Temporal Course of the Tourette Syndrome Clinical Triad

Brief Reports

Temporal Course of the Tourette Syndrome Clinical Triad

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Abstract

Background: Tourette syndrome (TS) is a disorder characterized by childhood onset of motor and phonic tics, often with improvement of tic symptoms by young adult years. The temporal course of tics and commonly comorbid behavioral symptoms is still not well characterized.

Methods: In order to clarify the time course of tics and comorbid attention deficit hyperactivity disorder (ADHD) or obsessive compulsive disorder (OCD) in TS, we administered a brief survey regarding the course of symptoms at a single point in time to 53 TS patients aged 13–31 years.

Results: Mean age ($\pm$SD) at symptom onset was 7.9 ($\pm$3.6) years for tics, 7.9 ($\pm$3.5) for ADHD, and 9.2 ($\pm$5.0) for OCD. Age at peak symptom severity was 12.3 ($\pm$4.6) years for tics, 10.8 ($\pm$3.8) for ADHD, and 12.6 ($\pm$5.5) for OCD. Tics, ADHD, and OCD were reported to be no longer present in 32.0%, 22.8%, and 21.0% of subjects, respectively. Decline in symptom severity began at age 14.7 ($\pm$3.7) years for tics, 13.9 ($\pm$2.9) for ADHD, and 15.1 ($\pm$5.0) for OCD. Remission of symptoms occurred at age 17.4 ($\pm$3.8) years for tics, 17.4 ($\pm$1.3) for ADHD, and 15.6 ($\pm$2.3) for OCD.

Discussion: Our data confirm and expand previously reported TS spectrum symptom milestones and may guide design of future research aimed at improving the course of TS.

Keywords: Tourette, obsessive compulsive disorder, attention deficit hyperactivity disorder, tic

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Introduction

Tourette syndrome (TS) is defined by childhood onset of multiple motor and vocal tics lasting more than one year.[1] Tics, attention deficit hyperactivity disorder (ADHD), and obsessive compulsive symptoms (OCS), comorbid in the majority of TS patients, constitute a TS neuropsychiatric spectrum and this combination is commonly known as the TS "clinical triad."[2] The mean age at onset of tics has been reported to be 6.4 years in patients with TS.[3] While the severity of tics typically waxes and wanes over time, many patients appear to experience a lessening of symptoms as they grow into adulthood. A peak in tic severity has been reported to occur between the ages of 10 and 13 years;[4,5] significant reduction in tic severity has been reported to begin at a mean age of 16 years, and between 26% and 50% of patients have been described as being essentially free of tics by early adulthood.[4,6,7] While substantial reductions in tic severity have been

called "tic remissions," many TS patients who report that their tics are in remission still have tics that are appreciated by an expert[8] or recur during times of psychosocial stress.[9] There are also reports of tics observed in individuals older than age 60, even after being reportedly absent for more than 40 years.[10,11] Little information is available regarding the natural course of the other components of the TS triad, comorbid ADHD, and OCD. In order to guide development of therapies aimed at hastening or increasing the likelihood of remission, we conducted a patient survey to gather more information on the temporal course of the full TS triad.

Methods

The University of Rochester Research Subject Review Board approved the study protocol and all subjects provided informed consent. Eligible subjects had a diagnosis of TS and were 13–35 years of age at the time of the survey. From August 2008 to January 2009,

we interviewed subjects identified during follow-up patient visits at the University of Rochester TS Clinic and from billing records of the clinic to identify other patients who would be adolescents or adults at the time of the survey. Selected subjects had been diagnosed by our clinicians using the Diagnostic and Statistical Manual of Psychiatry, 4th Edition as having TS (Tourette's disorder), OCD, or ADHD. There were no exclusion criteria. Severity of symptoms was not considered in subject selection. Information on medication treatment over time was not gathered. Subjects were interviewed directly either in-person (53%) or by telephone (47%) (for adolescents, a parent also joined the interview) using a standard questionnaire that included four main questions about tics, ADHD, and OCD: 1) age at onset, 2) age at peak severity, 3) age at which symptoms began to lessen, and 4) age at which symptoms were considered to be absent. The survey was conducted by a trained graduate student (L.A.R.) and subjects were informed about the purpose of the study, namely to obtain information about the course of their symptoms over time. In order to try to limit recall errors, the student also reviewed each subject's clinic records and any discrepancies were reviewed by calling the subject back. We used descriptive statistics to determine the frequency and the mean ages of occurrence for each of these milestones and the Pearson product–moment test to measure the strength of the relationship between these variables. An analysis of variance (ANOVA) was used to examine time course variables when factored by gender.

Results

The TS clinic included a total of 63 TS patients between the ages of 13 and 35 years. Fifty-three (84%) participants (79.2% male, mean age 19.4 [$\pm$5.3] years) completed the survey. Among the participants, 68% had been diagnosed with ADHD and 71.62% with OCD. Mean age ($\pm$SD) at symptom onset was 7.9 ($\pm$3.6) for tics, 7.9 ($\pm$3.5) for ADHD, and 9.2 ($\pm$5.0) for OCD. Age at peak symptom severity was 12.3 ($\pm$4.6) for tics, 10.8 ($\pm$3.8) for ADHD, and 12.6 ($\pm$5.5) years for OCD; 83.0% reported that their tics had lessened over time, and tics were reported to have stopped in 32.0%. Comorbid ADHD or OCD was reported to have resolved in 22.8% and 21.0% of subjects, respectively. Decline in symptom severity began at age 14.7 ($\pm$3.7) for tics, 13.9 ($\pm$2.9) for ADHD, and 15.1 ($\pm$5.0) for OCD. Resolution of symptoms occurred at age 17.4 ($\pm$ 3.8) for tics, 17.4 ($\pm$1.3) for ADHD, and 15.6 ($\pm$2.3) for OCD (Table 1.)

A Pearson product–moment test found significant correlations between several of the variables, and these are summarized in Table 2 (Table 2). Significance was found for age at tic onset and age at peak tic severity, age at tic onset and age at which tics began to lessen, and age at peak tic severity and age at which tics began to lessen (Table 2). Age at tic onset was also found to correlate with the age at OCD symptom onset, and OCD symptom onset correlated with ADHD symptom onset. The age at which tics were at their worst related to the age at which OCD and ADHD symptoms were peaking as well, and correlations were found between OCD peak symptom age and ADHD peak symptom age. Additionally, statistically significant relationships were found between the age at tic lessening and both age at OCD

Table 1. Summary of Results: The Temporal Course of TS

	Prevalence in Sample Population	Mean Age at Onset	Mean Age at Peak Symptom Severity	Mean Age at Symptom Lessening	Mean Age at Remission	% Symptom Lessening in Affected Subjects	% Remission in Affected Subjects
TS	100%	7.9 ($\pm$3.6)	12.3 ($\pm$4.6)	14.7 ($\pm$3.7)	17.4 ($\pm$ 3.8)	83%	32%
ADHD	68%	7.9 ($\pm$3.5)	10.8 ($\pm$3.8)	13.9 ($\pm$2.9)	17.4 ($\pm$1.3)	60%	22%
OCD	72%	9.2 ($\pm$5.0)	12.6 ($\pm$5.5)	15.1 ($\pm$5.0)	15.6 ($\pm$2.3)	68%	21%

ADHD, Attention Deficit Hyperactivity Disorder; OCD, Obsessive Compulsive Disorder; TS, Tourette syndrome.

Table 2. Correlations between temporal course milestones

		Tics Began	Age When Tics Were Worst	Age When Tics Lessened	OC Symptoms Began	ADHD Symptoms Began	ADHD Symptoms Worst	OC Symptoms Worst	OC Symptoms Lessened	ADHD Symptoms Lessened
Tics began	Pearson correlation	1	0.625**	0.444**	0.450**	0.270	0.260	0.455**	0.255	0.228
	Sig. (2-tailed)		0.000	0.003	0.005	0.117	0.157	0.009	0.209	0.320
Age when tics were worst Correlation	Pearson correlation	0.625**	1	0.776**	0.282	0.013	0.361*	0.635**	0.233	0.073
	Sig. (2-tailed)	0.000		0.000	0.086	0.940	0.046	0.000	0.252	0.753
Age when tics lessened	Pearson correlation	0.444**	0.776**	1	0.326	0.169	0.556**	0.520**	0.541**	0.653**
	Sig. (2-tailed)	0.003	0.000		0.073	0.363	0.003	0.005	0.006	0.002
OC symptoms began	Pearson correlation	0.450**	0.282	0.326	1	0.607**	0.479*	0.719**	0.672**	0.375
	Sig. (2-tailed)	0.005	0.086	0.073		0.001	0.013	0.000	0.000	0.125
ADHD symptoms began	Pearson correlation	0.270	0.013	0.169	0.607**	1	0.612**	0.276	0.468*	0.611**
	Sig. (2-tailed)	0.117	0.940	0.363	0.001		0.000	0.203	0.043	0.004
ADHD symptoms worst	Pearson correlation	0.260	0.361*	0.556**	0.479*	0.612**	1	0.611**	0.679**	0.826**
	Sig. (2-tailed)	0.157	0.046	0.003	0.013	0.000		0.002	0.002	0.000
OC symptoms worst	Pearson correlation	0.455**	0.635**	0.520**	0.719**	0.276	0.611**	1	0.927**	0.472
	Sig. (2-tailed)	0.009	0.000	0.005	0.000	0.203	0.002		0.000	0.076
OC symptoms lessened	Pearson correlation	0.255	0.233	0.541**	0.672**	0.468*	0.679**	0.927**	1	0.710**
	Sig. (2-tailed)	0.209	0.252	0.006	0.000	0.043	0.002	0.000		0.004
ADHD symptoms lessened	Pearson correlation	0.228	0.073	0.653**	0.375	0.611**	0.826**	0.472	0.710**	1
	Sig. (2-tailed)	0.320	0.753	0.002	0.125	0.004	0.000	0.076	0.004	

ADHD, Attention Deficit Hyperactivity Disorder; OC, Obsessive Compulsive.

*Correlation is significant at the 0.05 level (2-tailed).

**Correlation is significant at the 0.01 level (2-tailed).

symptom lessening and age at ADHD symptom lessening, as well as between OCD and ADHD symptom lessening (Table 2).

Only 63.6% of the female subjects experienced a lessening of their symptoms compared to 88% of the males, and just one female (9.0%) reported that her tics had stopped (male=38.0%). Significant gender differences were found for the categories of age at tic onset (F=4.84, p=0.032), age at which tics were at their peak (F=8.77, p=0.005), and age at which tics began to lessen (F=6.47, p=0.015), with males having younger ages at all points.

Discussion

The results of this survey study provide further data to define the expected temporal course for the symptoms of TS. An identical rate of tic remission (32%) was reported in a recent longitudinal study.[7] That study included a younger age group (16–23 years) of subjects at the time of follow-up, suggesting that it might be an underestimate since longer follow-up into adulthood might have yielded more subjects with remission. The current study adds to the knowledge of tic evolution by incorporating age-specific information about the timing of tic remission. This study is also the first to systematically gather time course data regarding the full TS clinical triad by including the common comorbidities ADHD and OCD. The results for mean age at tic onset (7.9 years) and peak tic severity (12.3 years) fall within previously reported ranges (6–8 and 10–13 years, respectively.)[3–8] The reported mean age at onset of ADHD (7.9 years) is older than standard diagnostic criteria for the condition (symptom onset before age 7 in DSM-IV).[1] This could reflect recall error or bias, as possibly evidenced by the fact that reported ages at onset for ADHD and tics were essentially identical. The mean age at tic improvement (14.8 years) is also similar to the previously reported 16 years.[6] We found that 22% of subjects with TS and ADHD reported remission of ADHD. Previous studies on the temporal course of ADHD in general (not comorbid with TS) differed from ours in that they did not use self-reports. Symptom improvement (defined as no longer meeting full diagnostic criteria for ADHD) was reported at 60–70% for young adults.[12,13] One previous longitudinal study (mean age at enrollment 12 years, mean follow-up interval 9 years) of individuals with OCD (and TS, as well as ADHD, comorbidity rates=40%) found that 44% had minimal symptoms and were classified as having experienced remission.[14] This study utilized a Yale Brown Obsessive Compulsive Score of less than 8 as the cut-off for defining remission. Our finding of a lower 21% rate of TS-associated OCD symptom resolution may reflect differences in methodology.

Although the number of female subjects in our study was small, our analyses suggest a difference between genders with respect to age at tic onset, age at peak tic severity, and age at which tics began to lessen, with male subjects having younger ages at all points. The proportion of females in our sample (21%) is comparable to that reported in a meta-analysis of larger TS population studies,[15] but further data are needed to clarify differences in temporal course or long-term outcome between the genders.

There are potential limitations to our study. Being retrospective, there may have been inaccuracies in recall by the subjects. In order to lessen this potential confound, we chose subjects in the age range of 13–35 so they would not be too many years beyond the times of their milestones. Also, to limit recall bias subject responses were verified with information in our medical records. Given that some of the participants had undergone new evaluation for tics as adults, our observed rate of reported tic remission may have been subject to referral bias. We did not retain data about the patients who declined to participate, so it is not possible to rule out some degree of selection bias. Investigator bias related to an expectation of finding tic, ADHD and OCD peaking and remission may have been introduced by the framing of the questions used in our survey. This may have resulted in unintended leading questions or conferring excess recall bias in favor of reporting remission of symptoms. We also did not consider medication treatment in our analyses and medications might potentially influence course of symptoms. Nevertheless, this study included the largest sample size to date that specifically investigated the natural course of TS and particularly comorbid ADHD and OCD and despite potential limitations provides new and important information.

Our study confirms previously reported data regarding the natural course of TS and provides new information about reported tic remission and the course of the common comorbidities ADHD and OCD. Until more objective, larger scale, and prospective research on the temporal course of TS can be completed, this data on the natural course of the TS triad can inform the design of experimental therapeutic trials aimed at improving the rate or time frame of remission of the illness.

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