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Long-term Outcomes of Behavior Therapy for Youth With Tourette Disorder

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Cognitive Control Processes in Behavior Therapy for Youth with Tourette's Disorder

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Abstract

Objective

To determine the long-term durability of behavior therapy for tics among youth with Tourette disorder and persistent (chronic) motor or vocal tic disorders.

Method

Of the 126 youth who participated in a randomized controlled trial of behavior therapy 11 years prior, 80 were recruited for this longitudinal follow-up. Consenting participants were interviewed in person or remotely (Web-based video) by trained evaluators to determine the course of tics, current tic severity, and tic-related impairment. Recruitment and data collection occurred between 2014 and 2019, with an average follow-up duration of 11.2 years.

Results

Treatment responders to both conditions in the original trial achieved partial, but not full, tic remission. Tic severity also decreased significantly across the sample, with 40% reporting partial remission. Behavior therapy responders (n = 21) in the original trial were more likely (67%) to achieve remission at follow-up (Total Tic Score = 12.52, SD = 10.75) compared to psychoeducation/supportive therapy responders (n = 6, 0%) at follow-up (Total Tic Score = 20.67, SD = 6.92) on the Yale Global Tic Severity Scale. Tic-related impairment decreased across the sample, with no significant differences between treatment groups or responders.

Conclusion

Despite limitations of unmeasured variables and veracity of self-report at follow-up, this study supports guidelines recommending behavior therapy as the first-line intervention for tics. Further investigation of behavior therapy as an early preventive intervention also merits attention.

Keywords

Tourette, tics, long-term follow up, youth

Introduction

Persistent tic disorders (PTD, including Tourette disorder) are chronic neurodevelopmental disorders characterized by motor and/or vocal tics. Tics are sudden, rapid, non-rhythmic movements (eg, eye blinking, facial grimacing) or vocalizations (eg, sniffing, grunting, words, or sounds) and may also include more complex patterns of movements or vocalizations. Tic onset usually begins between the ages of 5 and 7 years, with tic severity peaking between the ages of 10 and 13 years and then decreasing during late adolescence and early adulthood. Although significant distress and/or impairment is not required for diagnosis, individuals with tic disorders often experience distress and interference due to ticcing, and up to 85% meet lifetime criteria for comorbid psychiatric disorders.[1]

Antipsychotic medications (eg, haloperidol, risperidone, aripiprazole) and the Comprehensive Behavioral Intervention for Tics (CBIT) are currently the treatment modalities with the most research support.[2] Treatment effect sizes between these 2 approaches are comparable; however, antipsychotic medications are associated with various side effects such as weight gain, metabolic effects, fatigue, and sedation. Several academic/professional bodies with an interest in the treatment of tic disorders (eg, European Society for the Treatment of Tourette Syndrome,[3] Canadian Guidelines for the Evidence Based Treatment of Tourette Syndrome,[4] American Academy of Child and Adolescent Psychiatry,[5] and American Academy of Neurology[6]) recommend CBIT as the first-line intervention for individuals in need of treatment for PTDs.

CBIT comprises several components including psychoeducation, monitoring tics between sessions, functional assessment of antecedents to and consequences of ticcing, functional interventions to reduce the impact of environmental variables on ticcing, Habit Reversal Training,[7] relaxation training (both diaphragmatic breathing and progressive muscle relaxation), and relapse prevention. During Habit Reversal Training, providers work collaboratively with youth to increase awareness of tics and tic signals, to create incompatible actions (ie, competing responses) specific for each tic, and to practice implementation by including parents or other social supports to prompt and to praise competing responses as necessary.

In the largest RCT of CBIT for youth conducted to date,[8] 126 participants (aged 9−17 years) with PTD were randomized to receive 8 sessions over 10 weeks of either CBIT (n = 61) or a supportive and educational treatment (PST, n = 65). Evaluators masked to treatment assignment conducted structured clinical interviews and a standard tic severity rating instrument at posttreatment and at 3- and 6-month follow-up time points. CBIT led to a significantly greater decrease in severity (7.6 points) compared to that in the PST group (3.5 points) and significantly more CBIT than PST youth (52.5% vs 18.5%, respectively) were rated as being very much improved or much improved on measures of clinical improvement. Of those who responded to CBIT, 87% continued to maintain responder status at 6-month follow-up.

CBIT outcomes indicate that both youth[8] and adults[9] respond favorably and maintain gains up to 6 and 10 months, respectively, but no PTD treatment studies, psychotherapy or medication, have prospectively followed participants beyond 12 months to assess treatment durability. Furthermore, studies that have followed youth with PTDs over time have typically relied on retrospective chart review and/or self-report measures[10] instead of structured clinical interviews conducted by treatment-masked evaluators. Given that a significant proportion of youth with PTDs continue to experience tics into adulthood,[11] more research is needed to determine whether and how early intervention via CBIT might alter or influence tic severity over the lifespan. The purpose of the current study was to reassess youth who participated in the largest randomized controlled trial of CBIT in youth[8] both to characterize the long-term tic severity outcomes from childhood to adulthood, and to determine the influence of early successful behavioral management on the long-term course of PTDs.

Method

Participants

All 126 participants in the initial CBIT randomized clinical trial were eligible to participate. A total of 80 individuals (63.4%) completed the long-term follow-up (LTF) assessment a mean of 11.17 years after completing acute study treatment (SD = 1.25 years). A Sixteen individuals (12.7%) were contacted but declined to participate, and 30 individuals (23.8%) were lost to follow-up. There were no significant differences at pretreatment baseline between participants who completed the LTF assessment, those who declined to participate, and those lost to follow-up in terms of demographics, psychiatric comorbidity, treatment assignment, clinical severity, tic severity, impairment, or medication status (Table 1).

Table 1. Initial Characteristics of Participants Who Did and Did Not Complete the Long-term Follow-up Assessment (N = 126)

	Long-term follow-up (n = 80)	**Declined to participate (n = 16)**	**Lost to follow-up (n = 30)**	**χ^2**	***p***
	n (%)	**n (%)**	**n (%)**		
% White	69 (86.3)	13 (81.3)	25 (83.3)	0.34	.85
% Male	60 (75)	15 (94)	24 (80)	2.83	.24
% on a Tic medication[a]	29 (36.3)	6 (37.5)	11 (36.6)	0.01	.99
% Assigned to CBIT	38 (47.5)	9 (56.3)	14 (46.6)	0.46	.80
% OCD	15 (18.8)	3 (18.8)	6 (20)	0.30	.86
% ADHD	19 (23.8)	4 (25)	10 (33.3)	0.48	.79
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	***F***	***p***
Age (y)	11.61 (2.41)	11.84 (1.94)	12.01 (2.31)	0.34	.71
Baseline YGTSS Total Tic Score	24.83 (5.88)	22.00 (3.29)	25.63 (7.33)	1.99	.14
Baseline YGTSS Impairment	23.65 (8.25)	21.81 (6.62)	24.63 (9.75)	0.58	.56
Baseline CGI-S	4.44 (0.52)	4.19 (0.40)	4.57 (0.68)	2.46	.09
Posttreatment YGTSS Total Tic Score	19.20 (8.18)	15.31 (6.06)	21.09 (7.62)	2.22	.11
Posttreatment YGTSS Impairment	13.72 (10.13)	9.77 (6.86)	17.59 (11.36)	2.57	.08
Posttreatment CGI-S	3.58 (1.02)	3.46 (0.97)	3.95 (1.17)	1.31	.28

Note: ADHD = attention-deficit/hyperactivity disorder; CBIT = Comprehensive Behavioral Intervention for Tics; CGI-S = Clinical Global Impression of Severity; OCD = obsessive-compulsive disorder; YGTSS = Yale Global Tic Severity Scale.

[a] Tic medications included antipsychotic and α-agonist medications.

Participants who completed the LTF were 22.87 years of age on average *(*SD = 2.70) and predominantly male (n = 60, 75%). Most participants were non-Hispanic (n = 73, 91%) and came from several racial backgrounds (White, n = 69, 86.3%; Asian, n = 4, 5%; multi-racial, n = 4, 5%; Black, n = 1, 1.3%; and other racial background, n = 2, 2.5%). Few participants completed only partial high school (n = 1, 1.3%) or were high school graduates (n = 12, 15.0%). Most participants completed partial college coursework (eg, partial college, technical school; n = 32, 40.0%) and/or graduated from college (eg, 4-year college graduate and/or professional degree; n = 24, 30.0%) at the time of the LTF visit. Participants had a lifetime diagnosis of Tourette disorder (n = 76, 95%), persistent motor disorder (n = 3, 4%), or persistent vocal tic disorder (n = 1, 1%). Any use of tic influencing medication (eg, α-agonists, antipsychotics) during the interim period was reported by 27 participants (33.8%), and 8 (10%) were taking a tic-influencing medication at re-assessment (eg, α-agonist or antipsychotic medications). Although 47 participants (58.8%) received any mental health services during the follow-up period

(ie, cognitive behavior therapy, supportive therapy, multiple therapies), only 5 participants (6.25%) reported that this therapy was related to tics, and only 2 (2.5%) reported specifically receiving behavior therapy for tics. Collectively, 31 participants (38.8%) received an evidence-based treatment for tics during the follow-up period (ie, tic-influencing medication and/or behavior therapy for tics).

Measures

Yale Global Tic Severity Scale

The Yale Global Tic Severity Scale (YGTSS) is a clinician-rated measure of tic severity over the past week. Motor and vocal tics severity are separately rated across 5 dimensions. A total tic severity score (range 0−50) is the sum of motor and vocal ratings across all 5 dimensions. Aggregated tic-related impairment is rated on a 50-point, single-dimension scale. The YGTSS has been shown to have good reliability and validity.[12,13] Signal detection analyses show that a 25% reduction on the YGTSS Total Tic score corresponds with a clinically meaningful improvement.[14]

MINI International Neuropsychiatric Interview

The MINI International Neuropsychiatric Interview (MINI) is a standardized diagnostic interview recently updated to assess *DSM-V* psychiatric disorders and to track progress in clinical and research settings.[15] The instrument is composed of modules for 17 common psychiatric diagnoses, with previous research indicating acceptable reliability and validity.[16]

Clinical Global Impression of Severity and Clinical Global Impression of Improvement

The Clinical Global Impression of Severity (CGI-S)[17] is a clinician-rated scale used to measure overall clinical severity. Although a CGI-S rating of “moderate illness” (4) is commonly used as an inclusion criterion for treatment studies of TD,[8] items range from “no illness” (1) to “severe illness” (7). A Clinical Global Impression of Severity (CGI-I) score of “1” (very much improved) or “2” (much improved) defined treatment response in the original CBIT trial and is consistent with convention.[18]

Procedures

Recruitment for the follow-up study occurred over a period of 5 years (March 2014 to January 2019). Participants from the original trial were contacted using telephone, regular mail, e-mail, and social networking sites. Contacted participants completed an in-person or video (Skype) visit to determine current psychiatric diagnosis using a structured clinical interview, clinical history, and the severity of current tic symptoms using the YGTSS and CGI-S. All interviews were conducted by trained evaluators masked to participants’ original treatment assignment. Raters were trained to administer clinical interviews using the same methods in the original trial. This included initial didactic training and demonstration of reliable ratings on 2 consecutive administrations. All raters participated in monthly cross-site teleconferencing calls for ongoing supervision and ongoing consensus ratings to protect against rater drift. Participants received $100 for completing this assessment. All procedures were approved by the principal investigators’ institutional review boards.

Analytic Plan

The χ^2 test and 1-way analysis of variance were used to compare baseline differences between participants who completed the LTF assessment, declined to participate, and/or were lost to follow-up. One participant had missing data from the acute trial posttreatment assessment because of dropping out from the PST condition after the first therapy session, but completed the long-term follow-up visit. Four participants were missing tic medication and therapy history at the follow-up assessment, and were considered not to have received tic medication or therapy over the follow-up period. Given the large proportion of participants missing from the original trial at the long-term follow-up, lack of information on long-term follow-up more generally among youth with PTDs, and sufficient power to detect our primary outcomes with the data in hand, we conservatively

decided not to pursue multiple imputation or maximum likelihood estimation methods for the roughly 40% of participants who did not participate in the long-term follow-up. The change in tic severity (YGTSS Total Tic Score) and tic impairment (YGTSS Impairment Score) was examined using a mixed-model repeated-measures analysis that used an autoregressive error structure and restricted maximum likelihood estimations. Models included fixed effects for treatment group (2 levels), treatment response at posttreatment (2 levels), history of evidence-based tic treatment (tic-influencing medications and/or behavior therapy) over LTF (2 levels), and time (3 levels) was the repeated measure. A fixed effect for time (ie, number of months since the baseline assessment) was entered as a covariate into the model. A random effect for participant was included, allowing for individual variation in initial severity. Follow-up comparisons for significant effects and interactions were completed with Bonferroni corrections. We used χ^2 tests to examine whether participants at follow-up met criteria for "partial or full remission" (YGTSS Total Tic Score <14). Finally, the incidence of clinically meaningful change on the YGTSS Total Tic Score (ie, ≥25%; Jeon *et al.*[14]) and effect sizes were calculated for tic severity (YGTSS Total Tic score) and tic impairment (YGTSS Impairment score). All analyses were conducted using SPSS statistical software version 27.0.

Results

Course of Tic Severity and Impairment from Childhood to Early Adulthood

On average, participants, regardless of treatment condition, reported a mild-to-moderate level of tic severity (YGTSS Total Tic Score) and tic-related impairment (YGTSS Impairment Score) and mild illness on the CGI-S at the LTF assessment. In addition, 40% of participants met partial or full remission criteria (ie, a YGTSS total tic score <14).

Long-term Tic Severity Outcomes by Treatment Group and Responder Status

For tic severity outcomes on the YGTSS total tic score, there was a significant treatment group by treatment response by time interaction (Table 2, Figure 1). The CBIT treatment responders had lower tic severity at the LTF assessment compared to the PST responders (Table 3, Figure 1). Specifically, CBIT responders exhibited significant improvement at posttreatment and maintained this improvement over time, displaying large treatment effects over PST responders at the LTF visit ($mean_{diff}$ = 8.64, p = .015, d = 1.47). Although PST acute treatment responders also exhibited initial improvement at the posttreatment visit, this improvement was not maintained over time. There was no significant difference between treatment groups for nonresponders at the LTF visit (p = .32−.80), with only modest effects observed between treatment groups (d = 0.39) (Table 3).

Table 2. Mixed Model Effect for Tic Severity and Tic Impairment Over Time (n = 80)

	YGTSS total tic score			**YGTSS impairment**		
	Parameters	***F***	***p***	**Parameters**	***F***	***p***
Intercept	1	2.04	.16	**1**	**6.83**	**.01**
Time since baseline (mo)	1	2.32	.13	1	0.67	.41
Treatment condition	1	0.60	.44	1	0.05	.83
Treatment response status	**1**	**5.36**	**.02**	**1**	**5.09**	**.03**
EBT for tics	1	3.12	.08	1	1.95	.17
Time	**2**	**24.64**	**<.001**	**2**	**49.10**	**<.001**
Treatment condition ∗ treatment response status	1	0.97	.33	1	0.14	.71
Treatment condition ∗ EBT for tics	1	0.37	.55	1	1.48	.23
Treatment condition ∗ time	2	2.01	.14	2	1.21	.30

Treatment response status ∗ EBT for tics	1	0.61	.44	1	0.14	.71
Treatment response status ∗ time	**2**	**9.02**	**<.001**	**2**	**9.54**	**<.001**
EBT for tics ∗ time	2	0.38	.69	2	0.36	.70
Treatment condition ∗ treatment response status ∗ EBT for tics	1	0.29	.59	1	0.59	.44
Treatment condition ∗ treatment response status ∗ time	**2**	**4.30**	**.015**	2	0.06	.94
Treatment condition ∗ EBT for tics ∗ time	2	0.22	.80	2	0.34	.71
Treatment response status ∗ EBT for tics ∗ time	2	0.28	.76	2	1.67	.19
Treatment condition ∗ treatment response status ∗ EBT for tics ∗ time	2	0.24	.79	2	1.84	.16

Note: Boldface type indicates statistical significance. EBT for Tics = evidence-based treatment for tics during follow-up period; YGTSS = Yale Global Tic Severity Scale.

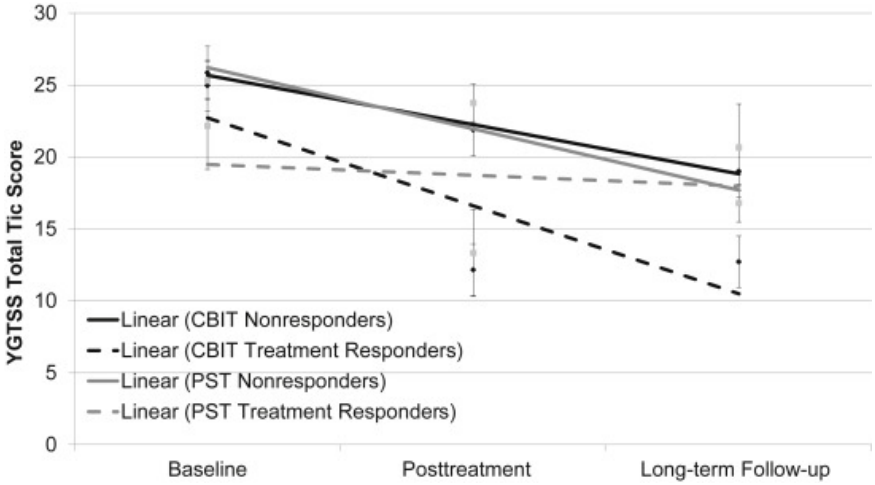

Figure 1. Yale Global Tic Severity Scale Total Tic Scores Across Time by Treatment Condition and Treatment Response Status

Note: *CBIT = Comprehensive Behavioral Intervention for Tics; PST = persistent tic disorders; YGTSS = Yale Global Tic Severity Scale.*

Table 3. Baseline, Posttreatment, and Long-Term Follow-up Tic Severity Scores by Treatment Condition and Treatment Response (n = 80)

Treatment responders[a]	CBIT (n = 21)		PST (n = 6)		Es[p.]
	Mean	**95% CI**	**Mean**	**95% CI**	
YGTSS total tic score					
Baseline	24.98	21.47–28.48	22.88	16.88–28.88	.36
Posttreatment	12.18	8.67–15.68	14.05	8.05–20.05	.32
Long-term follow-up	12.74	9.24–16.25	21.38	15.38–27.38	1.47
YGTSS impairment score					
Baseline	23.95	19.48–28.42	21.66	14.01–29.32	.28
Posttreatment	6.90	2.43–11.37	7.00	0–14.65	.01
Long-term follow-up	8.90	4.43–13.37	12.00	4.34–19.65	.38
Nonresponders[b]	**CBIT (n = 17)**		**PST (n = 36)**		**ES[a]**
	Mean	**95% CI**	**Mean**	**95% CI**	
YGTSS total tic score					

Baseline	25.59	21.99–29.19	25.00	22.40–27.60	0.10
Posttreatment	21.61	18.01–25.20	23.51	20.90–26.12	0.32
Long-term follow-up	18.73	15.14–22.33	16.43	13.83–19.03	0.39
YGTSS impairment score					
Baseline	26.31	21.72–30.90	23.48	20.17–26.79	0.34
Posttreatment	19.61	15.03–24.20	18.13	14.80–21.46	0.18
Long-term follow-up	10.52	5.93–15.10	11.15	7.84–14.46	0.08

Note: Data are presented estimated means for baseline, posttreatment, and long-term follow-up by treatment condition and treatment response status based on the mixed effects model. CBIT = Comprehensive Behavioral Intervention for Tics; ES = effect sizes; PST = Psychoeducation and Supportive Therapy; YGTSS = Yale Global Tic Severity Scale.

[a] Treatment response status was determined by the Clinical Global Impressions−Improvement score, which was administered by an independent evaluator masked to treatment condition.

[b] Effect sizes were calculated by subtracting the change in YGTSS scores in nonresponders from responders divided by the SD for the full sample at baseline.

There was a noticeable difference in clinically meaningful improvement experienced from baseline to the LTF visit for tic severity across the 4 groups. CBIT responders had a higher occurrence of clinically meaningful improvement (n = 17, 80.9%), whereas the other groups displayed a similar occurrence of clinically meaningful improvement (CBIT nonresponders: n = 9, 52.9%; PST responders: n = 3; 50%; PST nonresponders: n = 20; 55.6%). Follow-up comparisons between CBIT responders and PST nonresponders suggest that the between-group difference only approached statistical significance ($\chi^2 = 3.76$, $p = .05$, Cramer's $V = 0.26$).

Effect of Treatment Group and Responder Status on Partial Remission at LTF Assessment

For acute treatment responders, treatment condition was found to influence partial remission rates ($\chi^2 = 8.31$, $p < .004$, Cramer's $V = 0.56$). Specifically, 14 CBIT participants (67%) met this threshold, but no PST participants did. However, for acute treatment nonresponders, there was no difference between treatment groups and the rates of partial remission ($\chi^2 = 0.23$, $p = .63$).

Long-term Tic Impairment Outcomes by Treatment Group and Responder Status

The random intercept, main effect for treatment group and time, and the treatment by time interaction were all significant (Table 2). Follow-up comparisons revealed that treatment responders at week 10 had less tic impairment compared to treatment nonresponders ($mean_{diff} = 4.80$, $p = .027$). In addition, there was a decrease in tic impairment from baseline to posttreatment ($mean_{diff} = 10.94$, $p < .001$), with a nonsignificant increase from posttreatment to the LTF visit ($mean_{diff} = 2.27$, $p = .341$). Further examination of the treatment response by time interaction identified a significant difference between treatment responders and nonresponders at the posttreatment follow-up ($mean_{diff} = 11.93$, $p < .001$), but no significant differences were found at either baseline ($p = .44$) or the LTF ($p = .89$) between responders and nonresponders. Indeed, tic impairment decreased substantially for treatment responders at posttreatment, but all participants achieved comparable tic impairment scores by the long-term follow-up (Figure 2, Table 3).

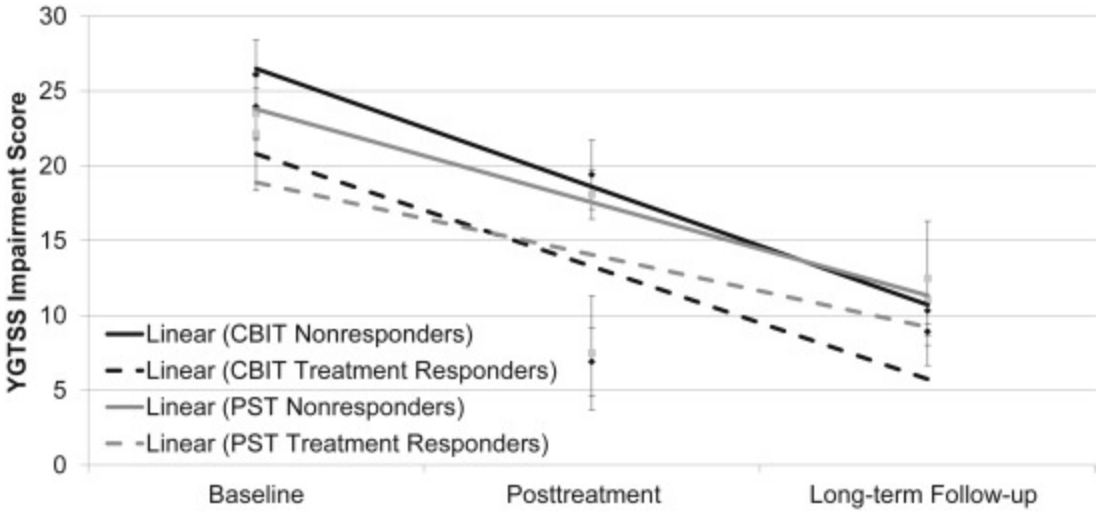

Figure 2. Tic Impairment Scores on the Yale Global Tic Severity Scale Across Time by Treatment Condition and Treatment Response Status

Note: *CBIT = Comprehensive Behavioral Intervention for Tics; PST = persistent tic disorders; YGTSS = Yale Global Tic Severity Scale.*

Discussion

This study is the first longitudinal study of a fully characterized and treated sample of children and adolescents with PTD. Among those who received CBIT, initially assessed in childhood (mean age = 11 years) and reassessed 11 years later, tic severity and impairment decreased significantly, with 40% reporting at least partial remission of their index tic disorder. It is notable that this rate of tic reduction was lower than the 60% to 80% partial remission rates reported in other longitudinal studies.[12,19] However, youth who responded to CBIT in the original trial were far more likely (67%) to achieve at least partial tic remission at follow-up than those who responded to supportive therapy (0%), even after controlling for potential effects of other interventions received over the 11-year follow-up interval. Although tic severity scores were significantly lower for CBIT as compared to PST responders at follow-up, tic impairment scores at follow-up did not differ across the 2 treatment groups, perhaps illustrating adaptation to tics that comes with age.[20]

Although this study lends support to the merits of early intervention for tics with behavior therapy, there are some notable limitations. First, these findings must be considered with the caveat that, although the proportion of initial CBIT and PST responders participating in this follow-up study was similar, the actual number of PST treatment responders included in these analyses was low (n = 6). Second, there were many participants who received some form of adjunctive intervention (eg, cognitive therapy, cognitive behavioral therapy, supportive therapy, multiple therapies) in the 11-year interim, and reducing concomitant problems such as stress or anxiety might also influence tic severity. Although the distribution of participants receiving adjunctive therapies was not significantly different between treatment groups (CBIT vs PST), between responders and nonresponders, or between those reporting high vs low severity at follow-up, the nature of our design cannot fully measure the effects of cumulative care. Third, the YGTSS reporting period of 1 week may not fully capture participants' tic severity, given the fluctuating nature of tics. Although evaluators use all available information when assessing participants' current level of functioning, tic severity, and tic impairment, the YGTSS remains the gold standard used in tic research, and this limitation is by no means unique to this study. Finally, other limitations include the potential effects of extraneous variables during the 10-year interim period and the veracity of recall among participants, many of whom were relatively young at the time of treatment. Despite careful assessment of the

time course and additional interventions received between posttreatment and follow-up, this study relied on subjective memory of participants instead of systematic periodic assessment.

Despite these limitations, this study represents the longest systematic prospective follow-up intervals of youth with PTDs, and the longest of its kind for individuals receiving CBIT.[21] Given the durability of treatment response among youth who receive behavior therapy at earlier ages, guidelines recommending CBIT as the first-line intervention appear to be warranted.[3, 4, 5, 6] There are currently no data available to suggest that similar long-term improvements are likely to be maintained a decade after discontinuing tic medications. Investigation of CBIT as an early preventive intervention also merits attention, as learning early tic suppression skills may change the course of tic severity over time.[22, 23, 24] In addition, future research is needed to determine the extent to which successful management of tics with CBIT may change the course of overall functional impairment, quality of life indicators, and later development or severity of comorbid conditions (eg, anxiety, depression, substance use). Further efforts should be undertaken by researchers, clinicians, and organizations with knowledge of PTDs to promote awareness and accessibility of CBIT.[25]

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