Course of Tic Severity in Tourette Syndrome: The First Two Decades

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ABSTRACT. *Objective.* **Prevalence studies indicate a 10-fold higher rate of Tourette syndrome (TS) among children compared with adults. The purpose of this investigation was to examine the course of tic severity during the first 2 decades of life.**

Method. **A birth-year cohort of 42 TS patients followed at the Yale Child Study Center was recontacted an average of 7.3 years after their initial clinical evaluation. Data concerning the onset and course of tic severity until 18 years of age were available on 36 TS patients. A variety of statistical techniques were used to model aspects of the temporal patterning of tic severity.**

Results. **Mean (SD) tic onset at 5.6 (2.3) years of age was followed by a progressive pattern of tic worsening. On average, the most severe period of tic severity occurred at 10.0 (2.4) years of age. In eight cases (22%), the frequency and forcefulness of the tics reached a severe level during the worst-ever period such that functioning in school was impossible or in serious jeopardy. In almost every case this period was followed by a steady decline in tic severity. By 18 years of age nearly half of the cohort was virtually tic-free. The onset of puberty was not associated with either the timing or severity of tics.**

Conclusions. **A majority of TS patients displayed a consistent time course of tic severity. This consistency can be accurately modeled mathematically and may reflect normal neurobiological processes. Determination of the model parameters that describe each patient's course of tic severity may be of prognostic value and assist in the identification of factors that differentially influence the course of tic severity.** ***Pediatrics*** **1998;102:14–19;** ***Tourette syndrome, natural history, growth curve analysis, puberty.***

ABBREVIATIONS. TS, Tourette syndrome; YCSC, Yale Child Study Center Tic Disorders Clinic; ADHD, attention deficit-hyperactivity disorder; OCD, obsessive-compulsive disorder; CGI, Clinical Global Impression (scale); SES, socioeconomic status; YGTSS, Yale Global Tic Severity Scale; ARRTS, annual rating of relative tic severity; STOBS-R, Schedule for Tourette and Other Behavioral Syndromes, Adult-on-Child Version, Revised; MSRPF, Modified Schedule for Risk and Protective Factors.

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Epidemiologic studies have indicated a higher prevalence rate of Tourette syndrome (TS) among children compared with adults. In children, prevalence rates as high as 50 per 10 000 have been reported.[1,2] Studies of adolescents and young adults have reported lower rates in the range 0.5 to 4.3 per 10 000.[3–5] In the one study that ascertained rates for both children and adults, using identical methods, a 10-fold difference was observed.[4,6] The reasons underlying this change in prevalence are not well-understood but likely reflect age-related variations in the natural history of the disorder that directly affect case ascertainment.[7,8]

By early adulthood, follow-up studies have consistently reported improvement in tic severity for a majority of TS patients.[9–11] Although a rough time course of tic severity has emerged, age-specific estimates of tic severity have not been reported. Typically, natural history studies of TS have included patients across a broad age range with widely varying follow-up intervals.[12] This cross-sectional, observational approach combined with the failure of most studies to identify key time points in the course of tic severity has made cross-patient comparisons difficult.

Gender- and stress-related hormonal factors have been implicated in the pathogenesis of TS.[13–16] Although speculation has focused on the role of gonadal androgens during the earliest stages of central nervous system (CNS) development in utero,[16,17] anecdotal case reports and evidence from clinical trials with antiandrogens support the view that alterations in the hormonal milieu during adolescence and adulthood can modulate tic severity.[18–20]

The present study was undertaken to document the time course of tic severity during the first 2 decades of life using data from a single birth-year cohort of TS patients. A birth cohort was selected to maximize our ability to make developmentally uniform cross-patient comparisons. In our analytic approach, we used a variety of statistical procedures to model these data to estimate the age of tic onset, the age when the tics were at their worst, as well as other model parameters. This model was then used to evaluate the a priori hypothesis that pubertal onset is associated with either the timing or degree of worst-ever tic severity.

METHOD

Subjects

Subjects in this study consisted of 36 patients with TS who had been diagnosed and evaluated at the Yale Child Study Center

(YCSC) Tic Disorders Clinic. Subjects were selected on the basis of their participation in a case-control study of TS in which extensive data were collected concerning the time course of tic severity. This study identified all TS patients born in 1975 who had ever been evaluated at this YCSC clinic. All patients were initially diagnosed with the *Diagnostic and Statistical Manual of Mental Disorders*, 3rd ed (DSM-III) or 3rd ed, revised criteria for TS using previously described methods.[21] A total of 42 TS cases were ascertained. Of this number, 36 cases (86%) had sufficient information to be included in these analyses (32 males and 4 females).

Procedures and Measures

Demographic and clinical information was collected from four sources: the clinic chart, a preliminary telephone interview with a parent, two in-person interviews with a parent, and an in-person interview of the TS patient.

Chart Review

A clinician with extensive experience with TS families (K.L.) abstracted information from the clinical record using a precoded form. Data recorded included demographic information; diagnostic status with regard to TS, attention deficit-hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and other comorbid conditions; and age of onset and severity at presentation of TS, ADHD, and OCD. Severity ratings were made using eight point ordinal Clinical Global Impression (CGI) scales previously developed at the YCSC for each of these disorders.[21] Relevant points on the TS-CGI scale include: *mild severity,* where the tic symptoms are judged not to interfere and not to be noticeable to most people; *moderate severity,* where the tics cause some problems in some areas of functioning (self-esteem, home life, peers relations, and/or school performance) and are noticeable to some people outside the family some of the time; *marked severity,* where the tic symptoms cause clear problems in more than one area of functioning and are frequent and quite noticeable in most situations most of the time; and *severe,* where the tic symptoms because of their frequency and forcefulness cause significant impairment in one or more area, such that functioning in usual settings is impossible or in serious jeopardy.

One clinic chart could not be located, but the case was clearly identified in the clinic roster permitting the case to be recontacted. In 10 randomly selected cases, another member of the research team (J.F.L.) independently reviewed the same record. Comparisons of age at evaluation, diagnostic status, age of onset, and scores on the respective CGI scales revealed a high level of agreement (Pearson correlations for age of tic onset and age at evaluation were $r = 0.98$ and $r = 0.83$, respectively). The interrater agreement for a diagnosis of TS was perfect, and the κ statistic values for the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed (DSM-IV) diagnoses of OCD and ADHD were excellent (0.83 and 0.77, respectively). The Spearman rank order correlations for the CGI scores were also excellent (ranging from $\rho = 0.79$ to $\rho = 1.00$). A comparison of data abstracted from the initial clinic evaluations of the 36 cases included in this analysis and the 6 remaining cases revealed no statistically significant differences with regard to age at evaluation, sex, socioeconomic status (SES), age of tic onset, or tic severity at initial evaluation.

Initial Follow-up Interview

After an initial letter describing the study and requesting consent, parents were contacted by telephone and inquiries were made concerning current demographic information; the history of the family's contact with the YCSC Tic Disorders Clinic; data concerning their child's tic disorder (age of onset, age when tics were at their most severe, medication history, and a rating of current tic severity using the Yale Global Tic Severity Scale [YGTSS][22]; comparable data concerning ADHD and OCD; and data concerning the onset and duration of puberty). The YGTSS is a standard clinical rating instrument for TS with excellent interrater agreement and other favorable psychometric properties including a high correlation with the TS-CGI scale.[22] A slightly modified and expanded form of the YGTSS was used in the telephone interview portion of the study.[23] This version has previously been shown to have a high level of agreement with YGTSS ratings independently made by experienced clinicians.[23,] At the conclusion of the interview, families were invited to participate in a more in-depth in-person interview to take place in the family's home. Interviewers were blinded to the information abstracted from the chart record.

Parent Interviews

After signed informed consent, parents participated in four semistructured in-person interviews. In the first interview, parents again reported on the course of their child's tic disorder (ratings of current and worst-ever tic severity using the YGTSS, annual rating of relative tic severity (ARRTS) using a 6-point ordinal scale (absent, least severe, mild, moderate, severe, and most severe) from which age of tic onset, and age of most severe tic symptoms were transcribed, and a current medication history). During the second interview, parents reported on comorbid conditions using a semistructured interview, the Schedule for Tourette and Other Behavioral Syndromes, Adult-on-Child Version, Revised (STOBS-R) that has been extensively used in family-genetic studies.[24,25] The STOBS-R also contains information concerning the onset of puberty. The third interview focused on putative risk factors, a main focus of the formal case control study, and used the Modified Schedule for Risk and Protective Factors (MSRPF) developed by John T. Walkup, J.F.L., and B.S.P.[26] In the final interview, parents were asked about their own tic histories as well as other psychopathology using the STOBS-R, child version. Because of the requirements of the case control study, different interviewers conducted the MSRPF and remained blinded to the information concerning tic severity. The results of the case-control aspects of this study will be reported elsewhere.

Patient Interview

The TS patient was interviewed in-person using the STOBS-R. This information was supplemented by current and worst-ever ratings of tic severity based on the YGTSS.

Best Estimate Diagnoses

All available diagnostic information on TS patients and their parents were blindly and independently evaluated by two investigators (J.F.L. and B.S.P.). The resulting DSM-IV diagnostic ratings were compared and discrepancies were resolved using a previously described consensus procedure.[27]

Data Analysis

Data analysis was conducted in several stages. An initial aim was to describe the sample and compare ratings across the three time points (clinical evaluation, initial follow-up interview, and in-person interviews with parents and patients). The test-retest reliability of key ratings of tic onset, timing of worst-ever tic severity, current and worst-ever tic severity (using the YGTSS) were then evaluated in an effort to validate the ARRTS.

Examination of the time course of the tic severity curves derived from the ARRTS ratings for individual TS patients led to the development of a mathematical model of tic severity characterized by the identification of an initial point of tic onset, followed by a period of increasing tic severity, followed by an inflection point (corresponding to the period of worst-ever tic severity), after which the tic severity steadily declined. A statistical bootstrapping technique was then used to assess the variability of the estimates for each model parameter.[28]

Once this model was established, the hypothesis that the course of tic severity is related to the timing of puberty onset was evaluated by including the main effect of the age of puberty onset and its interaction terms in the model. This computation was carried out in SAS using PROC MIXED (SAS, Cary, NC).

RESULTS

On average, the 36 members of the YCSC 1975 birth cohort were evaluated at age 11.0 years (range: 5.9–16.9; SD: 2.9). The initial telephone follow-up interview occurred when the TS patients were, on average, 17.7 years of age (range: 17–20; SD: 0.7); and the in-person interviews with the parents and the TS patients took place when the patients were, on average, 18.4 years of age (range: 17–20; SD: 1.0). The average interval between the initial YCSC evaluation

and the in-person interviews was 7.5 years (range: 1.2–12.1; SD: 2.7). All 36 patients met DSM-IV criteria for Tourette disorder. Of this number, 25 (69%) met lifetime DSM-IV criteria for ADHD (combined type–16 (44%), inattentive type–8 (22%), and hyperactive/impulsive type – 1 (3%)). Another 13 (36%) cases met lifetime DSM-IV criteria for OCD. Most the families were middle-class. The mean SES status of the families was 47.9 (range: 27–64; SD: 10.6).

Current Tic Status

At the time of the in-person interviews, when the TS patients were 18 years of age, tic symptoms for a majority of the 36 cases were minimal or absent. On average, the total tic score of the YGTSS assessed at the time of the in-person interviews with the parents and patients was 7.92 (actual range: 0–30 [possible range: 0–50]; SD: 9.53). Seventeen patients (47.2%) were entirely tic-free during the week before the in-person interviews. Another 4 patients (11.1%) had minimal tic symptoms (YGTSS total tic score of <10). Ten patients (27.7%) had mild symptoms (YGTSS total tic score of ≥ 10 but <20), and only 4 patients (11.1%) were judged to have a moderate or marked level of tic severity (YGTSS total tic score of ≥ 20 but <40).

Severity and Timing of Tics During the Worst Period

On average, the worst-ever total tic score on the YGTSS estimated at the time of the in-person interview was 29.8 (range: 4–49; SD: 10.9). Based on the frequency and forcefulness of their tics, 8 patients (22.2%) were judged during their worst period to have severe tics (YGTSS total tic scores ≥ 40 but <50) that were associated with a significant impairment in their primary social role such that functioning in usual settings was impossible or placed in serious jeopardy. Ten patients (27.8%) were judged during their worst period to have marked tic severity (tics frequent and quite noticeable in most situations most of the time; YGTSS total tic scores ≥ 30 but <40). Fourteen patients (38.9%) were judged during their worst period to have moderate tic severity (tics cause some problems and are noticeable to some people some of the time; YGTSS total tic scores ≥ 20 but <30). Only 4 patients (4.0%) were judged to have a mild level of tic severity during their worst period (YGTSS total tic score of <20).

Based on data collected during the initial telephone follow-up and the in-person interviews, the worst tics occurred between the ages of 6 and 15 years (mean: 10.0; SD: 2.4). Figure 1 presents a histogram of these data by year. The level of tic severity during the worst period was positively associated with the patient's age during the worst-ever period (Fig 2; Pearson $r = 0.58$, $N = 34$, $P < .0001$).

Predictive Value of Earlier Estimates of Tic Severity

Nine cases were judged to have mild tics during their initial clinic evaluation. Among this group, 3 cases continued to have only mild symptoms during their worst period. In each of these cases, no tics were evident at the time in-person interviews. In another 4 of the initially mild cases, their worst-ever tic severity was rated as moderate, and at the time of the in-person interviews tics were either absent ($N = 2$), minimal ($N = 1$), or mild ($N = 1$). Surprisingly, 2 cases judged to have mild tic severity at their YCSC evaluation were judged to have severe tic severity during their worst period, but fortunately in both cases at the time of the in-person interviews, their tic symptoms were either mild ($N = 1$) or moderate ($N = 1$) in severity.

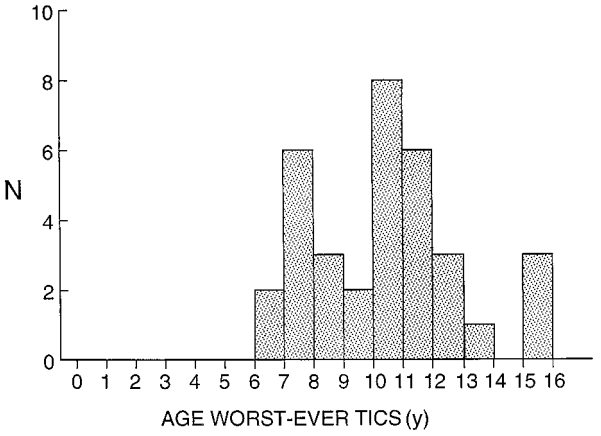

Fig 1. Age distribution of when tic symptoms were at their worst. This histogram presents the age at worst-ever tics as reported by parents during in-person interview.

Sixteen cases were judged to have moderate tic severity at the time of their initial YCSC evaluation. Among this group, 7 cases were judged to have either moderate ($N = 6$) or mild ($N = 1$) tic severity at the time of their worst symptoms. At the time of the in-person interviews, 5 of these cases were tic-free, 1 case had mild symptoms, and only 1 case continued with a moderate level of tic severity.

Of the 9 initially moderate cases remaining, 6 were judged to have marked tic severity during their worst period and 3 were judged to have severe tics. In this subgroup at the time of the in-person interviews, 1 case showed no tic symptoms, 3 had minimal symptoms, 4 had mild, and only 1 case continued with a moderate level of tic severity.

Ten cases presented at the time of their initial YCSC evaluation with a marked level of tics. Seven of these cases were judged to have either moderate ($N = 3$) or marked ($N = 4$) tic severity at the time of their worst symptoms. In this subgroup, 3 cases were tic-free at the time of the in-person interviews, three cases were rated has having mild tic severity, and in only 1 case did the tic severity remain at a marked level. The 3 remaining cases with marked severity at the time of their initial evaluation all had severe tic symptoms during their worst period. Remarkably, 2 of these cases showed no tic symptoms during their in-person interviews, and the remaining case had a mild level of tic severity at follow-up.

Tic severity at initial YCSC evaluation was not related to worst or current tic severity (worst: $F = 2.66$, $df = 2$, NS; current: $F = 0.05$, $df = 2$, NS). However, current tic severity was significantly correlated with both tic severity at the time of the initial telephone follow-up interview (Pearson $r = 0.66$, $P <$

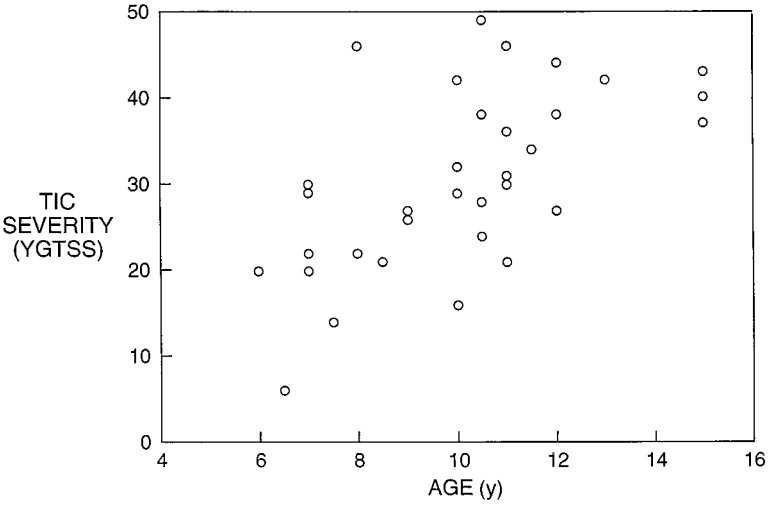

Fig 2. Association of age and level of worst-ever tic severity. This scattergram plots worst-ever tic severity versus age at worst-ever tic severity and suggests a positive association between these variables (Pearson r: 0.58, $N = 34$, $P < .0001$).

.0001) and with worst tic severity (Pearson $r = 0.37$, $N = 36$, $P < .03$).

Time Course of Tic Severity Ratings

A majority of TS patients displayed a consistent time course of tic severity. This consistency can be accurately modeled mathematically and may reflect normal biological processes that occur during the course of brain development. Using the ARRTS data collected at the time of the in-person interviews, individual growth curves of tic severity were generated. Figure 3 presents the mean and SDs of these curves.

In an effort to validate key points along this composite curve, test-retest comparisons were made between the age of onset estimates made at the time of the initial YCSC evaluation, at the initial telephone follow-up interview, and the onset point derived from the ARRTS curves. The mean values for each of these estimates showed a high level of agreement (mean [SD] age of tic onset: estimated from the chart review: 5.8 years (1.7); from the initial telephone follow-up interview: 5.8 years (2.8); and from the ARRTS curves: 6.0 (2.7)). The test-retest reliability of these estimates was reasonably good (ARRTS estimate vs initial telephone follow-up: Pearson $r = 0.67$, $N = 31$, $P < .0001$; and ARRTS estimate vs chart review data: Pearson $r = 0.58$, $N = 32$, $P < .0001$). Fewer estimates were available to judge the test-retest reliability of the age of worst tic symptoms. The mean values for each of these estimates showed a good level of agreement (mean [SD] age of worst tic severity estimated from the initial telephone follow-up interview: 10.0 years (2.4); and from the ARRTS curves: 10.8 (3.1)). However, the test-retest reliability of these estimates, was only fair (ARRTS estimate vs initial telephone follow-up: Pearson $r = 0.48$, $N = 31$, $P < .007$).

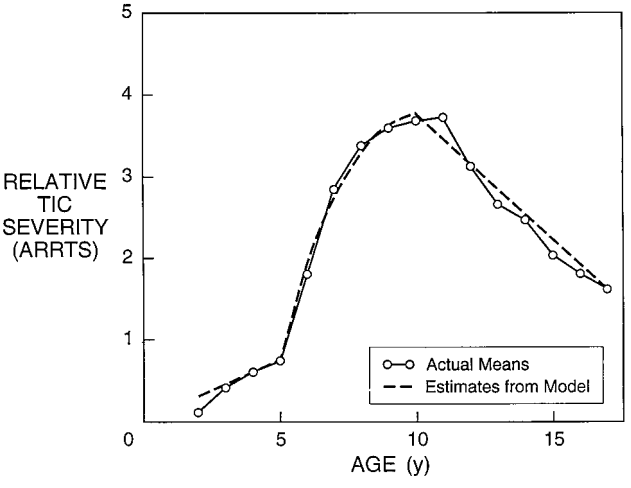

Fig 3. Plot of mean tic severity, ages 2 to 18 years. The solid line connecting the small circles plots the means of the annual rating of relative tic severity scores (ARRTS) recorded by the parents. The dashed line was generated using the modeling equations (Table 1) and the mean values for each of the coefficients and intercepts as determined by a statistical bootstrapping technique. Two inflection points are evident that correspond to the age of tic onset and the age at worst-ever tic severity, respectively.

Descriptively in 2 of the TS cases, the ARRTS curves had 2 points of maximal severity (relative tic severity = 5) separated by a period of 1 year or longer when the symptoms were not as severe. In both cases, rather than taking a mean value of these 2 points (and by doing so identifying a point in time when their tics were not as bad as either of the worst-ever points) a convention was established so that a worst-ever time point was selected on the basis of which period was of the longer duration. In another 5 cases, parents identified relative maximums in tic severity (relative tic severity <5) indicating a fluctuating course.

Mathematical Model of the Time Course of Tic Severity

Given the consistent time course of tic severity across patients, we formulated a mathematical model to describe precisely this pattern. This process is akin to comparing a patient's growth curve for height or weight to a composite curve for a larger number of patients. Based on an examination of the individual and composite ARRTS plots, the ARRTS

data were partitioned into three segments. Let t denote age in years. The tic time course, $f(t)$ is characterized by:

$$f(t) = \begin{cases} \alpha t & \text{if } t \le \tau_1 \\ \beta_0 + \beta_1 t + \beta_2 t^2 & \text{if } \tau_1 < t \le \tau_2 \\ \gamma_0 + \gamma_1 t & \text{if } t > \tau_2 \end{cases} \quad (1)$$

where τ_1 refers to the age-at-onset and τ_2 is closely related, but not necessarily equal, to the age at which their tics were at their worst. Table 1 displays the parameter distributions of the tic time course function obtained from the bootstrap procedure.[28] A plot of this function is included in Fig 3. Individual growth curves were also generated. Mean values for each of the parameters obtained from individual curves were in close agreement with estimates obtained by bootstrap methods.

Timing of the Onset of Puberty and the Course of Tic Severity

The present study was undertaken, in part, to evaluate the a priori hypothesis that pubertal onset is associated with the period of worst-ever tic severity. This hypothesis was not supported in this group of patients. Age at pubertal onset was not associated with the age when the tics were at their worst (r = 0.02, NS) or degree of worst-ever tic severity (r = 0.08, NS). Similarly, when the timing of puberty onset was included in the time course model (Fig. 3), neither its main effect nor its interactions with any of the other parameters were significant.

In an effort to validate the age of pubertal onset, test-retest comparisons were made between the age of pubertal onset estimates made at the time of the initial telephone follow-up interview and during the in-person parental interview. The mean values for each of these estimates showed a high level of agreement (mean [SD] age of puberty onset: estimated from the initial telephone follow-up interview: 13.0 years (1.3); and the direct parental interview: 13.7 (1.7)). The test-retest reliability of these estimates was also reasonably good (direct parental interview estimate vs initial telephone follow-up: Pearson $r = 0.67$, $N = 31$, $P < .0001$).

DISCUSSION

The natural history of TS and other chronic tic disorders is not well-understood. In this report we present an explicit model of the time course of tic severity over the first 2 decades of life. This model extends the findings of previous follow-up studies by offering age-specific tic severity estimates and by defining a period of maximal tic severity that usually occurs between the ages of 8 and 12.[7–11] If confirmed, this pattern of ascending severity followed by a near linear decline may also clarify the differences in TS prevalence that are found when adult versus child populations are studied using similar methods.[4,6] By early adulthood, tic severity may have declined sufficiently that a TS diagnosis may no longer be warranted.

TABLE 1. Parameters for the Time Course of Tic Severity Function

Parameters	Mean (SD)
Age at onset (τ_1)	4.8 (0.50)
Age when tics were at their worst (τ_2)	9.9 (0.85)
Onset slope (α)	0.15 (0.05)
Intercept for quadratic function (β_0)	−11.9 (8.6)
Ascending slope (β_1)	3.5 (2.4)
Ascending quadratic coefficient (β_2)	−0.19 (0.16)
Intercept for linear decline (γ_0)	6.5 (1.1)
Slope for linear decline (γ_1)	0.29 (0.07)

Before discussing the clinical implications of this study and its potential value, we should take note of its limitations. Recall bias may have influenced the parents' and the patients' reporting. Our use of test-retest procedures to determine the reliability of key informants and the use of blinded interviews of multiple informants (parents vs patients) support the accuracy of our findings. The documented decline in the YGTSS ratings from the initial telephone follow-up to the time of the in-person interviews directly supports the validity of the ARRTS ratings. Likewise, the consistency of the parental reports (in only 3 cases was there an inconsistency between the level of tic severity observed at evaluation and the family's estimate of tic severity during the worst period) lends support to validity of the time course of tic severity that emerges from this report.

A limitation concerning the mathematical modeling approach is that in a small number of cases (N = 2) more than one worst-ever time point was reported. In 5 other cases, relative maximums in tic severity were reported. Rather than seeing these as exceptional cases, it is probably better to consider the unimodal distributions of relative tic severity (seen in all the remaining cases) as being composed of multiple relative maximums in tic severity that are undetectable at this level of temporal scaling. This view is supported by the well-known waxing and waning pattern of tics that occur over weeks to months. This discussion raises the potentially important point that the temporal occurrence of tics may be determined by nonlinear dynamical processes.[29] One of the characteristic features of these nonlinear, chaotic, systems is that they are fractal in nature—that regardless of the temporal scaling (seconds, hours, weeks, months, years) a similar bursting intermittency is evident.[30] The tics occur in bouts, the bouts of tics occur in larger superbouts, and so forth. Viewed from this perspective, the unimodal tic severity curves seen in this study may be a reflection of the same processes that underlie both the occurrence of tics in bouts (temporal scaling at the level of seconds and milliseconds) and their waxing and waning pattern (temporal scaling at the level of weeks to months).

The processes that underlie tic onset and the usual time course of tic severity are largely unknown. Hormonal and neurochemical factors active early in CNS development have been the subject of speculation.[16,17,31] For example, exposure of the developing CNS to gonadal steroids has been implicated.[17–19] Although indirect evidence from this study may argue against increasing levels of gonadal androgens during male pubescence as a major risk factor for tic exacerbation, the complexity of hormonally medi-

ated events in the brain surrounding adrenarche and puberty urge caution.[32] The consistency of the pattern observed across patients strongly suggests the presence of an underlying process. It is intriguing to speculate that this time course may reflect neurobiological events that normally occur during the course of brain development and that are overtly expressed only because of the patient's TS vulnerability.

Caution is warranted in the interpretation of the data concerning puberty onset because these data were not ascertained directly by physical examination or Tanner staging. If confirmed in subsequent studies, the data presented in this report may influence clinical practice. In our experience, families find comfort in the realization that tic severity will likely decline through adolescence. Such knowledge is likely to help families and pediatricians live with the tics and to delay the decision to begin psychotropic medications. Ages 8 through 12 are likely to be critical. If medications can be avoided through this period, the patient may have a good chance of never needing them. Although anti-tic medications are available, none are ideal. Over the longer term, starting medications may do more harm than good, given their potential adverse effects and the difficulties associated with medication withdrawal. This is particularly true of the standard neuroleptic agents such as haloperidol and pimozide.[33]

As discussed by Goetz and co-workers,[8] it is important to be mindful that tic severity early on is not necessarily a good predictor of later tic severity. For example, 20% of the mild cases at clinic evaluation, went on to have severe tics. More importantly, 90% of the patients with marked tic severity at evaluation had mild or no tics by 18 years of age. The finding of an association between age of the patient when their tics were at their worst and the level of tic severity during that same period may have limited predictive value except when older adolescents present with severe tic symptoms—heralding a relatively poor prognosis.

The results of this study only extend to the end of the second decade. A minority of TS patients go on to have catastrophic outcomes in adulthood. Whether any of the parameters examined in this study have predictive value for the early identification of these individuals awaits further investigation.

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