

CHILD AND DEVELOPMENTAL PSYCHIATRY (M GRADOS, SECTION EDITOR)

Behavioral Therapy for Tourette Disorder: An Update

Michael B. Himle¹ · Matthew R. Capriotti²

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Abstract

Purpose of Review The past decade has realized substantial progress in understanding and treating Tourette disorder (TD). The goal of this review is to highlight recent research on behavioral approaches for treating TD and to identify limitations to this treatment approach and directions for future research.

Recent Findings Two large randomized controlled trials provide the most compelling evidence to date of the efficacy of behavior therapy for reducing tic severity in both children and adults with TD. Historical concerns regarding adverse treatment side effects have been examined and are not supported. However, treatment response remains incomplete and studies have shown that access to trained providers and the burden associated with treatment are significant barriers to utilization. Abbreviated treatment protocols and remote delivery have been investigated and have shown promise for addressing these issues.

Summary Behavior therapy is an efficacious treatment for TD, a better understanding of the behavioral and biological mechanism(s) by which behavior therapy operates will likely lead to improved outcomes. Additionally, it is critical to continue to identify barriers to implementation and improve dissemination of this efficacious treatment option.

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Introduction

Persistent tic disorders (PTD), including Tourette Disorder (TD), are a class of childhood-onset neurodevelopmental movement disorders characterized by involuntary motor and/ or vocal tics [1]. Prevalence estimates suggest that PTDs affect 0.5-1 % of school-aged children, disproportionately affect boys, and take a fluctuating course [2]. Although many individuals report some remission of tic symptoms in adolescence and early adulthood, tics persist into adulthood in many individuals. The mechanisms underlying improvement or persistence are unclear [3, 4]. In moderate to severe cases, PTDs are associated with considerable functional impairment and a decreased quality of life [5, 6]. The cause of PTDs remains unknown; however, family, twin, and segregation studies provide strong evidence of polygenic inheritance, although the specific genes involved are yet to be identified [7]. From a neurocognitive perspective, converging lines of research implicate failed inhibition within cortico-striato-thalamo-cortical (CSTC) pathways in the pathogenesis of tics [8].

Based on the biological conceptualization of TD, pharmacotherapy, and, in particular, anti-dopaminergic agents, have historically been considered the first-line of treatment [9]. For less severe tics, alpha agonist preparations can be utilized. While pharmacotherapy is beneficial for many patients, it rarely results in complete or sustained symptom remission and is limited by concerns of unwanted side effects [10], emphasizing the need for ancillary and/or alternative approaches to treatment. Recently, behavior therapy has garnered strong empirical support as an efficacious treatment for TD and is now recommended as a first-line intervention by several

¹ Department of Psychology, University of Utah, 380 S. 1530 E., BehS #502, Salt Lake City, UT 84112, USA

² Department of Psychology, San Jose State University, San Jose, CA, USA

international groups [11–13]. Rather than offering an explanation for the underlying cause of tics, behavioral approaches target environmental (i.e., behavioral) processes believed to maintain and exacerbate tics. A primary assumption of the behavioral model is that the frequency, complexity, and forcefulness of tics can be reduced by eliminating (or altering) environmental/social reinforcers that exacerbate tics and reinforcing the use of specific tic suppression strategies [14].

Overview of Behavioral Approaches to Treating TD and Their Rationale

Although behavior therapy for the treatment of tics has received increased attention over the past decade, the idea that tics can be managed with behavioral techniques is not new. Early research reports demonstrating the successful application of behavior therapy for reducing tics date back to the early 1970s when Nathan Azrin and colleagues described the use of habit reversal training (HRT) to successfully treat tics and other repetitive behaviors [15]. Similarly, early investigations by researchers in the UK demonstrated the efficacy of a behavioral tic suppression procedure known as exposure and response prevention (ERP), which shares some similarity (and differences) with HRT [16, 17]. The central idea behind both HRT and ERP is that tics are strengthened through negative reinforcement [16-18]. The negative reinforcement conceptualization of tics stems from studies showing that most adults and children report that their tics are preceded by aversive premonitory urges that are reduced, at least temporarily, when tics are performed [19, 20]. Based on this conceptualization, both HRT and ERP employ specific therapeutic techniques to teach individuals to become more aware of their tics and associated urges and suppress their tics, for example, by engaging in a physically incompatible behavioral response prior to tic onset [14, 16]. The intent is to facilitate habituation to premonitory urges and break the negative reinforcement cycle [21], much in the same way that repeated and prolonged exposure to a feared stimulus reduces physiological arousal and avoidance behavior characteristic of an anxiety response [22].

More recently, an expanded version of HRT, known as comprehensive behavioral intervention for tics (CBIT), was developed [14]. Although HRT is a primary therapeutic component of this intervention package, CBIT extends beyond the negative reinforcement (i.e., urge-reduction) conceptualization of tics by emphasizing the role of contextual factors (e.g., particular settings, activities, or social reactions that worsen tics) in determining TD severity and impairment. For example, the CBIT model posits that when tics are performed, they often elicit reactions from others. When such reactions are delivered contingent upon tics, they can exacerbate the intensity and frequency of tics and premonitory urges through the same operant reinforcement processes that influence voluntary behavior [23••]. In addition, although the specific mechanism remains unclear, there is substantial evidence that tics are exacerbated by psychological factors such as stress, anticipation, anxiety, boredom, and other affective and mood states [24]. To address these tic-exacerbating factors, along with HRT, CBIT includes a set of function-based therapeutic strategies to systematically identify and reduce contextual tic exacerbations [14].

Emerging Evidence for the Negative Reinforcement Hypothesis in TD

Although the negative reinforcement hypothesis has been difficult to test directly, several recent laboratory investigations have examined the effect of tic suppression (and execution) on premonitory urges using variations of a reinforced tic suppression paradigm [25, 26]. Within this paradigm, token rewards are provided when individuals suppress their tics for brief periods of time, essentially setting up a competition between suppressing tics and tolerating aversive premonitory urges while earning rewards versus allowing tics to occur in order to reduce urges and forgoing rewards. In one early pilot study, children with TD were asked to provide periodic urge ratings during alternating periods of tic suppression and a free-to-tic control condition. This study found that urge ratings were higher during periods of tic suppression relative to the freeto-tic condition [27]. This is consistent with the idea that tic performance decreases urges, as tic rates were lower during suppression than under free-to-tic conditions.

A more recent study replicated this finding in 15 children with TD/PTD [28•]. In addition to reinforced suppression and free-to-tic conditions, this study included a third "escape" condition in which children were allowed to initiate 10-s breaks from the reinforced suppression protocol (i.e., were allowed brief periods to tic) without losing the rewards they earned by suppressing their tics. Results were consistent with earlier findings [27] and showed that urge ratings were higher during periods of suppression and escape relative to the freeto-tic condition. Furthermore, during the escape condition, urge ratings increased during suppression (i.e., just before breaks) and decreased when ticcing resumed (i.e., just after breaks). In another recent investigation urge ratings were collected continuously during conditions of free-to-tic and tic suppression in 17 patients with TD [29•]. In both conditions, urge intensity was found to increase prior to, and decrease shortly after, tics were performed.

While the above studies provide support for the negative reinforcement hypothesis, it is noteworthy that at least two recent studies have failed to show a significant relationship between premonitory urge severity and tic suppressability [30, 31] and yet another study found considerable individual variability in urge-tic relationships with some individuals showing increased urge ratings during suppression (consistent with the negative reinforcement hypothesis) and others showing *decreases* in urge ratings during suppression [32]. Studies are also mixed regarding whether premonitory urges decrease during and after periods of tic suppression and/or behavior therapy. While some treatment studies have shown decreases in premonitory urges both during and after behavior therapy [17, 33], at least one laboratory-based study failed to find decreases in urge ratings during a 40 min of tic suppression [34]. These findings emphasize the need for more research to understand the role and course of premonitory urges in TD.

Functional (Contextual) Factors Associated with Tic Severity

As noted above, the CBIT model posits that although tics are involuntary, they can nonetheless be influenced by the same reinforcement processes that influence voluntary behavior. For many years, evidence for this view was largely inferred from early operant research on other "involuntary" behaviors [35] and from a heterogeneous group of small studies suggesting relations between environmental influences and tics [36]. However, several more recent studies have investigated ticenvironment relations more systematically. Results from these studies strongly support the idea that reactions from others can function to increase tic severity within a particular context.

In one recent study, parents and children with TD were interviewed using a structured protocol and were asked to keep daily records of situational tic exacerbations [23••]. Consistent with findings from previous research [37], all participants reported that their child's tics reliably increased in specific settings and/or during specific activities (e.g., at home after school, in public places, when in the classroom, and/or when engaged in activities such as playing videogames or completing homework). Importantly, almost all respondents were also able to identify one or more tic-contingent consequences (i.e., reactions) associated with these tic exacerbations, with most reporting that their child received some form of attention for tics (e.g., provided comfort or told to stop) or was allowed to escape a non-preferred task (e.g., homework) or continue a preferred task (e.g., videogame) when tics worsened. The number of consequences endorsed also correlated with motor tic frequency and interference [23••].

Consistent with these findings, two additional independent studies of children with TD and their caregivers found that higher scores on the Tic Accommodation and Reactions Scale (TARS), an assessment instrument designed to assess the number and frequency of consequences experienced for ticcing, were positively correlated with tic severity as well as measures of tic-related impairment [38, 39]. In addition, one of these studies [39] reported that children with internalizing problems (e.g., anxiety) experienced more tic-related consequences than those without comorbid internalizing problems, perhaps partially explaining the association between anxiety and increased tic severity [24]. The second author and colleagues are currently collecting longitudinal data to more definitely evaluate whether naturally occurring consequences for ticcing prospectively affect future tic severity.

Efficacy of Behavior Therapy for TD

Over the past 30 years, numerous investigations have demonstrated the efficacy of HRT and ERP for reducing tics [40]. However, most of these studies were limited by small sample sizes and methodological shortcomings. To address this, investigators in the USA recently reported the results of two large, multi-site, randomized controlled trials comparing the efficacy of CBIT to a supportive psychotherapy control condition [41..., 42...]. In both trials, patients with TD or PTD were randomized to eight sessions (10 weeks) of CBIT or supportive therapy followed by three monthly booster sessions. Assessments were conducted by condition-blind independent evaluators at baseline, post-treatment, and at 3- and 6month follow-up. The primary outcome measure was the gold-standard Yale-Global Tic Severity Scale (YGTSS) [43]. Responder status was determined using the Clinician Global Impressions-Improvement (CGI-I) Scale, with ratings of "very much improved" and "much improved" indicating responder status. In the child trial, 126 children (ages 9–17) were randomized. Results showed that CBIT was associated with a significantly greater decrease on the YGTSS at posttreatment (effect size = 0.68). Further, 53 % of children receiving CBIT were rated as treatment responders versus 19 % in the control group, and 87 % of responders maintained treatment gains at 6-month follow-up. In the adult trial, 122 adults (ages 16-69 years) were randomized to the same conditions (CBIT versus supportive therapy). Results showed that CBIT led to a significantly greater decrease on the YGTSS (effect size = 0.57) and 38 % of patients receiving CBIT were rated as treatment responders versus 6 % in the control group. Similar to the child trial, 80 % of participants receiving CBIT maintained treatment gains at 6 months post-treatment. In addition, two recent meta-analytic studies of behavior therapy for TD reported medium to large effect sizes for behavior therapy relative to comparison conditions [44•, 45].

Neural Correlates of Behavior Therapy for TD

To date, few studies have directly investigated the neural changes associated with response to behavior therapy for TD. In one small investigation, eight participants (from the aforementioned adult CBIT trial) completed a measure of response inhibition (the visuospatial priming task, VSP) during fMRI [46•]. Results were compared to eight healthy control participants matched for age, gender, education, and IQ, before and after a 10-week waiting period. Relative to controls, TD subjects showed greater putamen activation during the VSP task prior to treatment, less activation at post-treatment, and a significant decrease in putamen activation was observed pre- to post-CBIT in TD patients. Though preliminary, these results suggest that CBIT might alter aberrant brain activation within CSTC circuitry. Interestingly, the study also found that greater tic reduction during CBIT (as measured by the YGTSS) was associated with less change in VSP taskrelated activation in the inferior frontal gyrus (Broadman's area 47) pre- to post-treatment. Given that studies with healthy controls have found increased engagement in this (and other) cortical regions while performing the VSP task in adults [47], the authors interpreted these later findings to suggest that adequate inferior frontal gyral activation might be a necessary prerequisite for CBIT to be efficacious. Another study used EEG to examine motor- and event-related electrocortical response while completing a stimulus-response compatibility task administered pre- and post-treatment to 20 TD patients receiving a cognitive-behavior therapy for TD [48]. Results were compared to 20 healthy controls matched on age, gender and IQ. Results showed that TD patients, relative to controls, demonstrated delayed stimulus-locked LRP onset latency and larger response-locked LRP peak amplitude during inhibition processing, both of which corrected after treatment. Evidence for frontal overactivation during the NoGo (inhibition) portion of the task was also observed, but remained unchanged pre- to post-treatment.

Disseminating and Implementing Behavior Therapy for TD

Although CBIT has shown to be efficacious for reducing tics, large survey studies have shown that it is not widely available. A pair of recent online surveys involving adults (N = 672) and parents of youth (N = 740) with a self-reported diagnosis of TD or PTD, conducted in the USA, found that only 17 % of treatment-seeking adults had received behavior therapy for tics, with only 4 % reporting that treatment included habit reversal training [49]. Among parents, only 24 % of treatment-seeking families reported having received behavior therapy, with only 7 % reporting that treatment included habit reversal training. Among the most commonly cited reasons for having not received behavior therapy were lack of access to knowledgeable and trained treatment providers and concerns that behavior therapy would cause new tics to emerge (i.e., tic substitution), tic worsening, or exacerbation of co-occurring psychiatric symptoms, which are known to commonly cooccur in TD [50]. Dissemination and implementation efforts

have begun to examine the safety and tolerability of CBIT as well as novel approaches to dissemination and implementation, including modifying the CBIT protocol to increase feasibility of implementation and delivering CBIT remotely through telehealth.

Addressing Common Misperceptions Regarding Behavior Therapy for Tics

One of the primary barriers to widespread adoption of behavior therapy as a first-line intervention for TD has been lingering concerns that treating tics using behavioral methods will lead to the emergence of new symptoms and/or a paradoxical increase in tics [51, 52]. To address these concerns, the CBIT clinical trials investigators conducted an empirical examination of symptom substitution in 228 participants from the CBIT randomized controlled trials using four indices: (1) the onset of new tic symptoms during treatment, (2) the occurrence of adverse events, (3) changes in tic medications during the study, and (4) worsening of co-occurring psychiatric symptoms [53•]. Results of this analysis showed several interesting and encouraging findings. First, across both treatment conditions, participants in the CBIT trials exhibited an average of 1.25 new bothersome tics over the 10-week trial period; a finding that is not particularly surprising given that tics are known to take a fluctuating and changing course [3]. Importantly, behavior therapy did not differ from supportive psychotherapy on the likelihood of new tic onset or the number of newly emerged tics, and treatment response following CBIT was not uniquely associated with new tic onset. Second, tic worsening during the 10-week study period was rare across both treatment conditions. Among those receiving behavior therapy, only one child participant (2 %) and four adult participants (6 %) reported tic worsening during the study, rates that were comparable to, if not slightly lower than, what was reported in the supportive therapy condition in which four children (6 %) and four adults (7 %) reported tic worsening. Third, there were no differences between the two treatment conditions in the number of children or adults who reported changes or initiation of tic medication during the study. Finally, there were no statistically significant differences between the two treatment conditions on any measure of cooccurring psychiatric and behavioral symptoms following treatment or at 6-month follow-up, and measures of ADHD, OCD, ODD, depression, and anxiety were all modestly improved at post-treatment in both treatment arms [54]. Collectively, the results of this investigation suggest that behavior therapy does not result in tic worsening nor does it confer increased risk for the onset or development of new tics and demonstrates the safety and tolerability of behavior therapy for TD.

Implementation Research

To address accessibility problems, research has begun to examine novel methods for implementing CBIT via new settings and new modalities. These efforts have examined two primary avenues: increasing the number and breadth of providers trained in administering behavior therapy for TD, and using technology to deliver CBIT remotely. Given that neurology and pediatric clinics are typically the first point of therapeutic contact for most patients with TD, training medical professionals who practice in these clinics to deliver behavior therapy is a potentially fruitful way to increase accessibility. However, time constraints and limitations on reimbursement are likely to prohibit a full course of treatment as described in published manuals [14] and commonly delivered in behavioral health clinics. A recently published case series demonstrated that an abbreviated CBIT protocol (referred to as CBIT-NP) could be effectively and feasibly delivered by nurse practitioners and physicians practicing in neurology and developmental pediatric clinics [55•]. In this study, 14 youth (ages 9-17) with TD received 4-6 sessions of CBIT delivered over 6-8 weeks, with each session lasting 20-25 min. Of the nine participants who completed at least four treatment sessions, five were rated as treatment responders by independent evaluators, using ratings of "very much improved" or "much improved" on the Clinician's Global Impressions Improvement Scale as the criterion for responder status. Patient and parent satisfaction ratings with CBIT-NP were high. However, even with the abbreviated protocol, time constraints remained a burden to implementation. Poor patient adherence to treatment was also reported to be a problem in some cases. Another study evaluated the efficacy of CBIT delivered by occupational therapists trained in CBIT [56]. In this study, 30 children (ages 7–19) with TD received eight sessions of standard CBIT. A significant reduction in the number of tics, overall tic severity, and subjective discomfort from tics was observed. In addition, significant improvements were noted across various occupational domains, such as the ability to complete schoolwork, socialize, and complete basic activities of daily living. These findings are encouraging, but more work is needed to determine how to best modify the CBIT protocol to enhance feasibility and improve adoption across various practice settings while also maintaining the integrity of the treatment.

A second emerging area of implementation research is the use of technology to deliver CBIT to those who do not have access to a trained CBIT therapist in their area. A recent randomized controlled pilot trial with 20 youth with TD compared CBIT delivered face-to-face (F2F) to CBIT delivered via high-speed videoconference [57, 58]. In this study, videoconference patients traveled to a local clinic and interfaced with a clinician in a remote location via specialized telehealth equipment. That study found that both delivery modalities were equally efficacious, with both groups showing

reductions in tic severity similar to what was observed in the child CBIT trial and treatment gains were maintained at 1month follow-up. In addition, patient and parent acceptability ratings for both delivery modalities were high and comparable across groups. Another study tested another telehealth model that even further reduced travel burden for patients, by having them attend sessions from their homes via their personal computers. This randomized waitlist-controlled trial with 20 youth with TD examined the efficacy and acceptability of CBIT delivered remotely into the patients' homes using voice over internet protocol (VoIP) [59]. Significantly greater reductions in clinician- and parent-rated tic severity were observed in the CBIT VoIP condition relative to waitlist. However, only one third of those receiving CBIT-VoIP were rated as treatment responders, which is lower than the response rate reported in the large CBIT child trial [41...]. Patient and parent satisfaction with VoIP delivery were high; however, the authors noted that the study therapists experienced audio-visual difficulties and challenges with respect to patient distraction that might have impacted the effectiveness of treatment. Finally, the first author and his colleagues are currently testing the efficacy of an interactive, self-guided, online CBIT program, called Tichelper.com, in a randomized controlled trial. Results are forthcoming.

Conclusion

The past decade has seen an exciting, exponential growth in the evidence supporting the utility of behavior therapy for TD. Recent research has firmly established the efficacy of behavioral interventions, allayed concerns about untoward side effects, and provided insights into contextual and neural variables that influence symptom expression. So, where to now in the next decade? Much work remains to be done. Basic science research efforts are needed to more fully elucidate the processes that underlie TD. Applied research is needed to go beyond showing that behavior therapy for TD works, but also showing how it can be brought to scale and have maximum public health impact. Moreover, bidirectional translation between basic behavioral and neuroscientific findings and applied research will likely lead to novel and more effective treatments going forward.

Compliance with Ethical Standards

Conflict of Interest Dr. Himle has received grants from the National Institutes of Health and the Tourette Association of America. Dr. Capriotti reports grants from the American Academy of Neurology, outside of the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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