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Current controversies on the role of behavior therapy in Tourette Syndrome

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Abstract

Comprehensive Behavioral Intervention for Tics (CBIT) is a safe and effective treatment for managing the tics of TS. In contrast to most current medications used for the treatment of tics, the efficacy of CBIT has been demonstrated in two relatively large, multisite trials. It also shows durability of benefit over time. Similar to psychopharmacological intervention, skilled practitioners are required to implement the intervention. Despite concerns about the effort required to participate in CBIT, patients with TS and parents of children with TS appear willing to meet the

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requirements of the CBIT program. Efforts are underway to increase the number of trained CBIT providers in the United States. Based on available evidence, recent published guidelines suggest that CBIT can be considered a first-line treatment for persons with a tic disorders.

Keywords

Tourette syndrome; tics; habit reversal therapy; evidence-based treatment

Motor and phonic tics are the defining neurological symptoms of Tourette syndrome (TS).¹ Historically, pharmacotherapy has been used to modulate the function of brain circuits presumed to underlie tics. Behavior therapy, based on Habit Reversal Training, offers another approach to tic reduction. Many patients with TS report an unpleasant sensation or warning preceding some or all of their tics. Patients also report that the execution of the tic temporarily relieves these unwanted sensations. Habit Reversal Training (HRT) promotes strategies intended to disrupt this pattern of unwanted premonitory sensations and temporary relief following the performance of tics. Early reports provided encouraging results for HRT.² Several critical reviews concur that HRT is effective for reducing tics in children and adults.³⁻⁵ In addition, treatment guidelines from professional societies in Europe and Canada recommend HRT as a first line treatment for tics.^{6,7}

Comprehensive Behavioral Intervention for Tics (CBIT), which integrates HRT with procedures designed to mitigate influences of daily life that worsen tics, has been evaluated for the treatment of tics in two large-scale randomized trials.^{8,9} In the first trial, 126 subjects (age 9 to 17 years) were randomly assigned to CBIT or a psychoeducational control condition. Using the same design, the second trial included 122 subjects (age 16 to 69 years). In these trials, tic severity on the Yale Global Tic Severity Scale (YGTSS) and overall response on the Clinical Global Impression-Improvement scale (CGI-I) were rated by clinicians who were blind to treatment assignment.

The YGTSS is a semi-structured, clinician-rated measure of tic severity that is the most commonly used outcome measure in TS treatment trials. It includes a review of motor and phonic tics and several dimensions such as number, frequency, forcefulness, complexity and degree of interference to derive a Total Tic score ranging from 0 to 50 with higher scores indicating greater severity.¹⁰

The YGTSS Total Tic score declined by 31% in the CBIT group in the child trial (effect size = 0.68) and by 26% (effect size = 0.57) in the adult trial. These decreases were significantly greater than the 14.2% and 11.4% for the control condition in the child and adult trials, respectively. On the CGI-I, 52.5% of children in the CBIT group showed a positive response compared to 18% of children in the control condition.⁸ In the adult trial, 40% of subjects in CBIT showed a positive response compared to 7% in the control condition.⁹

Each of the CBIT trials was larger than any prior medication study focused on tic reduction (see Table 1).^{8,9,11-19} In addition, CBIT is among the few interventions demonstrating a positive effect on tic severity in more than one study. Despite these findings, questions about the efficacy and safety of HRT-based therapy in TS persist.^{20,21} Common objections

include: 1) CBIT is only useful for patients with mild tics; 2) CBIT requires considerable effort by the patient; 3) reduction in tic severity following CBIT is modest and gains may not endure over time; 4) CBIT may result in tic substitution or tic worsening. We examine each of these claims using data from the CBIT trials and results from selected placebo-controlled medication trials. Other concerns about CBIT include lack of trained professionals to deliver it effectively, lack of insurance reimbursement, and the possibility that dissemination of CBIT as an effective behavior therapy would lead to recasting TS as a psychological (versus neurological) disorder.

CBIT is only useful for patients with mild tics

The two CBIT trials enrolled a total of 221 subjects with TS and 27 subjects with Chronic Tic Disorder (CTD). To compare results from the CBIT trials with those of medication trials listed in Table 1, we excluded subjects with CTD and including only subjects with TS. The mean baseline YGTSS Total Tic scores for subjects with TS in the child CBIT trial was 25.3 ± 5.62 and 24.4 ± 5.83 in the adult trial. Although not shown in Table 1, these baseline tic severity scores are comparable to mean baseline YGTSS Total Tic scores for these placebo-controlled medication trials.

CBIT requires considerable effort for patients

This critique implies a contrast between the effort required to take medication versus the effort required to participate in CBIT. CBIT does indeed require participation in therapy sessions and practice between sessions. However, attrition in the CBIT trials was relatively low (9.5% and 13.9% in the child and adult trial, respectively) suggesting that effort did not hinder subject retention. In the placebo-controlled medication trials presented in Table 1, attrition is in a similar range with the exception of trials by Silver et al.¹² and Jankovic et al.¹⁹ both of which exceeded 30%. Moreover, the implication that medication treatment is simple and well-accepted by patients with TS is not supported by a parent survey on 740 children with TS.²² In that survey, 36% of parents reported that medication treatment was difficult for their child due to drug-induced side effects and 43% of parents expressed avoidance of tic medication due to concerns about adverse effects.

Gains in tic severity are likely to be modest and may not endure over time.

As shown in Table 1, the effect sizes in the CBIT trials were lower than several studies listed, but similar or higher than others. The sample sizes in the CBIT trials, however, were larger than any previous placebo-controlled trials focused on tic reduction. Moreover, most of the medication studies in Table 1 enrolled medication-free subjects from a single site. In order to promote more generalizable results, the CBIT trials were multisite studies that included subjects on stable tic medication and stable medication for co-occurring anxiety, depression or obsessive-compulsive disorder. Although these entry criteria enhanced the generalizability of the CBIT trials, these design decisions posed a more difficult test for the efficacy of CBIT due to increased variability. Furthermore, the inclusion of subjects on tic medication in the CBIT trials may have limited the effects of CBIT, as some gains would have already been realized from the medication.

Most placebo-controlled medication studies focused on tic reduction were 6-8 weeks in duration. Thus, there is insufficient information on enduring benefit for current medications used for the treatment of tics. Combining data from both CBIT trials, the overall rate of positive response (defined by a rating of Much Improved or Very Much Improved by a blinded rater) was 45.2% (56 of 124) for subjects in the CBIT group. Of these, 38 subjects returned for six-month post-treatment follow-up and 32 (84.2%) showed continued benefit. In PST, 12 of 65 (18.5%) were rated as Much Improved or Very Much Improved at Week 10. Ten subjects returned for the six-month follow-up assessment and 70% continued to show a positive response. It is possible that subjects with continued benefit were more likely to return for the six-month follow-up visit. Furthermore, post-treatment follow-up did not include subjects who did not show a positive response in the acute study phase. Thus, these encouraging longer-term results support, but do not prove, the enduring positive effects of CBIT.

CBIT may result in tic substitution or tic worsening.

This concern appears to be based on early reports of tic worsening following behavioral intervention.²³ Here we are reminded of the long-held prohibition of using methylphenidate for the treatment of ADHD in children with TS due to concern about tic worsening.²⁴ It was only when stimulants were examined in controlled trials that the long-held prohibition was revised.^{25,26} Tic worsening was systematically evaluated in the CBIT trials with the YGTSS, CGI-I and documentation of spontaneous report by study subjects by clinicians blind to treatment assignment. Over the entire sample of 248 participants, tic worsening was detected in 5 of 124 subjects (4%) in CBIT and 8 of 124 subjects (6.4%) in the control condition. These findings indicate that CBIT does not result in tic worsening.

Tic substitution would also be detected by the YGTSS. If one or more tics were simply exchanged for other tics, the Total Tic score would not decline over time with treatment. Improvement in the YGTSS scores in these trials does not support tic substitution.

Another closely related issue is concern about tic rebound following efforts to suppress tics.²⁷ This was tested in a sample of 20 subjects with TS by Verdellen and colleagues (2007).²⁸ In that study, subjects were treated with exposure and response prevention. This behavioral intervention instructs patients to refrain from performing the tic for extended period of time rather than respond. Using video recordings and tic counts, the investigators compared tic frequency in a 15-minute period before and after each tic suppression therapy session. In all ten therapy sessions, the mean post-session tic counts were lower than the baseline.

Trained CBIT practitioners and insurance coverage for CBIT are lacking.

Of course, only competent and trained practitioners should administer CBIT. The challenge of disseminating evidenced-based treatments, including appropriate use of medication in neurology and psychiatry, is a problem that is not unique to CBIT. Concerted effort by the Tourette Syndrome Association (TSA) and the US Centers for Disease Control are underway to enhance the availability of trained CBIT providers.^{29,30} There are also encouraging results from pilot telemedicine applications of CBIT in remote regions.³¹

The discussion of insurance coverage for CBIT is complicated by regional differences, the multitude of health plans that are currently available, and the fact that health care financing is rapidly changing.³² The demonstrated benefit of various psychosocial interventions for a range behavioral health conditions is having a positive impact on reimbursement and may have greater impact in the future as insurance companies acquiesce to the weight of evidence.³³ The accumulating evidence supporting the efficacy and safety of CBIT may empower consumers to demand insurance coverage.

Effective behavior therapy could lead to recasting TS as a psychological disorder rather than a neurological condition

Given the longstanding effort to emphasize the neurological underpinnings of TS, there is concern that dissemination of CBIT could lead to a reconceptualization of TS as a psychological disorder.²¹ This important concern presents a challenge for public and professional education about the false dichotomy between psychological and neurological systems that influence human behavior. The success of behavior therapy for symptom reduction and rehabilitation in other neurological conditions such as epilepsy and multiple sclerosis underscores the essential interaction between psychological and neurological systems.^{34,35}

Although the neurobiological mechanisms of behavior therapy for tics have not been identified, frontal cortical and striatal mechanisms are likely to be involved. There is evidence that CBT for anxiety and obsessive-compulsive disorder alters frontal and striatal circuits and that the changes are similar to those seen with pharmacotherapy for those disorders.³⁶ Furthermore, successful response to behavior therapy requires transition from a cognitive strategy (practice) to an unconscious, automatic performance of the learned response. This transition likely involves striatal mechanisms involved in habit learning.³⁷

Final note

Roughly half of the subjects in the CBIT trials did not show a positive response. Additional research is needed to delineate the mechanism of CBIT and to identify strategies that can expand the rate of positive response to CBIT. Although it is not true in all cases many children do indeed “grow out” of their tics.³⁸ Nonetheless, tics can have adverse social consequences. These adverse consequences may endure even after the tics subside in early adulthood. CBIT offers an option for children, their families and adults to manage tics in a manner that may reduce tic severity and negative social consequences. Results presented in Table 1 suggest that drug treatment is also in need of further study. Thus, a balanced approach to intervention research that includes drug development, dissemination of CBIT and strategies for refractory cases is warranted.

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Table 1

Randomized clinical trials focused on tic reduction as measured by the YGTSS Total Tic^{a,b,c,d,e} score using parallel group design, raters blind to treatment and sample sizes of 20 or greater.

Author, year	Drug	N	# of Weeks	Effect Size ^f	% Improvement ^g	Active > Placebo ^h	# Drop Outs N (%)
Sallee et al., 2000 ¹⁰	ziprasidone	28	8	0.87	34.8	Yes	2 (7.1)
Silver et al., 2001 ¹¹	mecamylamine	61	8	NR	13.0	No	23 (37.7)
Cummings et al., 2002 ¹²	guanfacine	24	4	0.81	37.2	No	NR
Scahill et al., 2003 ¹³	risperidone	34	8	0.91	32.3	Yes	2 (5.9)
Gilbert et al., 2003 ¹⁴	pergolide	51	8	0.60	23.7	No	6 (11.8)
Hoekstra et al., 2004 ¹⁵	IVIG	30	14	0.40	19.6	No	2 (6.7)
Nicolson et al., 2005 ¹⁶	metoclopramide	28	8	0.98	38.5	Yes	4 (14.3)
Toren et al., 2005 ¹⁷	ondansetron	30	3	0.24	27.2	No	3 (10)
Jankovic et al., 2010 ¹⁸	topiramate	29	10	1.05	53.6	Yes	9 (31)
Piacentini et al., 2010 ⁸	CBIT-child	126	10	0.68	31	Yes	12 (9.5)
Wilhelm et al., 2012 ⁹	CBIT-adult	122	10	0.57	26	Yes	17 (13.9)

^a Atomoxetine, guanfacine, selegiline trials focused on ADHD and were excluded.

^b Crossover trials of pergolide and levetiracetam were excluded because reports did not provide data for the first arm of the trial.

^c Pramipexole trial did not provide baseline or endpoint scores and was excluded.

^d Botulinum toxin, THC trials did not use YGTSS Total Tic score and were excluded.

^e Verdellen et al., 2004 compared two active treatments (Habit Reversal vs Exposure and Response Prevention); unclear if raters were blind to treatment assignment and was not included.

^f (Change in active – change in placebo) ÷ std deviation at baseline estimated for the full sample at baseline.

^g Change in active ÷ mean score at baseline for the active treatment group × 100.

^h CBIT trials had a psychoeducational control condition with responses consistent with placebo in medication trials.