity and complexity of their tics than those observed in patients with STD. Indeed, some tics such as eye-blinking, jaw tics and head jerks were markedly more common in patients with TS as compared to those with STD. Eye tics have been deemed as a core feature of TS and seem to support this diagnosis in patients with tics (Martino et al. 2012; Baizabal-Carvallo and Jankovic 2022). Despite these differences, there does not seem to be a single feature that has an absolute accuracy to discriminate between patients with TS and STD. We tested the diagnostic accuracy of individual clinical features for the diagnosis of TS. Simple phonic tics had the greatest diagnostic accuracy for TS. However, oromandibular tics showed a high specificity for TS diagnosis, when compared with all STD or functional tics only (Fig. 1). Oromandibular tics have shown to be markers of greater TS severity (Baizabal-Carvallo et al. 2023). These findings should tested in further studies.

Although tics may be observed in a number of other disorders besides TS, it is likely that the underlying pathophysiology varies among etiologies. Experimental studies in animals have shown that, disinhibition of the cortico-striato-thalamo-cortical circuits as a result of GABAergic deficiency leads to tic-like movements (Pogorelov et al. 2015). Furthermore, various imaging and neurophysiologic studies have suggested that the dorsal anterior insula may be part of the urge-tic network and could influence the urge- and tic-related cortico-striato-thalamic regions in TS (Jackson et al. 2020). Disturbance of cortical-basal ganglia-cerebellar networks probably underlies the pathophysiology of tics irrespective of underlying etiology.

Several clinical and pathophysiological differences have been proposed between patients with TS and functional tics. From a biochemical standpoint, patients with TS have evidence of increased dopaminergic activity in basal ganglia as dopamine receptor blockers consistently improve motor and phonic tics (Maia and Conceição 2018); moreover, pathological and neuroimaging evidence of impairment in the inhibitory neuro-transmitter GABA provides a biochemical basis for decreased inhibition in patients with TS (Lerner et al. 2012). However, a consistent abnormality in neurotransmitters has not been identified in patients with functional movement disorders, including functional tics, and these patients do not show improvement with pharmacological manipulation of inhibitory or excitatory neurotransmitters (Baizabal-Carvallo et al. 2019).
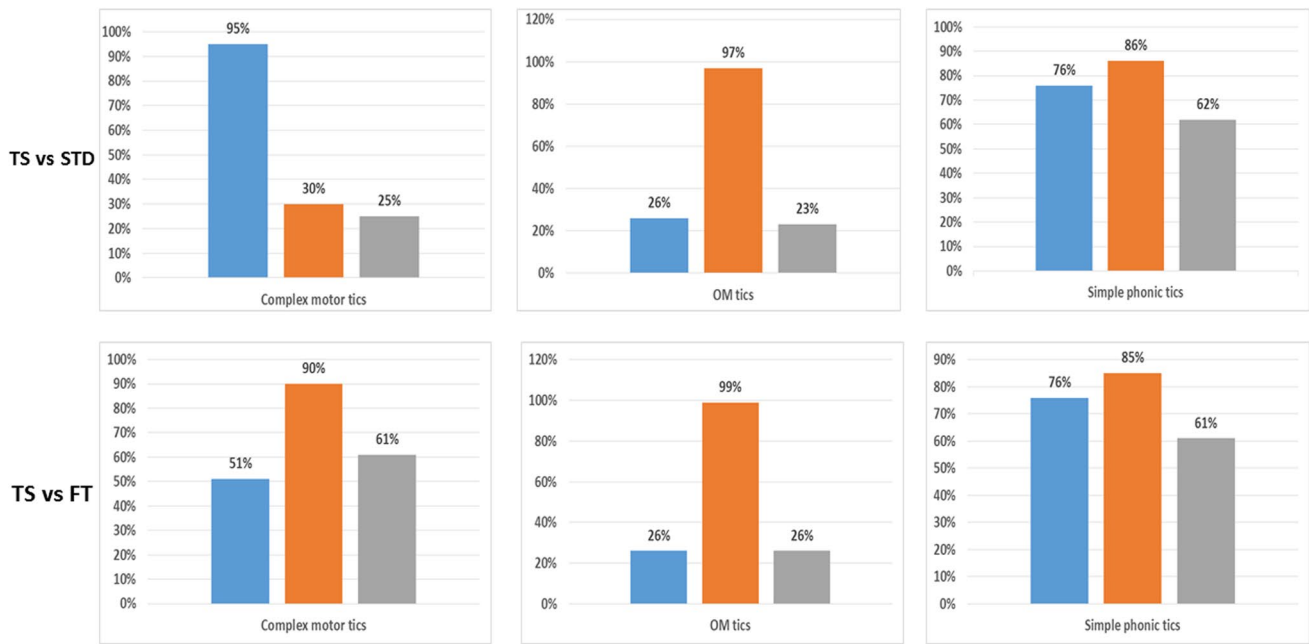
Fig. 1 Diagnostic performance of complex motor tics, oromandibular (OM) tics and simple phonic tics for the diagnosis of Tourette syndrome vs secondary tics disorders (upper row) and Tourette syndrome vs functional tics (FT) (bottom row). Sensitivity: blue; specificity: orange; J value: gray

Our study has some limitations. For example, patients with STD may have fragments of other movements (i.e. chorea) besides tics and most have functional tics (Baizabal-Carvallo 2021). Our study did not include the so called "TikTok tics", a form of functional neurological disorder that characterizes by rapid-onset of exaggerated tic-like behaviors that follows exposure to a social media personality (Hull and Parnes 2021). We are not aware of this kind of exposure in our patients. An analysis of most viewed videos from that social network showed several atypical features such as unusually frequent coprolalia, strong environmental influence, aggression, object throwing, self-injurious behavior and uttering long phrases (Zea Vera et al. 2022). Moreover, when compared with patients with TS, these individuals showed a greater severity on tic-scale (Pringsheim et al. 2021). In our study, we compared TS patients with patients with non-TikTok functional tics. Another limitation is that we did not assess systematically premonitory sensations. This premonitory sensory phenomenon has been consistently reported in over 90% of patients with TS (Kwak et al. 2003) and were reported only in 19% of patients with functional tics and in only 13.15% in patients with STD in our study, pointing to diverse mechanisms underlying tics between groups.

Conclusions

In summary, patients with TS are more likely males, have a wider anatomic distribution of tics, and greater severity and complexity of tics than those with STD. Despite some overlap in clinical features, the two forms of tics can be differentiated not only etiologically but also phenomenologically.

Declarations

Ethics approval The Baylor College of Medicine Internal Review Board provided consent for case publications after written approval by patients or family members.

Consent to participate Patients provided written informed consent to participate in scientific research.

Consent for publication Patients provided written informed consent for publication in a scientific journal.

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