Behavior Therapy for Children With Tourette Disorder

A Randomized Controlled Trial

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Context Tourette disorder is a chronic and typically impairing childhood-onset neurologic condition. Antipsychotic medications, the first-line treatments for moderate to severe tics, are often associated with adverse effects. Behavioral interventions, although promising, have not been evaluated in large-scale controlled trials.

Objective To determine the efficacy of a comprehensive behavioral intervention for reducing tic severity in children and adolescents.

Design, Setting, and Participants Randomized, observer-blind, controlled trial of 126 children recruited from December 2004 through May 2007 and aged 9 through 17 years, with impairing Tourette or chronic tic disorder as a primary diagnosis, randomly assigned to 8 sessions during 10 weeks of behavior therapy (n=61) or a control treatment consisting of supportive therapy and education (n=65). Responders received 3 monthly booster treatment sessions and were reassessed at 3 and 6 months following treatment.

Intervention Comprehensive behavioral intervention.

Main Outcome Measures Yale Global Tic Severity Scale (range 0-50, score >15 indicating clinically significant tics) and Clinical Global Impressions–Improvement Scale (range 1 [very much improved] to 8 [very much worse]).

Results Behavioral intervention led to a significantly greater decrease on the Yale Global Tic Severity Scale (24.7 [95% confidence interval {CI}, 23.1-26.3] to 17.1 [95% CI, 15.1-19.1]) from baseline to end point compared with the control treatment (24.6 [95% CI, 23.2-26.0] to 21.1 [95% CI, 19.2-23.0]) ($P<.001$; difference between groups, 4.1; 95% CI, 2.0-6.2) (effect size=0.68). Significantly more children receiving behavioral intervention compared with those in the control group were rated as being very much improved or much improved on the Clinical Global Impressions–Improvement scale (52.5% vs 18.5%, respectively; $P<.001$; number needed to treat=3). Attrition was low (12/126, or 9.5%); tic worsening was reported by 4% of children (5/126). Treatment gains were durable, with 87% of available responders to behavior therapy exhibiting continued benefit 6 months following treatment.

Conclusion A comprehensive behavioral intervention, compared with supportive therapy and education, resulted in greater improvement in symptom severity among children with Tourette and chronic tic disorder.

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TOURETTE DISORDER IS A CHRONIC neurologic disorder characterized by motor and vocal tics. Prevalence estimates in school-aged children range from 1 to 10 per 1000, with a rate of 6 per 1000 replicated in several countries.[1,2] Tics are usually brief, rapid movements (eg, blinking, facial grimacing) or vocalizations (eg, throat clearing, grunting) but can include more complex movements and vocalizations. Tics begin in childhood; severity peaks in early adolescence and often declines in young adulthood.[3] Epidemiologic and clinical data indicate that Tourette disorder can be associated with considerable impairment[2] and social isolation[4] in school-aged children. Tics are commonly preceded by premonitory urges or sensations that are experienced as noxious and relieved on completion of the tic.[5,6]

The most effective treatments for reducing tic severity are antipsychotic

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medications such as haloperidol, pimozide, and risperidone, although these medications rarely eliminate tics and are often associated with unacceptable sedation, weight gain, cognitive dulling, and motor adverse effects.[7] In addition, nearly all previous randomized medication trials targeting tics in children with Tourette disorder have been brief, ranging from 4 to 8 weeks, and included fewer than 50 participants.[7] Few trials have provided controlled (or even open maintenance) data beyond acute treatment. Thus, data on long-term outcomes of medication for tics are limited.

The most promising behavioral intervention for reducing tic severity is habit reversal training.[8] Habit reversal acknowledges the neurologic basis of tics but proposes that situational factors, including the reaction of others to the tics, as well as the internal experience of premonitory urges, play an important and ongoing role in tic expression.[9-11] Establishing the effectiveness of behavioral treatments for reducing tic severity in children would advance public health by broadening treatment options and expanding the types of clinicians who can effectively treat tic disorders. This trial was designed to evaluate the efficacy of a comprehensive behavioral intervention for tics (CBIT),[12] based on habit reversal training, for reducing tics and tic-related impairment in a large sample of children and adolescents with Tourette disorder.

METHODS

Design

This was a 2-phase, multicenter, randomized controlled trial for children and adolescents with Tourette or chronic tic disorder.[13] Phase 1 was a 10-week acute comparison of the behavioral intervention, with a structured control condition consisting of supportive therapy and education about tics. The control treatment was selected to control for time and attention. In addition, we presumed that it would be acceptable to children and families. Phase 2 was a 6-month, naturalistic observation period for participants exhibiting a positive response to either study intervention. The assessments at 3 and 6 months following treatment provided an estimate of the durability of treatment response. Children who did not exhibit a positive response to either intervention in the randomized trial were not assessed after completing phase 1.

The study was implemented at 3 sites: Johns Hopkins School of Medicine (Baltimore, Maryland), the University of California, Los Angeles, and the University of Wisconsin–Milwaukee. Collaborating investigators provided training of clinical raters, data management and analysis (Yale University, New Haven, Connecticut), therapist supervision (Massachusetts General Hospital/Harvard Medical School), and coding of secondary outcome measures (University of Texas Health Science Center at San Antonio).

The Tourette Syndrome Association provided grant management and recruitment support. An independent data and safety monitoring board provided regular oversight. The trial was approved by the institutional review boards at each site. Before enrollment, study personnel provided a detailed description of study procedures, risks, and benefits to interested families, after which interested parents/guardians provided informed consent and children provided informed assent.

Objectives

The primary study aim was to evaluate whether CBIT[12] would prove superior to supportive therapy and education for reducing tics and tic-related impairment in children and adolescents with a chronic tic disorder. We were also interested in evaluating the effect of the behavioral intervention on children receiving stable medication for tics.

Participants

Eligible participants were aged 9 through 17 years, with Tourette or chronic tic disorder of moderate or greater severity, as measured by a Yale Global Tic Severity Scale[14] total score greater than 13 (>9 for children with motor or vocal tics only), English fluency, and IQ greater than 80. Co-occurring attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, other anxiety disorders, depressive disorders, or oppositional-defiant disorder was allowed unless the disorder required immediate treatment or change in current treatment. Children receiving psychotropic medications for tics or allowed psychiatric disorders were eligible if the dose was stable for 6 weeks, with no planned changes during study participation. The lack of data regarding premedication tic severity did not allow us to establish the degree of previous symptom reduction in medicated children. Exclusion criteria included an unstable medical condition, current diagnosis of substance abuse/dependence, lifetime diagnosis of pervasive developmental disorder, mania or psychosis, or 4 or more previous sessions of habit reversal training.

Treatments

The primary component of CBIT[12] is habit reversal training. The primary components of habit reversal are tic-awareness and competing-response training.[15] Awareness training entails self-monitoring of current tics, focusing on the premonitory urge or other early signs that a tic is about to occur. Competing-response training is based on the observation that performance of a tic results in a decrease in the premonitory urge. Over time, the reduction in the urge after completion of the tic reinforces repetition of the tic (ie, a negative reinforcement cycle).[9] Competing response training involves engagement in a voluntary behavior physically incompatible with the tic, contingent on the premonitory urge or other signs of impending tic occurrence. Competing-response training is distinct from deliberate tic suppression in that it teaches the patient to initiate a voluntary behavior to manage the premonitory urge (and disrupt the negative reinforcement cycle) rather

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than simply suppressing the tic. Initially, patient and therapist create a tic hierarchy and rank tics from most to least distressing, with more distressing tics addressed earlier in treatment.

Awareness training and competing response training are then implemented and practiced in session one tic at a time. For example, a child with a neck-jerking tic may be taught to look forward with his chin slightly down while gently tensing neck muscles for 1 minute or until the urge goes away. The competing response can be initiated when the patient notices that a tic is about to occur, during the tic, or after the tic has occurred. For vocal tics, slow rhythmic diaphragmatic breathing is the most common competing response. Patients are encouraged to use their competing responses throughout the day. Optimally, competing responses are compatible with maintaining participation in ongoing activities but incompatible with execution of the tic. With practice, patients are able to complete the competing response without disengaging from routine activities.

In addition to habit reversal training, CBIT also included relaxation training and a functional intervention to address situations that sustained or worsened tics. The functional intervention first identified situational antecedents and consequences influencing tic severity and then developed individualized behavioral strategies to reduce the influence of these factors.[16,17] For example, parents were taught to manage tic increases often occurring when their child returned home from school by encouraging and praising the child for practicing behavioral intervention techniques. Parents were also taught to manage their own reactions to the tics and to prevent the tics from exerting undue influence on family life.

The control treatment—supportive psychotherapy and education—provided information about tic disorders and was designed to mimic recommended adjunctive components of psychopharmacologic treatment.[18] Children and their parents were allowed to discuss tics and related issues, but therapists were prohibited from providing direct instructions about tic management.[19]

Both treatments were delivered in 8 sessions during 10 weeks and matched for session length and duration. The first 2 sessions were 90 minutes long to facilitate rapport building and information gathering. The remaining sessions were 60 minutes long. The first 6 sessions occurred weekly; the remaining 2, biweekly. Although both interventions focused on the child, parents were included for all or part of a session, depending on session content. After systematic training and certification, therapists with masters-level or higher education implemented both interventions according to detailed treatment manuals. Therapists also received weekly site-level and cross-site supervision, with an emphasis on maintaining the integrity of both interventions. Independent raters completed treatment integrity ratings on a random 13% sample of video-recorded therapy sessions, using a detailed checklist outlining the required and prohibited elements of each treatment session in both treatment conditions. Overall, 88% of behavioral intervention sessions and 98% of control treatment sessions were rated as good or better.

Randomization and Blinding

The data center randomly assigned eligible children by computer algorithm to treatment in a 1:1 ratio. The randomization was done within site and stratified by medication status to ensure that equal numbers of participants receiving tic medication would be in each treatment group. Children, their parents, and therapists were aware of assigned treatment condition. Independent outcome evaluators were masked to treatment assignment. Several methods were used to maintain the treatment blind, including segregation of assessment and treatment staff and instructions to children and parents to avoid discussion of treatment assignment with the independent evaluators.

Outcome Measures

Demographics, symptom severity, psychiatric diagnoses, and psychosocial functioning were obtained via self-report and clinical interview from children and their parents at screening and baseline. Children's racial/ethnic status was collected to provide comparability with similar studies and designated by parents on a parent-report questionnaire. Diagnostic eligibility was established with a *Diagnostic and Statistical Manual*–based, semistructured clinical interview[20] administered separately to parent and child and modified to cover Tourette and other tic disorders.[21]

Outcome assessments were repeated at weeks 5 and 10. The primary outcome measures were the Yale Global Tic Severity Scale Total Tic score[14] and the Clinical Global Impressions–Improvement scale.[22] The Yale Global Tic Severity Scale is a clinician-rated measure that begins with the completion of a checklist of all tics present in the past week. Current motor and vocal tics are then rated on 5 dimensions (number, frequency, intensity, complexity, and interference; range, 0-5 each), which are summed to yield separate motor and vocal tic scores (range, 0-25) and a combined total tic score (range, 0-50). An associated impairment scale (range 0-50) assesses tic-related disability during the past week. Functional status was also assessed with the clinician-rated Children's Global Assessment Scale (score 0-100).[23] Scores of 60 or lower indicate a need for treatment; scores above 70 reflect normal functioning. The Clinical Global Impressions–Improvement scale was used to assess overall treatment response. Lower scores indicate improvement and higher scores indicate worsening. By convention, scores of "very much improved" (1) or "much improved" (2) define positive response.[23]

Parents completed the Parent Tic Questionnaire,[24] which lists 28 motor and vocal tics to be marked as present or absent during the past week and is rated on a 1 to 4 severity scale (range, 0-112). With a 3-item scale (total score from 3-15), parents in both treatment

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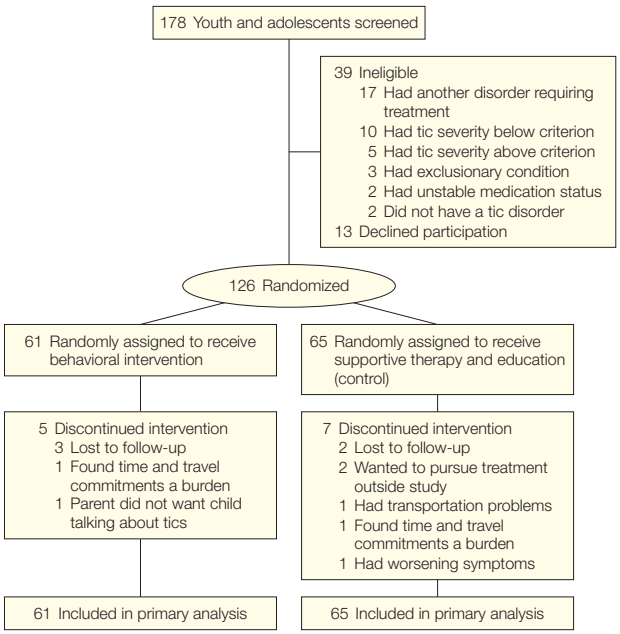
Figure. Flow of Patients Through the Trial



groups also rated how much they expected their child's assigned treatment to be beneficial at the end of their first therapy session.

Tic outcomes were rated by independent evaluators who were masked to treatment condition, were clinicians with at least a masters-level degree, and were trained to reliability. After didactic training and demonstration of reliability on 3 videotaped assessments, evaluators received ongoing supervision within site and via biweekly cross-site teleconference. All study interviews were recorded and 13% were randomly selected during the course of the study and independently rated for quality on a 7-item checklist with a 0 to 3 scale, with higher scores reflecting better quality. The mean item score of 2.33 reflects high quality and uniformity in the study outcome assessments; there were no site differences.

Adverse Events

Adverse events were monitored at each therapy session. Therapists asked about recent health complaints, behavioral changes, visits for medical/mental health care, need for concomitant medications, change in ongoing medications, and hospitalizations and offered the opportunity for spontaneous report of any other problem. Affirmative responses prompted further inquiry concerning the onset, severity, and outcome of the adverse event and measures taken to address it. Tic worsening was rated as an adverse event when child or parent spontaneously reported worsening inconsistent with the child's usual waxing and waning pattern.

Statistical Analysis

Our sample size calculation was based on examination of recently completed placebo-controlled medication trials for tics in children with Tourette syndrome. These trials report mean baseline Yale Global Tic Severity Scale Total Tic scores between 24 and 28, with standard deviations of 6 to 8 points. Change scores with medications superior to placebo range from 7 to 9 points compared with 2 to 4 points for placebo, yielding effect sizes of 0.9 to 1.0.[25-27] In this study, we planned to enroll medication-free children and those receiving tic-suppressing medication, which would predictably result in greater variability at baseline. In addition, we predicted that the supportive treatment condition would provide greater benefit than typically observed for pill placebo in medication trials. Therefore, we proposed a minimally significant effect size of 0.55, resulting in a sample size of 60 per group, given 10% attrition, significance level of 5%, and power of 80%.[28]

Baseline characteristics were compared between groups with *t* tests for continuous variables and χ^2 tests for categorical variables. Outcome data are presented as least squares means from a mixed-model repeated-measures analysis,[29] which assumes that missing data are missing at random and is more robust than other alternatives, such as analysis of completers only or using the last observation carried forward.[30] The effect of treatment on the primary outcome, Yale Global Tic Severity Scale Total Score, as well as the secondary outcomes, was tested with mixed-model repeated-measures analyses adjusted for baseline scores.[31] These efficacy analyses were conducted on the modified intention-to-treat population (ie, all participants with at least one postrandomization visit), with all participants analyzed in their assigned treatment condition. The models included fixed effects for treatment (2 levels), time (5 and 10 weeks), site, and time-by-treatment interaction and a random effect for participant. Treatment-by-site interactions were not significant for any of the outcome variables and were excluded from the models. Comparison of least squares means at week 10 were conducted with orthogonal contrasts. Sensitivity analyses were conducted with the last observation carried forward, which resulted in the same conclusions and are therefore not presented. Separate analyses examined modification of treatment effect by presence of tic medication at baseline by examining the 2- and 3-way interactions of treatment with time and medication status. Effect sizes were estimated by subtracting the 10-week baseline-adjusted least squares

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mean in the control group from the mean change in the treatment group and dividing by the pooled standard deviation for the entire study sample (N = 126) at baseline. The proportion of positive responses on the Clinical Global Impressions–Improvement Scale was compared across time with Mantel-Haenszel χ^2 to adjust for site. Comparisons of adverse event rates were made with Fisher exact tests. Data regarding treatment durability were examined with all participants who exhibited a positive response at week 10 and participants who returned for follow-up assessment. Because of low power, between-group comparisons of Clinical Global Impressions–Improvement positive response rates and Yale Global Tic Severity Scale scores during the follow-up period were not made. All analyses were performed with SAS version 9.1 (SAS Institute Inc, Cary, North Carolina) at the 2-sided .05 level of significance. There was no adjustment for multiple comparisons for testing secondary outcomes.

RESULTS

Baseline Characteristics

During the 30-month period from December 2004 to May 2007, 178 children and adolescents were screened and 126 were randomly assigned to 1 of the 2 treatment conditions (FIGURE). Enrollment across sites was similar (TABLE 1). Participants ranged in age from 9 through 17 years (mean [SD], 11.7 [2.3] years); 99 (78.6%) were boys, 106 (84.1%) were white, and 118 of 126 (93.7%) met criteria for Tourette disorder. Overall, 36.5% of children who entered the trial were receiving stable antitic medication. There were no significant between-group differences in baseline demographic or clinical characteristics, including tic medication status. Attrition in the behavioral intervention group was 8% (5/61) vs 11% for the control treatment (7/65). Children in the behavioral intervention attended 94.1% of scheduled sessions compared with 93.7% for the control condition. Two (3.3%) participants in the behavioral

Table 1. Baseline Demographic and Clinical Characteristics by Treatment Group[a]

Characteristic	No. (%) Behavioral Intervention (n = 61)	No. (%) Control (n = 65)
Study center		
Johns Hopkins University	20 (32.8)	21 (32.3)
University of California, Los Angeles	21 (34.4)	24 (36.9)
University of Wisconsin–Milwaukee	20 (32.8)	20 (30.8)
Demographics		
Age, mean (SD), y	11.6 (2.3)	11.7 (2.3)
WASI IQ, mean (SD)	111.7 (13.5)	108.6 (14.0)
Male sex	46 (75.4)	53 (81.5)
Race/ethnicity		
White, non-Hispanic	51 (83.6)	56 (86.2)
White, Hispanic	6 (9.8)	3 (4.6)
Black	1 (1.6)	3 (4.6)
Asian/Pacific Islander	2 (3.3)	2 (3.1)
Other	1 (1.6)	1 (1.5)
Two-parent family	50 (82)	57 (87.7)
Parent occupation[b]		
Laborer/homemaker/clerical	4 (6.6)	2 (3.1)
Craftsperson/artist	1 (1.6)	3 (4.6)
Technician/skilled laborer	5 (8.2)	9 (13.8)
Professional	51 (83.6)	50 (76.9)
Parent education[b]		
High school	4 (6.6)	1 (1.5)
Technical school/some college	7 (11.5)	13 (20)
College graduate	21 (34.4)	17 (26.2)
Graduate or professional school	29 (47.5)	34 (52.3)
Tic disorder		
Tourette disorder	56 (91.8)	62 (95.4)
Chronic motor tic	4 (6.6)	3 (4.6)
Chronic vocal tic	1 (1.6)	0
Yale Global Tic Severity Scale, mean (SD)		
Total score	24.7 (6.2)	24.6 (6.0)
Total motor	14.6 (4.4)	14.6 (3.2)
Total vocal	10.1 (4.5)	10.0 (4.7)
Other diagnoses[c]		
Attention-deficit/hyperactivity disorder	20 (32.8)	13 (20.0)
Obsessive-compulsive disorder	8 (13.1)	16 (24.6)
Generalized anxiety	10 (16.4)	15 (23.1)
Separation anxiety	6 (9.8)	5 (7.7)
Social anxiety	13 (21.3)	14 (21.5)
Receiving tic medications at entry	23 (37.7)	23 (35.4)
No medication	38 (62.3)	42 (64.6)
Antipsychotic[d]	8 (13.1)	3 (4.6)
α-Agonist[d]	11 (18.0)	14 (21.5)
Anticonvulsant[d]	1 (1.6)	1 (1.5)
Benzodiazepine[d]	0	1 (1.5)
α-Agonist + antipsychotic[e]	3 (4.9)	2 (3.1)
α-Agonist + levetiracetam	0	1 (1.5)
Antipsychotic + donepezil	0	1 (1.5)

Abbreviation: WASI, Weschler Abbreviated Scale of Intelligence.
[a] There were no significant between-group differences for any of the listed variables.
[b] "Parent occupation" and "education" classifications were based on the parent with the highest level in 2-parent homes or parent of primary resident in single-parent homes.
[c] Some participants had more than one coexisting diagnosis.
[d] Antipsychotics included haloperidol, pimozide, risperidone, aripiprazole, olanzapine; α-agonists: guanfacine, clonidine; anticonvulsants: valproate, levetiracetam; benzodiazepine: clonazepam.
[e] One child was receiving an α-agonist and 2 antipsychotic medications.

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intervention and 4 (6.2%) in the control group reported a change in their tic medication type or dose during acute treatment. Because of the low frequency of medication changes, no adjustments were made in the analysis.

Outcomes

After 10 weeks of treatment, the Yale Global Tic Severity Scale Total Tic score was significantly reduced in the behavioral intervention group compared with that in the control group ($P<.001$). Behavior therapy was associated with a 7.6-point decrease in the Yale Global Tic Severity Scale Total Tic score compared with a 3.5-point decrease in the control treatment. This 4-point difference between groups is similar to that in placebo-controlled medication trials and was clinically meaningful, as suggested by an effect size of 0.68.[32] Moreover, the rate of positive treatment response as measured by a rating of 1 (very much improved) or 2 (much improved) on the Clinical Global Impressions–Improvement Scale was significantly higher for the behavioral (52.5%; 32/61) vs control (18.5%; 12/65) intervention ($P<.001$). For behavior therapy, this difference reflects a number needed to treat of 3 and an absolute risk reduction of 34%.

TABLE 2 displays mean scores, effect sizes, and confidence intervals (CIs) on the difference between CBIT and the control condition for all study outcomes. Positive results for CBIT relative to control treatment were again evident on motor tics, phonic tics, and tic-related impairment. Children randomized to behavioral intervention exhibited a 51% decrease (25.0 to 12.2) on Yale Global Tic Severity Scale–Impairment from baseline to week 10 compared with a 30% decrease (23.4 to 16.4) for the control treatment ($P=.004$; effect size=0.57). Both groups exhibited improvement on the clinician-rated Children's Global Assessment Scale. However, children and adolescents in the CBIT group exhibited greater improvement on the Children's Global Assessment Scale compared with the control treatment (59.0 to 69.4 vs 59.3 to 64.1, respectively; $P<.001$; effect size=0.64). There were no treatment differences across sites. In addition, neither the presence of tic-suppressing medication nor tic severity at baseline significantly moderated treatment outcome. Parents indicated a moderately high degree of expected benefit for each treatment (behavior therapy: mean=11.3, 95% CI, 10.8-11.8; control treatment: mean=10.4, 95% CI 9.9-10.9). Although statistically significant ($P=.02$), this small difference was not clinically meaningful.

Table 2. Baseline, Week 5, and Week 10 Scores on Key Outcome Measures[a]

	Mean (95% CI)			
	Behavioral Intervention (n = 61)	Control (n = 65)	Group Difference at Week 10 (95% CI)	Effect Size[b]
Yale Global Tic Severity Scale				
Total tic score				
Baseline	24.7 (23.1-26.3)	24.6 (23.2-26.0)		
Week 5	19.7 (17.6-21.7)	22.8 (20.7-24.9)	3.3 (1.2-5.4)	0.54
Week 10	17.1 (15.1-19.1)	21.1 (19.2-23.0)	4.1 (2.0-6.2)	0.68
Total motor				
Baseline	14.6 (13.5-15.7)	14.6 (13.8-15.4)		
Week 5	12.2 (10.8-13.6)	13.6 (12.4-14.7)	1.3 (0.1-2.7)	0.34
Week 10	10.7 (9.3-12.1)	12.5 (11.5-13.5)	1.9 (0.4-3.3)	0.49
Total vocal				
Baseline	10.1 (9.0-11.2)	10.0 (8.9-11.1)		
Week 5	7.4 (6.2-8.6)	9.3 (7.9-10.6)	2.0 (0.7-3.3)	0.43
Week 10	6.5 (5.4-7.6)	8.6 (7.4-9.8)	2.2 (0.9-3.6)	0.50
Impairment				
Baseline	25.0 (22.6-27.4)	23.4 (21.6-25.2)		
Week 5	16.8 (14.0-19.5)	20.1 (17.6-22.7)	3.8 (0.7-6.8)	0.47
Week 10	12.2 (9.8-14.6)	16.4 (13.8-19.0)	4.7 (1.6-7.8)	0.57
Parent Tic Questionnaire total score				
Baseline	34.2 (29.5-38.9)	35.7 (30.3-41.1)		
Week 5	25.8 (21.5-30.1)	33.7 (27.8-39.6)	7.3 (1.5-13.1)	0.28
Week 10	20.0 (16.3-23.7)	27.6 (23.0-32.2)	7.8 (1.9-13.8)	0.30
Children's Global Assessment Scale[c]				
Baseline	59.0 (57.1-60.9)	59.3 (57.3-61.3)		
Week 10	69.4 (66.9-71.9)	64.1 (59.5-68.7)	5.8 (2.8-8.8)	0.64

Abbreviation: CI, confidence interval.
[a] Data are presented as least square mean values and 95% CIs and standard deviations for each assessment point. Group differences with 95% CIs are also presented.
[b] Effect sizes were calculated as follows: change from baseline in behavior therapy minus change in the control group divided by the pooled standard deviation for the entire study sample at baseline.
[c] Children's Global Assessment Scale administered only at baseline and week 10.

Adverse Events

Two hundred adverse events were reported during the 10-week phase 1 trial. Of these, 193 were rated as mild or moderate and 7 as severe (broken bones, n=3; concussion, n=1; neck pain, n=1; neck injury, n=1; nausea and vomiting, n=1); none of the severe events was considered study related. There were no serious adverse events. Tic worsening above and beyond usual fluctuation was spontaneously reported by 1 participant (1.6%) receiving behavioral intervention and by 4 participants (6.2%) in the control treatment (TABLE 3).

Treatment Durability

Acute-phase positive responders received 3 monthly booster treatment sessions and were reevaluated at 3 and 6 months following treatment. Of the 32 children classified as positive responders to CBIT at week 10, 28 returned for assessment at 3 months and 23 returned at 6 months following treatment. In the control group, all 12 children classified as positive responders at week 10 returned for assessment at

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3 months and 8 returned at 6 months following treatment. As shown in TABLE 4, 20 of 32 (62.5%) positive responders to CBIT and 20 of 23 (87%) available responders (9 children were lost to follow-up) exhibited continued benefit at 6 months. In the control group, 6 of 12 (50%) responders and 6 of 8 (75%) available responders (4 children were lost to follow-up) exhibited continued benefit. Considering only individuals with complete data in the CBIT group (n=23), the mean score on the Yale Global Tic Severity Scale was 13.7 (95% CI, 10.5-16.9) at week 10 and 13.9 (95% CI, 10.4-17.3) and 13.3 (95% CI, 9.8-16.8) at months 3 and 6, respectively. For the control, 6 children with complete data had a mean score on the Yale Global Tic Severity Scale of 13.0 (95% CI, 9.3-16.7) at week 10 and 9.9 (95% CI, 2.1-15.7) and 10.4 (95% CI, 2.6-18.2) at months 3 and 6, respectively.

COMMENT

A comprehensive behavioral intervention based on habit reversal training was effective in reducing tics and tic-related impairment in children and adolescents with Tourette or chronic tic disorder of moderate or greater severity. Benefits of the behavioral intervention were observed in independent masked-clinician and parent ratings regardless of tic-medication status and were durable during a 6-month follow-up interval for children who exhibited a positive response to acute treatment. The findings of this trial validate those of several smaller studies.[8,33] Given the more active control treatment in this trial, the magnitude of response in this study is comparable to results of controlled trials with antipsychotic medications for Tourette disorder.[25,27] The absolute decrease of 7.6 points (31% from baseline) on the Total Tic score of the Yale Global Tic Severity Scale in the CBIT group is only slightly less than the decrease caused by effects of antipsychotic medications in children with Tourette disorder. Recent placebo-controlled trials reported a decrease of 8.6 points (35%) and 9.7 points (36%) after 8 weeks of treatment with ziprasidone[27] and risperidone,[25] respectively. In addition, the number needed to treat of 3 found for behavior therapy in the present study compares favorably with that found in recent trials for other child psychiatric disorders.[21,34-36]

The sample included children with a range of tics and associated impairment, as well as co-occurring psychiatric conditions, suggesting that the study results are applicable to clinical populations of children with moderate to severe Tourette disorder. The generalizability of our findings is further supported by the fact that, unlike previous psychopharmacologic trials for Tourette disorder that excluded children receiving medication,[37] 38% of children in our study were receiving stable tic-suppressing medication at study entry. The lack of data on premedication tic severity in this subgroup is a study limitation. Parents reported high expectation for positive outcome for both treatments, and the attrition rate was low for both interventions, suggesting that each was acceptable and well tolerated by children and families. The relative absence of tic worsening in the behavioral intervention should reassure clinicians, patients, and families who might be concerned that behavioral strategies to reduce tic severity are inadvisable or contraindicated.[38] The low attrition rate in the supportive therapy and education condition suggests that children and families also found this interven-

Table 3. Adverse Events by Treatment Group

Adverse Event[a]	Behavioral Intervention (n = 61) No.	Behavioral Intervention (n = 61) % (95% CI)	Control (n = 65) No.	Control (n = 65) % (95% CI)	*P* Value[b]
Upper respiratory tract infection	21	34.4 (22.7-47.7)	27	41.5 (29.4-54.4)	.47
Irritability and explosive behavior	10	16.4 (8.2-28.0)	10	15.4 (7.6-26.5)	.99
Headache	10	16.4 (8.2-28.0)	14	21.5 (12.3-33.5)	.50
Muscle or joint pain	9	14.8 (7.0-26.2)	13	20.0 (11.1-31.8)	.49
Falls and athletic injuries	7	11.5 (4.7-22.2)	19	29.2 (18.6-41.8)	.02
Anxiety and nervousness	4	6.6 (1.8-15.9)	3	4.6 (0.9-12.9)	.71
Disruptive behavior[c]	4	6.6 (1.8-15.9)	4	6.2 (1.7-15.0)	.99
Sore throat	4	6.6 (1.8-15.9)	7	10.8 (4.4-20.9)	.53
Nausea, vomiting	2	3.3 (0.4-11.3)	5	7.7 (2.5-17.0)	.44
Stomach discomfort	2	3.3 (0.4-11.3)	9	13.8 (6.5-24.7)	.06
Dermatologic problems[d]	1	1.6 (0.04-8.8)	5	7.7 (2.5-17.0)	.21
Tic worsening	1	1.6 (0.04-8.8)	4	6.2 (1.7-15.0)	.37
Tiredness, fatigue	1	1.6 (0.04-8.8)	4	6.2 (1.7-15.0)	.37

Abbreviation: CI, confidence interval.
[a] Defined as mild (new event that did not interfere with activities of daily living), moderate (new event that posed some interference or required intervention to prevent interference), or severe (new event that posed interference and required intervention).
[b] By Fisher exact test (2-sided).
[c] Increase in impulsive and oppositional behavior.
[d] Rash, dermatitis, sunburn.

Table 4. Children Exhibiting Continued Positive Response on the Clinical Global Impressions–Improvement Scale at 3 Months and 6 Months Following Treatment

	No./Total (%)			
	Behavioral Treatment		Control	
	3 Months	6 Months	3 Months	6 Months
Available participants[a]	24/28 (85.7)	20/23 (87.0)	11/12 (91.7)	6/8 (75.0)
All acute-phase responders	24/32 (75.0)	20/32 (62.5)	11/12 (91.7)	6/12 (50.0)

[a] The proportion of continued positive response is expressed over available participants, as well all acute-phase responders. Study participants who were lost to follow-up were not counted as positive responders.

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tion meaningful.[18] Although it did not have a significant effect on tic severity, the control treatment was associated with a 31% decrease in tic-related impairment. Thus, it is unlikely that the superiority of active treatment was mediated by differences in parental expectancy or treatment acceptability.

Our results have several clinical implications. First, the efficacy of the behavioral intervention expands available treatment options for tic disorders. Second, by emphasizing the development of skills that promote autonomy and mastery, this intervention offers patients and their families an active role in treatment. Third, the dissemination of the behavioral intervention may improve public health by increasing access to care through expanding the range of practitioners who can treat children with Tourette and chronic tic disorder. Published treatment manuals and existing educational outreach funded by the Centers for Disease Control and Prevention will aid dissemination to trained behavioral therapists.

The 10-week duration of the acute efficacy phase compares favorably with that of recent randomized medication trials targeting tic severity in children, all of which ranged from 4 to 8 weeks.[25,27,39,40] Although the behavioral intervention demonstrated efficacy in this trial, a sizeable number of children did not benefit. In addition, although neither baseline tic severity nor medication status moderated treatment outcome, future analyses may provide guidance on patient selection and future research may provide insight about the underlying mechanism of this intervention.

The durability of treatment is an important consideration in treatment choice but to date has been poorly studied for chronic tic disorder.[41] Although our study design did not include evaluation of all children posttreatment, resulting in a loss of randomization, findings provide preliminary support for the durability of response to behavioral intervention.

The observation in the 1960s that haloperidol was effective in reducing tic severity led to a fundamental reconceptualization of Tourette disorder as a neurotransmitter-based neurologic disorder[42,43] and stimulated a generation of neurobiological research. The results of this study may prompt a similar reconceptualization of tic disorders and provide a new platform for future research. However, acknowledging that behavioral and learning processes play a role in tic severity does not imply that tics have a purely psychological etiology or that patients can suppress tics by force of will. Rather, our study lends clinical support to advances in basic science that emphasize the role of both cortical[44-46] and basal ganglia[47-49] circuitry on motor function and habit formation.

Author Contributions: Dr Piacentini had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Piacentini, Woods, Scahill, Wilhelm, Peterson, Chang, Ginsburg, Deckersbach, Dziura, Walkup.
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