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We've all been wrong about Provisional Tic Disorder

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Abstract

Background: Provisional Tic Disorder (PTD) is common in childhood. The received wisdom among clinicians is that PTD is short-lived and mild, with at most a few tics, and rarely includes complex tics, premonitory phenomena or comorbid illnesses. However, such conclusions come from clinical experience, with biased ascertainment and limited follow-up.

Methods: Prospective study of 89 children with tics starting 0–9 months ago (median 4 months), fewer than half from clinical sources. Follow-up at 12 (± 24, 36, 48) months after the first tic.

Results: At study entry, many children had ADHD (39), an anxiety disorder (27), OCD (9) or enuresis (17). All had at least two current tics, with a mean total since onset of 6.9 motor and 2.0 phonic tics. Forty-one had experienced a complex tic, and 69 could suppress some tics. Tics were clinically meaningful: 64 had tics severe enough for a clinical trial, and 76 families sought medical attention for the tics.

At 12 months, 79 returned, and 78 still had tics. Of these, 29 manifested no tics during history and extended examination, but only via audio-visual monitoring when the child was seated alone. Only

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Conflicts of interest

No relevant conflicts.

12/70 now had plans to see a doctor for tics. Most who returned at 2–4 years still had tics known to the child and family, but medical impact was low.

Conclusions: Our results do not contradict previous data, but overturn clinical lore. The data strongly argue against the longstanding but arbitrary tradition of separating tic disorders into recent-onset versus chronic.

Keywords

Tourette syndrome (MeSH); Tic disorders / classification (MeSH); Tic disorders / psychology (MeSH); Provisional Tic Disorder

1. Introduction

Tourette's disorder (Tourette syndrome, TS) is defined by tics—brief, repetitive unwanted movements or vocalizations—that develop in childhood and have persisted for at least a year [1]. About 1 in 200 children age 5–14 years old have TS [2–6]. However, tics are much more common, affecting at least 20% cross-sectionally and arguably most children over time [7, 8]. These observations, taken together, have led to the conclusion that tics usually disappear after a few months. When tics have lasted for less than a year, Provisional Tic Disorder (PTD) can be diagnosed. A major concern of parents is whether the recent onset of tics heralds a transient or a chronic tic disorder.

The received wisdom among clinicians has been that PTD is generally short-lived and mild, includes few tics, and rarely includes complex tics, premonitory phenomena, or comorbid illnesses [7, 9]. However, such conclusions come from clinical experience, which unfortunately is necessarily biased. Many tics go unnoticed or are attributed to allergies, hyperactivity, or other problems. Parents are less likely to take a child with mild tics to a physician. Additionally, symptoms other than tics are quite frequent in these children; "the majority of patients do not seek help for the tics but rather for other problems" [10]. The most common co-occurring conditions are ADHD and OCD, but anxiety disorders are also quite common [11]. Thus many children with tics are not diagnosed within the first year after tic onset. For instance, half of children with ADHD have tics [12], yet many fewer are diagnosed with tics. Therefore, the conclusions clinicians draw from their experience are strongly affected by sampling bias. Clinical follow-up is perhaps even more biased, as "these patients, characteristically, do not return for follow-up contacts" [13]. They may not return because tics improved, but parents also may have become accustomed to the tics or no longer feel anxious about them. Thus, clinicians may erroneously assume a full remission even when tics persist.

Given these biases, only a prospective study can accurately describe the features of PTD: a study that records tic severity, tic distribution, and comorbidities, both near tic onset and over an extended period of time, with special attention to persistence and remission. We conducted the New Tics study, enrolling children whose tics had begun 0–9 months before a screening visit at which several clinical, psychological, and biological measures were collected, and following these children for several years [14]. For comparison, we enrolled participants of the same age who had already had tics for at least one year, and children with

no tics. We have previously reported some of the findings from about half the patients at one year after tic onset [9, 15–17]. However, several additional clinical observations surprised us as we completed data collection from the full sample, including data from a subset seen in follow-up 2–4 years after tic onset. Here, we report novel, clinically focused analyses from the New Tics study that we believe will be of substantial practical interest to clinicians and support a change in the accepted nosology of tic disorders.

2. Methods

2.1 Subjects

The New Tics study was conducted at Washington University in St. Louis, and used a longitudinal design to investigate recent-onset tics. We actively recruited from 2010–2022 using physician referrals, flyers in public locations, school district e-flyers to parents, electronic medical records search, search engine advertising, and word of mouth. These methods were designed to recruit children with recent onset of tic disorder, many of whom do not come to immediate medical attention for the tics. We enrolled children aged 5–10 years into one of three groups: (1) the NewTics group: children with tic onset 0–9 months before the first study visit; (2) the TS/CTD group: children experiencing tics for at least one year and met criteria for either Tourette's Disorder or Persistent Tic Disorder; (3) the tic-free control (TFC) group: children who after parent and self-reported history, clinical examination, and audiovisual observation had no tics or immediate family member with tics. Though not an aspect of the original study design, we additionally started to track a fourth group, (4) the LaterPTD group: children with tic onset 9 to 11.5 months before the baseline visit.

2.2 Ethics approval

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the Washington University Human Research Protection Office (IRB), protocol numbers 201109157 and 201707059. Each child assented and a parent (guardian) gave informed consent.

2.3 Protocol

The study protocol was registered after the first, pilot sample was enrolled (https://osf.io/cdx3n; 03 Oct 2016), and methods were described previously [14].

Participants in the NewTics group completed a baseline visit within 9 months of tic onset. They returned at the 1-year anniversary of their first tic (as nearly as possible). Those enrolled after the pilot sample were also asked to return at the 2-, 3- and 4-year anniversaries of their tic onset. Public health measures for the COVID-19 pandemic prevented some of these later follow-up visits.

The TS/CTD group completed a screening visit with the same procedures as the NewTics group and a follow-up visit at the 12-month anniversary of the tic onset of the NewTics participant they were matched to in terms of age, sex, and handedness.

The TFC group completed a screening visit and a 12-month follow-up visit that coincided with the 12-month anniversary of the tic onset of the NewTics participant they were matched to. Parents of the TFC participants were asked to complete an annual online survey (up to 4 years) about possible development of tics or any other new conditions.

The LaterPTD group, with tic onset 9–11.5 months before the screening visit, returned for a follow-up visit 3 months after screening, and were invited to return at the 2–, 3–, and 4–year anniversaries of their tic onset.

2.4 Assessments

2.4.1 Screening visit—Demographic information was collected including medical and surgical history, maternal and birth history, socioeconomic status, family history of tics, ADHD, and OCD, and descriptions of both current and past symptoms experienced by the participant. Study data were collected and managed using REDCap electronic data capture tools hosted at Washington University in St. Louis [18, 19]. Surveys completed by the parent or guardian, with a recommendation to involve the child, included the Edinburgh Handedness Inventory [20], the Barratt Simplified Measure of Social Status [21], parent-rated adaptations of the Yale Global Tic Severity Scale (YGTSS) and CY-BOCS (current and worst ever) [22], ADHD Rating Scale [23] rated for the time in the child's life when ADHD symptoms were most severe ("lifetime worst"), Social Responsiveness Scale (SRS) [24], Child Sensory Questionnaire (adapted from the Adult Sensory Questionnaire) [25], the American Psychiatric Association DSM–5 Parent/Guardian-Rated Level 1 Cross-Cutting Symptom Measure, Pediatric Quality of Life Inventory™ (PedsQL) [26], Child Behavior Checklist (CBCL) ages 6 through 18 (or Y-CBCL Age 5) [27], and the Premonitory Urge Tics Scale (PUTS) [28].

A standard tic suppression protocol (TSP) was performed with a clinician observing by remote video as the child sat alone under several 5-minute conditions: tic freely, verbal request not to tic ("verbal"), immediate reward for every disjoint 10-second period without a tic (Differential Reinforcement of Other behavior, DRO), and, in some participants, a non-contingent response (NCR) condition that presented the same number and timing of rewards as occurred in the DRO condition regardless of tic occurrence during the NCR session [29]. Further details appear in ref. [15].

Other assessments administered by staff at baseline included K-SADS-PL, a semi-standardized diagnostic interview with separate child and parent interviews [30], Purdue Pegboard test [31, 32], Kaufman Brief Intelligence Test Second Edition (KBIT-2) [33], the Conners Continuous Performance Test II (CPT-II) [34], a probabilistic classification task [35], and for later participants, the Physical and Neurological Examination for Subtle Signs [PANESS; 36]. The investigator (author KJB, for > 95% of study visits) performed a brief neurological exam and completed the following measures: Diagnostic Confidence Index (DCI) [37], ADHD Rating Scale (ARS), CY-BOCS [38], questions about tic outcome, and

the YGTSS [39]. For later participants, the YGTSS was rated both before and after the TSP, in which case analyses used the post-TSP YGTSS ratings.

We invested substantial effort into determining as accurately as possible the date of tic onset [15]. We sought information on tic start date in semi-standardized interviews with the child and parent separately. We specifically asked them to consider major life events, birthdays, and holidays, we asked them to look up the date of physician visits, and we asked whether teachers had observed tics. We asked the parents to examine any home videos. When this information led to a range of possible onset dates, such as "after Thanksgiving, but before New Year's," the investigator chose a most likely start date within that "confidence range." After the first few participants, the investigator also began recording the beginning and ending date of that range.

Diagnoses for ADHD, OCD, and tic disorders were determined by two methods. In addition to the K-SADS-PL diagnoses, author KJB recorded a clinical diagnosis based on all data collected prior to and during the visit, including the K-SADS interviews.

2.4.2 Follow-up visits—Measures and assessments administered at most follow-up visits included the PedsQL, CBCL, Premonitory Urge Tics Scale, parent-rated CY-BOCS, medical history since the previous visit, a brief neurological exam, YGTSS (before and after the TSP), standard CY-BOCS, ARS, DCI, and the TSP.

After several participants had enrolled, we added questions about clinically relevant tic outcomes, such as "Are you planning to take your child to the doctor now or in the near future because of tics?" (also counted as positive if there was a recent such visit). We defined tics as "clinically meaningful" at a given visit if any of the following criteria were true: YGTSS total tic score (TTS) > 13 (an inclusion criterion for a large TS clinical trial) [40], YGTSS impairment score of 20 ("mild") or higher, parent planning to take child to the doctor because of his or her tics, or clinician judgment that in the week prior to the visit, tics impaired function in a life role or caused marked distress.

Late in the study, follow-up visits were shortened due to pandemic safety restrictions, and thereafter included only the PedsQL, PUTS, parent-rated CY-BOCS and ARS, medical history, DCI, outcome data, a single 5-minute remote observation of the child sitting alone in the room (free to tic), and YGTSS ratings both before and after that 5-minute observation. The clinician also reviewed psychiatric history since the previous visit and updated diagnoses as needed.

2.5 Tic diagnosis

Author KJB recorded final diagnoses for tic disorders, as described above. Prior to mid-2017, tic diagnosis was by DSM–IV–TR criteria, a few children ages 11–14 were enrolled, and potential participants discovered to have tic onset > 6 months prior to screening were excluded unless their prior tic history consisted only of a single possible tic, over a year prior, lasting for no more than 2 months. After mid-2017, participants in the New Tics group had DSM–5 PTD with tic onset ≤9 months prior to screening.

2.6 Statistical analyses

Descriptive statistics, group comparisons and correlations were conducted using Excel (version 2016) or R Studio (R version 3.6.1, 2019-07-05).

3. Results

Eighty-nine NT participants enrolled in the study, with a mean duration since tic onset of 118.3 days (median 111, range 22–268; Figure S1). The mean confidence range around tic duration was 28.8 days (median=16.5, range=0–123, N=72); *i.e.*, for half of participants, the onset date was felt to be accurate within 8 days (Figure 1A). Two of the 89 participants were initially scheduled as TFC (*i.e.,* on a brief screening telephone call, parents knew of no current or past tics), but were moved to the NT group when tics were observed at the screening visit (see Table S3). Nineteen participants were scheduled as NT, but enrolled as TS/CTD when a longer tic history was identified at the screening visit, an indication of how carefully we worked to assess onset date. Similarly, 3 participants were reassigned at screening from TFC to TS/CTD, and 1 from TS/CTD to LaterPTD.

Seventy-nine of the 89 NT participants returned at 12 months. Two additional participants returned at 24 or 36 months, and parents of 4 more children reported tics on a phone call scheduled 3 months after the screening visit, leaving only 4 children with no follow-up.

Table 1 summarizes participant characteristics other than tics. Most had ADHD (39), an anxiety disorder (27), enuresis (17) or OCD (9). Average ASD symptom scores were near the population mean (SRS T-score 50.4 ± 10.0). The average PANESS score was higher than has been reported for children with autism (p=.02) or ADHD (p<.0001) [41], though that study excluded most psychiatric comorbidity, and the children were older, mean age 10.3 (autism) and 10.7 (ADHD). PANESS scores correlate inversely with age, so we estimated what the NT scores might have been at 10.3 and 10.7 years. These age-corrected NT scores were similar to scores from autism (p=.68) but higher than from ADHD (p=.007).

Table 2 reports the tic features present at the baseline and follow-up visits. At the baseline visit, every NT participant had at least 2 known lifetime tics, including a phonic tic in over 80%. The number of tics known by the end of the screening visit tended to correlate with the 12-month TTS, controlling for the screening TTS (p=0.078). Controlling for the TTS at screening may have reduced the significance of this correlation somewhat, since the TTS includes items for number of motor and phonic tics, and hence is not independent of the number of tics observed. Tics most commonly involved movements of the eyes, mouth and neck (Figure S2A), similar to the distribution in the TS/CTD group (Figure S2B) except that more children in the chronic group had developed tics in the eyes, face, throat, neck, hands, and thighs/legs (Supplemental Table S1).

The situation had changed at follow-up. After observing the child during history and physical exam at the 12-month visit, the PI was confident of a past-week tic in only 33 of 56 NT participants (59%; Table 3). However, tics often became obvious when the child was observed by remote audiovisual monitoring while seated alone in a room (during the TSP). Thus, by the end of the 12-month visit, the YGTSS TTS increased by almost 2 points

from before to after the TSP (mean), and all but one of the NT participants had a known tic in the past week. In other words, all but one now had a chronic tic disorder. The clinical import of the tics had waned, however. The YGTSS TTS exceeded 13 in 40/79, impairment was “mild” or greater in only 7/79, the investigator deemed impairment or marked distress to be present in the past week in 3/69, and only 12/70 had proximate plans to see a physician for tics.

Most participants still had tics at their 24, 36, and 48-month follow-up visits. These tics were, in most cases, apparent to both the parent and the clinician (Table 3). In a few participants, however, tics were observed only on the TSP, when the child was observed remotely while seated alone (2 of 32 at 2 years, 1 of 31 at 3 years, and 2 of 23 at 4 years). By 2–4 years after initial tic onset, YGTSS scores were low for most participants: 53%–67% had a TTS score > 13, and only 15%–20% had impairment scores of 20 (“mild”) or higher. Many parents no longer viewed tics as a major concern; only 8%–12% were planning on taking their child to the doctor because of the tics.

An additional 10 children with DSM–5 PTD but with tics beginning 9–11.5 months prior to the first visit (LaterPTD) are described in Supplementary Table S2. Their baseline and follow-up clinical features are similar to those of the NT group.

4. Discussion

The present report describes the largest prospective study of Provisional Tic Disorder.

4.1 Results that are *not* surprising

The fraction of children with “clinically meaningful” tics, as we defined it, dropped from 74% at screening to 28% at the 1-year anniversary of the first tic. On average, 12-month total tic scores declined by 29% relative to the screening visit. In other words, on average, the prognosis for PTD at 1 year after tic onset is good, even if at least occasional tics remain in essentially all the children at follow-up.

We found a M:F sex ratio of 2.6:1. In Tourette syndrome, this ratio is reported closer to 4:1, but previous studies of PTD similarly found a lower sex ratio, with values ranging from 1.2 to 4.0 [42–46]. Among several possible explanations for this difference, we could hypothesize that girls are more likely than commonly thought to have a first tic (*i.e.*, to develop PTD), but that earlier maturation of inhibitory pathways and better attention to social feedback allows their tics to improve earlier, especially in the presence of others.

4.2 Results that are surprising

Based on the first half of these data, we reported that all NT children followed up in person at 12 months still had tics [9]. Here we confirm that observation in a much larger sample, in which 98% had tics at 12 months. The earlier report discusses several reasons for the apparent mismatch of these prospective data with the widespread clinical teaching that tics usually disappear within weeks to months of onset [1, 43, 47 (p. 171), 48–55]. Underreporting of tics by parents partially explains the mismatch. In 0–10% of NT children, both parent and child reported no tics in the week prior to a study visit, but tics were seen

at the visit. We did not track how often only the child or only the parent reported past-week tics, but anecdotally this seemed to occur at about half of visits. Similarly, 9 parents reported absence of past-week tics 3 months after the first study visit, but their children all had tics at a subsequent in-person visit (Figure S1). Thus face-to-face observation is essential for studies attempting to measure complete tic remission. However, parent or child unawareness of ongoing tics is not the only factor. On 11–32% of NT visits, the investigator observed tics during the TSP after seeing none during ~45 min of observation prior to the TSP (Table 3). Similarly, 23% of TS patients in a clinical trial showed tics only when the examiner left the room [56]. Our data are corroborated by the few previous studies to follow up PTD, none of which involved direct examination of every patient [7, 47 (p. 188), 57, 58].

In addition to presence or absence of tics at follow-up, the observed tic variety and severity are also unexpected. Experienced tic clinicians have usually viewed Provisional Tic Disorder as a mild condition with few tics, usually without an urge to tic, that does not cause marked distress or impair function (e.g., refs. [54, 59, 60]). Although almost all adults with tics report premonitory urges or sensations [61], the prevalence of premonitory urges in children with tics has been reported as 20%–40% in children under age 8, and as 24%–62% at age 8–10 [62–64]. In our sample of children ages 5–10, 65% had premonitory urges at the initial visit, when completion of the assessment was assisted by the experimenter.

PTD has traditionally been thought to involve only one or a few tics. For instance, in a consecutive sample of 60 children with TS, 60% recalled that their first “tic episode” included only a single motor tic [65]. By contrast, in our study, by the end of the screening visit, every child had experienced more than one tic, with a mean of 8.9. We attribute this to the exceptionally thorough assessment in the New Tics study. Fewer tics may possibly predict a better outcome: in one report, 6 of 11 cases of spontaneously remitting tics had only a single tic identified [66], and in an epidemiological study set in an elementary school, multiple tics were thought to portend a worse prognosis [67]. However, our observations suggest that within weeks of onset, children almost always have experienced multiple tics. Additionally, almost all the children experienced at least one phonic tic (82% at screening and 87% at 12 months).

Comorbidities were also surprisingly common, including a high prevalence of anxiety disorders and past or current enuresis (Table 1). Anxiety is common in children with TS [68, 69], and tics generally worsen with anxiety [70]. In our sample, a current or past anxiety disorder at screening predicted more severe tics at 12 months [9]. We hypothesize that in part, the association of tic outcome with baseline anxiety is explained by the fact that anxiety is characterized by strong negative reinforcement learning. Negative reinforcement (specifically, the temporary alleviation of the urge to tic when a tic occurs) has been hypothesized to be a key construct in explaining the persistence of tics over time and the mechanism of behavior therapies for tics. Anxiety was not significantly greater in girls than in boys, whether measured by diagnosable anxiety disorders (p=.18) or by symptom severity (CBCL or YCBCL anxiety scale T score; p=.63). Enuresis has been noted previously to be common in TS, and more common than in children without tics [71–73], but we suspect we were not the only clinicians who had failed to appreciate this point, especially as enuresis has been proposed as supporting a diagnosis of streptococcal-induced tics [74].

Thirty-three of our 89 PTD participants (37%) had a first-degree relative with tics, specifically a parent in 18 (20%). One child had tics in both parents. These fractions are immensely higher than the rate of tics in the general adult population, but within the range of family history rates reported in *chronic* tic disorders. A family history of chronic tics, of tics persisting into adulthood, and of tics in both parents have all been proposed as possible predictors of worse outcome for PTD [75, 76].

4.3 Data that bear on controversies

Traditionally, the aversion to lumping transient and chronic tics has been strong. PTD is "generally viewed as a separate entity" [50], "not commonly considered as a part of the TS spectrum" [77]. However, "the exact time criteria, *i.e.* tics are present shorter or longer than 1 year … have never been supported by valid data such as a longitudinal study on tics in an epidemiological sample" [78]. Our data shed light on this arbitrary separation of tic disorders at one year's duration. Of course, the number of tics children had experienced at screening was greater in those who had had tics longer (Figure 1B) and increased with longer follow-up (Table 2). The DCI score similarly increased from the initial visit to subsequent visits (Table 2). Otherwise, however, clinical features, follow-up outcomes, psychological testing, and family history were all more similar than different in the PTD and TS/CTD patients. In other words, the present results support the conclusion that PTD and TS/CTD are best considered different points in time along the temporal unfolding of the same disorder, rather than two distinct conditions [79]. Testing whether genetic burden or treatment response differ between PTD and TS/CTD could further strengthen this conclusion.

One might hypothesize to the contrary that perhaps duration matters, but one year is the wrong choice. As we wrote previously, "plausibly full tic remission … takes 1.5, 2 or 10 years," rather than one [9]. However, these new follow-up data suggest that PTD rarely remits completely even as late as 4 years after tic onset.

Another controversy was summarized recently by He and colleagues: "Some have argued that because not all individuals with TS experience premonitory urges, tics cannot be caused by premonitory urges. … However, by adulthood, up to 98% [of] individuals with TS report experiencing premonitory urges, suggesting that low estimates of premonitory urges experienced in TS may be partially because of difficulties describing premonitory urges in early childhood and adolescence" [80, 81]. In favor of the latter interpretation, two thirds of the young children in this study endorsed premonitory urges within months of tic disorder onset.

4.4 "Social tic suppression"

Anecdotally, most NT children on follow-up visits showed zero or few tics during a 40- to 60-min session with the PI, talking about their tics, but then had numerous tics within moments of closing the door on them for remote observation. In TS, Goetz and colleagues [56] counted 73% fewer tics when the examiner was present. Unfortunately, we did not quantify tic frequency or severity during the interview and physical examination. We did record that on follow-up visits, about 1/4 of children had zero tics observed prior to the

TSP (Table 3). We hypothesize that this phenomenon (minimal ticcing during observation by others) increases with maturation of social awareness and inhibitory capacity, which may partially explain the improvement seen over the first year of a tic disorder. This “social tic suppression” ability would be expected to improve more in children with fewer autism-like characteristics, and in fact 12-month tic severity was lower in children with lower SRS scores at baseline [9]. Indeed, “social tic suppression” is so typical shortly after tic onset that its opposite (tics much worse when observed by others) is a useful diagnostic feature of functional tic-like symptoms [82].

4.5 Limitations

The main limitation is that our sample was not randomly chosen from the population; possibly we oversampled children with more severe tics or from families with better access to medical care. But in fact our sample appears representative of children whose parents notice a tic. “Tic severity was fairly low at study entry, with a mean TTS < 20; about a third of the children came from families experienced with tics (positive family history or a physician parent); and disadvantaged minorities are represented at or above the frequency predicted from regional demographics” [14].

Judging tic onset retrospectively is not trivial. However, we sought information on tic start date in semi-standardized interviews with the child and parent separately, and probed extensively (see Methods). Often volunteers arrived thinking tic onset was 2–3 months ago, but on further discussion, we identified tics for more than 6 or even 12 months. After careful probing, the median “confidence range” for onset date was only 16 days.

Could we be coming to the fire scene too late? That is, could we have missed the expected remitting (transient) tics because they remit before we could enroll them? Our data do not support this hypothesis. Tic outcomes were not significantly better for children enrolled in the study sooner after tic onset (Figure 1C, $p = 0.09$). No remissions occurred in the children enrolled soonest, including 4 children first seen 22–28 days after onset. Conceivably the tic disorders that remit do so only in the first 3 weeks after onset. However, although data are limited [83], tics lasting less than 4 weeks have been called an “aberrancy” [59], and the data we provide here support that view.

5 Conclusion

Provisional Tic Disorder does generally have a favorable prognosis. However, its phenomenology and course resemble Tourette’s Disorder much more closely than previously recognized. The evidence base now supports changing the nosology to include only a single diagnosis for all primary, childhood-onset tic disorders regardless of duration.

Changing the nosology to reflect this conclusion will have practical implications. It will direct etiological and pathophysiological research to earlier time points in the course of tic disorders. Since PTD is so common, for instance, genetic studies may need to focus more on why tics improve over the first year, rather than on why they start. Second, if we knew why tics improve so substantially, on average, over the first year after onset, we could design a treatment to mimic that process in patients with more severe tics. Third, unifying PTD and

TS/CTD will more accurately inform patients and parents that on average tics improve over time but are not expected to disappear completely.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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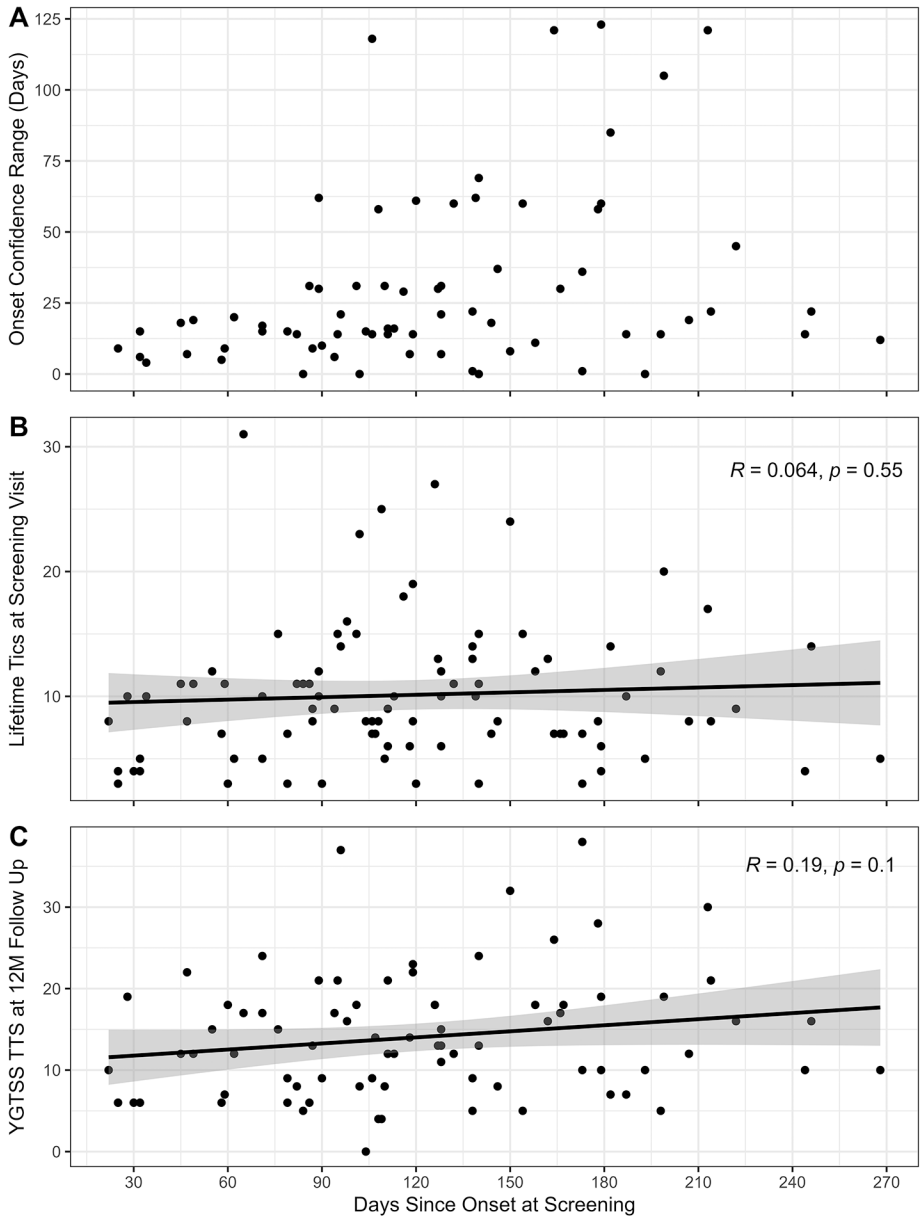

Figure 1.

A. Confidence range around tic onset date, by time since tic onset

Careful probing determined a first and last likely date of tic onset, *e.g.* "After Halloween, but before the visit to the doctor on November 12." The duration of that interval (in this example, 11 days, for Nov. 1–12) is plotted below against the time since tic onset at screening. Two thirds of onset dates were judged to be accurate within 2 weeks. As expected, more remote dates were recalled somewhat less precisely.

B. Number of tics known at the screening visit, by time since tic onset.

More lifetime tics were identified in children who had had tics longer.

C. YGTSS Total Tic Score (TTS) at 12 months, by time since tic onset at screening.

TTS at the 12-month follow-up visit was not significantly lower in children whose tics had lasted a shorter time at the initial screening visit (p=.091). More importantly, if such a difference exists, it is most likely to be relatively small in magnitude over the first few months after tic onset (~2 points difference in mean TTS at 12 months between those enrolled at 1 *vs.* 4 months after tic onset).

Table 1.
Participant characteristics other than tics for the NT participants over time.

Children with tics for 0–9 months at screening. Values indicate number or mean ± SD unless indicated otherwise.

Characteristic	Baseline	Baseline (returned at 12 months)	12-month follow-up	24-month follow-up	36-month follow-up	48-month follow-up
Demographics						
N	89	79	79	37	36	32
Age	7.88 ± 2.05	7.74 ± 1.97	8.45 ± 1.94	9.13 ± 1.47	10.19 ± 1.58	11.69 ± 1.56
Sex (M:F)	64:25	55:24	55:24	28:9	26:10	26:6
Handedness (R:non-R)	77:12	68:11	68:11	31:6	28:8	27:5
Non-white	15	13	13	5	5	3
OCD and ADHD						
Family history of OCD	14	13	-	-	-	-
Family history of ADHD	25	22	-	-	-	-
ADHD, K-SADS (current)[a]	48	42	-	-	-	-
ADHD, K-SADS (past)	2	2	-	-	-	-
ADHD, clinician	39	32	35	16	14	11
ADHD Severity	14.8 ± 12.34	14.39 ± 12.53	15.28 ± 11.52	16.23 ± 14.19 (N=31)	14.0 ± 12.46 (N=27)	10.7 ± 10.88 (N=10)
OCD, K-SADS (current)	27	22	-	-	-	-
OCD, K-SADS (past)	0	0	-	-	-	-
OCD, clinician	9[b]	7	13	5	5	6
OCD severity (CY-BOCS)	4.12 ± 6.46	3.89 ± 6.37	6.2 ± 8.08	4.48 ± 6.82 (N=33)	6.17 ± 7.51 (N=29)	5.17 ± 8.36 (N=12)
Other psychiatric diagnoses						
Anxiety disorder, K-SADS, lifetime[c]	39	37	-	-	-	-
Enuresis (current), K-SADS	17	14	-	-	-	-
Enuresis (past), K-SADS	12	10	-	-	-	-
DMDD, K-SADS[d]	2 (1 current, 1 past)	2 (1 current, 1 past)	-	-	-	-
ODD, K-SADS[e]	12 (11 current, 1 past)	12 (11 current, 1 past)	-	-	-	-
SRS total T scores	50.35 ± 10.02 (N=88)	50.2 ± 9.82	-	-	-	-
Number of comorbid psychiatric diagnosis classes [84]	1.24 ± 0.95	1.19 ± 0.96	-	-	-	-
Other						
Barratt SES	51.57 ± 9.92	51.76 ± 10.14	-	-	-	-
IQ estimate (K-BIT)	108.36 ± 12.5 (N=88)	108.43 ± 12.09	-	-	-	-

Characteristic	Baseline	Baseline (returned at 12 months)	12-month follow-up	24-month follow-up	36-month follow-up	48-month follow-up
PANESS total score	40.79 ± 11.33 (N=47)	40.67 ± 10.36 (N=40)	-	-	-	-
Brain-active medications[f]	24	21	25	9	11	5

[a] K-SADS entries in this table include diagnoses recorded as definite, probable, or in partial remission. ADHD includes combined, hyperactive, inattentive, and non-specific subtypes.

[b] Clinical diagnosis including “subthreshold OCD” = 26 of 89

[c] Does not include OCD

[d] Disruptive mood dysregulation disorder

[e] Oppositional-defiant disorder

[f] Includes medications like diphenhydramine, melatonin and magnesium in addition to prescription medication for ADHD, tics or anxiety disorders

Table 2.

Tic characteristics for the NT participants over time. Children with tics for 0–9 months at screening.

Values indicate number or mean ± SD unless indicated otherwise.

Characteristic	Baseline	Baseline (returned at 12 months)	12-month follow-up	24-month follow-up	36-month follow-up	48-month follow-up
N	89	79	79	37	36	32
Time since tic onset at screening						
Days since tic onset (range)	22–268	22–268	346–594	663–961	959–1404	1351–1854
Median days since tic onset	111.0	111.0	370.0	738.0	1101.0	1468.0
Mean days since tic onset	118.33 ± 55.80	120.56 ± 57.24	380.09 ± 31.28	755.27 ± 25.18	1115.83 ± 63.75	1502.94 ± 103.99
Mean months since tic onset	3.9 ±1.83	4.02 ± 1.91	4.02 ± 1.91	4.48 ± 2.08	4.27 ± 2.14	4.29 ± 1.85
Tic diagnosis						
DSM–IV–TR TS or CTD	0	0	65 TS, 6 CTD	24 TS, 5 CTD	24 TS, 5 CTD	16 TS, 3 CTD
DSM–5 TS or CTD	3	2	70 TS, 7 CTD, 1 other[a]	26 TS, 5 CTD, 1 other	29 TS, 3 CTD, 1 other	26 TS, 1 CTD (N=30)
Number of tics						
Total number of lifetime tics known by end of visit	8.92 ± 4.26	9.09 ± 4.28	12.33 ± 7.12 (N=36)	14.81 ± 7.54	17.15 ± 9.0 (N=33)	16.24 ± 7.41 (N=29)
Number of lifetime motor tics known by end of visit	6.9 ± 4.09	6.95 ± 4.15	9.22 ± 6.25 (N=36)	10.84 ± 5.77	12.06 ± 5.91 (N==33)	12.21 ± 5.56 (N=29)
Number of lifetime phonic tics known by end of visit	2.01 ± 1.38	2.13 ± 1.39	3.11 ± 2.48 (N=36)	3.97 ± 3.33	4.79 ± 4.13 (N=33)	3.62 ± 3.09 (N=29)
Number of different tics in the last week[b]	3.98 ± 2.21	3.97 ± 2.20	4.05 ± 3.13	4.38 ± 4.27	5.08 ± 4.42	4.12 ± 3.60
YGTSS motor tic number score (0–5) past week	1.98 ± 0.96 (N=88)	1.95 ± 0.98 (N=78)	1.8 ± 1.16 (N=79)	2.14 ± 1.23 (N=37)	2.28 ± 1.43 (N=36)	2.06 ± 1.39 (N=32)
YGTSS motor tic number score (0–5) (post-TSP)	2.35 ± 0.87 (N=66)	2.37 ± 0.89 (N=59)	2.34 ± 0.96 (N=70)	2.39 ± 1.08 (N=36)	2.56 ± 1.37 (N=32)	2.48 ± 1.05 (N=25)
YGTSS phonic tic number score (0–5) past week	1.11 ± 1 (N=88)	1.15 ± 1 (N=78)	0.97 ± 1 (N=79)	1.05 ± 1 (N=37)	1.06 ± 1 (N=36)	0.81 ± 1 (N=32)
YGTSS phonic tic number score (0–5) (post-TSP)	1.44 ± 1 (N=66)	1.49 ± 1 (N=59)	1.13 ± 1 (N=70)	1.22 ± 1 (N=36)	1.25 ± 1 (N=32)	0.56 ± 1 (N=25)
Tic severity						
YGTSS motor tic intensity (pre-TSP)	2.28 ± 0.97 (N=88)	2.26 ± 1.0 (N=78)	1.84 ± 1.1 (N=79)	2.16 ± 1.21 (N=37)	2.14 ± 1.15 (N=36)	2.22 ± 1.18 (N=32)
YGTSS motor tic intensity (post-TSP)	2.55 ± 0.9 (N=66)	2.54 ± 0.92 (N=59)	2.27 ± 0.85 (N=70)	2.42 ± 1.05 (N=36)	2.25 ± 0.98 (N=32)	2.28 ± 1.02 (N=25)
YGTSS phonic tic intensity (pre-TSP)	2 ± 1.23 (N=88)	2 ± 1.23 (N=78)	1 ± 1.26 (N=79)	1 ± 1.3 (N=37)	1 ± 1.3 (N=36)	1 ± 1.38 (N=32)
YGTSS phonic tic intensity (post-TSP)	1.88 ± 1.2 (N=66)	1.92 ± 1.21 (N=59)	1.31 ± 1.23 (N=70)	1.47 ± 1.34 (N=36)	1.84 ± 1.37 (N=32)	0.88 ± 1.3 (N=25)
YGTSS motor tic interference (pre-TSP)	0.95 ± 1.07 (N=88)	1.04 ± 1.1 (N=78)	0.85 ± 0.98 (N=79)	0.7 ± 0.88 (N=37)	1.14 ± 1.15 (N=36)	1.12 ± 1.29 (N=32)

Characteristic	Baseline	Baseline (returned at 12 months)	12-month follow-up	24-month follow-up	36-month follow-up	48-month follow-up
YGTSS motor tic interference (post-TSP)	0.91 ± 1.02 (N=66)	1.0 ± 1.03 (N=59)	0.84 ± 1.0 (N=70)	0.72 ± 0.88 (N=36)	1.12 ± 1.18 (N=32)	1.16 ± 1.37 (N=25)
YGTSS phonic tic interference (pre-TSP)	1 ± 0.94 (N=88)	1 ± 0.96 (N=78)	1 ± 0.97 (N=79)	1 ± 1.14 (N=37)	1 ± 1.0 (N=36)	0 ± 0.76 (N=32)
YGTSS phonic tic interference (post-TSP)	0.61 ± 0.97 (N=66)	0.64 ± 1.0 (N=59)	0.5 ± 0.96 (N=70)	0.61 ± 1.13 (N=36)	0.53 ± 0.92 (N=32)	0.36 ± 0.7 (N=25)
Tic history						
First tic: motor, phonic, or both at same age	29, 12, 20 (N=61)	21, 12, 18 (N=51)				
Tics began above the shoulders	79	71	71	32	33	28
Current complex tic	40 (N=88)	36 (N=78)	35	21	21	18
Current motor tic	85 (N=88)	75 (N=78)	73	34	33	30
Current phonic tic	67 (N=88)	60 (N=78)	52	23	24	15
At least 1 phonic tic lifetime	73	65	69	34	33	30
Ever had a complex tic	41	36	52	26	29	25
Ever had a complex motor tic	35	30	47	24	27	25
Ever had a complex phonic tic	13	12	18	10	12	10
Multiple motor tic body locations	46	41	55	28	27	25
DCI score	33.21 ± 13.09	33.15 ± 13.15	43.31 ± 14.83 (N=77)	50.35 ± 17.12	52.44 ± 15.9	53.97 ± 16.46
Tics suppressible	69	62	70 (N=78)	33	35	31
Premonitory urge						
Premonitory Urge (current)	60 (N=82)	51 (N=72)	58 (N=75)	27 (N=36)	29 (N=35)	22 (N=31)
PUTS Score	14.01 ± 4.97 (N=82)	13.76 ± 4.84 (N=72)	15.15 ± 5.7 (N=75)	14.47 ± 5.83 (N=36)	15.26 ± 5.65 (N=35)	15.87 ± 5.58 (N=31)
YGTSS scores						
Pre-TSP YGTSS Total Tic Score (TTS)	15.41 ± 5.72 (N=88)	15.63 ± 5.65 (N=78)	12.14 ± 8.05	14.38 ± 9.44	15.42 ± 9.24	13.0 ± 9.16
Pre-TSP YGTSS Impairment	7.65 ± 8.02 (N=88)	7.86 ± 8.27 (N=78)	4.18 ± 6.48	6.22 ± 10.3	7.92 ± 10.65	6.25 ± 11.36
Pre-TSP TTS, post-TSP score recorded	15.32 ± 5.78 (N=63)	15.73 ± 5.8 (N=56)	11.7 ± 7.99 (N=70)	14.03 ± 9.33 (N=36)	15.19 ± 9.76 (N=32)	11.4 ± 8.75 (N=25)
Post-TSP YGTSS TTS	17.22 ± 5.56 (N=63)	17.7 ± 5.53 (N=56)	13.83 ± 7.59 (N=70)	15.56 ± 8.64 (N=36)	16.66 ± 9.04 (N=32)	12.72 ± 8.4 (N=25)
Post-TSP YGTSS Impairment	7.46 ± 8.365 (N=63)	7.84 ± 8.5458 (N=56)	4.21 ± 6.5770 (N=70)	6.57 ± 10.4935 (N=36)	8.59 ± 11.0232 (N=32)	6.0 ± 11.2725 (N=25)
Δ in TTS from pre- to post-TSP	1.9 ± 2.12 (N=63)	1.96 ± 2.17 (N=56)	2.13 ± 2.86 (N=70)	1.53 ± 2.65 (N=36)	1.47 ± 2.36 (N=32)	1.32 ± 1.86 (N=25)
Children whose TTS increased after TSP	47 (N=63)	42 (N=56)	41 (N=70)	17 (N=36)	15 (N=32)	13 (N=25)
Other						

Characteristic	Baseline	Baseline (returned at 12 months)	12-month follow-up	24-month follow-up	36-month follow-up	48-month follow-up
Number of new tic types seen on TSP	2.00 ± 2.42	2.08 ± 2.47	1.34 ± 1.94	0.71 ± 0.99	1.00 ± 1.25	0.89 ± 2.12
Medication for tics[c]	4	4	3–4	0–1	2–3	1

[a] One motor tic plus phonic tics [85].

[b] Estimated in some cases from the motor number and phonic number items on the YGTSS.

[c] In 3 cases, at a follow-up visit it was not clear whether a medication was for tics or for another purpose.

Table 3.

Tics in the NT participants: how identified, and consequences. Children with tics for 0–9 months at screening.

Values indicate number or mean ± SD (Range) unless indicated otherwise. N is given in a cell if it differs from the overall N for that column.

Measure	Baseline	Baseline (returned at 12 months)	12-month Follow-up	24-Month Follow-up	36-Month Follow-up	48-Month Follow-up
N	89	79	79	37	36	32
Tic Identification						
Parent or child reported any tics in past three months?	60 (N=62)	54 (N=54)	58 (N=70)	33	33	27 (N=31)
Parent or child noticed any tics in past week (before intensively reviewing symptoms with the clinician)	59 (N=62)	53 (N=54)	56 (N=70)	32	33	24 (N=31)
Positive history, after clinical interview, for tics in the past week	60 (N=62)	54 (N=54)	58 (N=70)	33	33	27 (N=31)
Positive exam (before TSP)	80 (N=87)	70 (N=77)	55 (N=79)	25 (N=36)	29	19 (N=31)
Tics observed in a parent[a]	0 (N=8)	0 (N=7)	3 (N=14)	3 (N=20)	4 (N=23)	0 (N=22)
Tic Suppression Paradigm						
Tics observed on TSP	66	58	32 (N=37)	33 (N=36)	27 (N=33)	21 (N=28)
No positive history or positive exam, but tics were observed on TSP	18 (N=85)	16 (N=75)	9 (N=37)	12 (N=35)	5 (N=30)	8 (N=24)
Number of lifetime tics known before TSP	6.78 ± 3.82	6.76 ± 3.81	11.03 ± 5.63 (N=35)	14.05 ± 7.37	16.3 ± 8.96 (N=33)	15.31 ± 7.19 (N=29)
Participants with tics first observed during TSP	45	42	17 (N=37)	12 (N=36)	13 (N=33)	12 (N=32)
Number of tics first observed during TSP	2.04 ± 2.73	2.22 ± 2.83	1.58 ± 2.2 (N=36)	0.76 ± 1.06	0.85 ± 1 (N=33)	0.9 ± 2.06 (N=29)
# of tics in the past week that were known previously, but before TSP were thought not to have happened in the past week	0.12 ± 0.90	0.14 ± 0.96	0.32 ± 0.87	0.09 ± 0.28	0.15 ± 0.51	0.26 ± 0.53
Investigator confident they had tics before the TSP	49 (N=59)	42 (N=51)	36 (N=57)	29	28	22 (N=31)
Clinically Meaningful						
Planning to see doctor because of tics	76	68	12 of 70	6	3	2 of 31
YGTSS Impairment ≥20	13 (N=88)	13 (N=78)	7	7	8	6
YGTSS TTS >13	66 (N=88)	60 (N=78)	40	21	24	17
Impairment or marked distress (ever)	33	28	39	28	24	23
Impairment or marked distress (past week)	7 of 62	7 of 54	3 of 69	6	9	6 of 31
Clinically meaningful tics	64	57	22	14	16	10

[a]Data collected only in the last 5 years of the study. In most cases, only one parent was present at the visit.