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

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Abstract

Background: Cognitive control processes are implicated in the behavioral treatment of Tourette's Disorder (TD). However, the influence of these processes on treatment outcomes has received minimal attention. This study examined whether cognitive control processes and/or tic suppression predicted reductions in tic severity and treatment response to behavior therapy.

Method: Fifty-three youth with TD or a pervasive tic disorder participated in a randomized wait-list controlled trial of behavior therapy. Following a baseline assessment to evaluate psychiatric diagnoses, tic severity, and cognitive control processes (e.g., response selection, inhibition, and suppression), youth were randomly assigned to receive 8 sessions of behavior therapy (n=23) or a waitlist of equal duration (n=28). Youth receiving immediate treatment completed a post-treatment assessment to determine improvement in tic severity. Meanwhile, youth in the waitlist condition completed another assessment to re-evaluate tic severity and cognitive control processes, and subsequently received 8 sessions of behavior therapy followed by a post-treatment assessment to determine improvement.

Results: A multiple linear regression model found that pre-treatment inhibition/switching on the Delis-Kaplan Executive Function System Color Word Interference Test predicted reductions in tic severity after behavior therapy (β=−0.36, t=−2.35, p=0.025, η^2 =0.15). However, other cognitive control processes and tic suppression did not predict treatment response and/or reductions in tic severity. Small non-significant effects were observed in cognitive control processes after behavior therapy.

Conclusion: Cognitive control processes may influence tic severity reductions in behavior therapy. Notably, even when other cognitive control processes are impaired and youth are initially unable to voluntarily suppress their tics, youth with TD can still benefit from behavior therapy. Findings offer implications for clinical practice and research for TD.

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Keywords

Cognitive control; inhibitory control; inhibition; tic suppression; behavior therapy

Introduction

Tourette's Disorder and other persistent tic disorders (collectively referred to as TD) are neurodevelopmental conditions characterized by involuntary motor movements and/or vocalizations. Evidence suggests that TD develops in childhood and affects almost 2% of youth (Knight et al., 2012; Scahill, Specht, & Page, 2014). Youth with TD often experience co-occurring psychiatric conditions such as attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and anxiety disorders (Freeman et al., 2000; Specht et al., 2011). Tics and co-occurring conditions can cause significant impairment for youth with TD (Cloes et al., 2017; Stiede et al., 2018) and contribute to a reduced quality of life (Conelea et al., 2011; Storch et al., 2007). Therefore, effective treatments are critical for youth with TD.

Behavior therapy is recommended as the first line intervention for youth with TD by numerous professional organizations (Murphy, Lewin, Storch, Stock, & AACAP Committee on Quality Issues, 2013; Pringsheim et al., 2019). Behavioral therapies such as habit reversal training (HRT) and its successor the Comprehensive Behavioral Intervention for Tics (CBIT; (Woods et al., 2008) have demonstrated moderate-to-large reductions in tic severity that maintain over time with no significant adverse effects or risk for symptom substitution (McGuire et al., 2014; McGuire et al., 2019; Peterson et al., 2016; Piacentini et al., 2010; Woods et al., 2011). Despite its therapeutic benefit, only 50% of youth with TD exhibit a positive treatment response to behavior therapy and many treatment responders continue to experience bothersome tics (Piacentini et al., 2010). Therefore, it is critical to understand the factors that influence treatment response to behavior therapy. This knowledge can provide critical insights into underlying therapeutic mechanisms and inform the development of strategies to optimize treatment outcomes.

Behavior therapy is predicated on a neurobehavioral model of TD. This model acknowledges the neurological origin of tics and TD (see Augustine & Singer, 2018 for a review of the neurobiology of TD), and highlights that internal and external contextual factors influence the expression and maintenance of tics (Conelea & Woods, 2008; Woods et al., 2008). These internal (e.g., premonitory urges, mood states) and external factors (e.g., situations, activities) serve as key targets in behavior therapy to reduce tic expression. For instance, youth with TD often experience internal aversive sensations called premonitory urges, which precede tics and are alleviated by tic expression (Capriotti, Brandt, Turkel, Lee, & Woods, 2014; Himle, Woods, Conelea, Bauer, & Rice, 2007; Leckman, Walker, & Cohen, 1993; McGuire et al., 2016; Specht et al., 2013; Woods, Piacentini, Himle, & Chang, 2005). Consequently, tic expression can become unintentionally reinforced due to the reduction in premonitory urge, which leads to the increased likelihood of tic expression in response to subsequent premonitory urges. A similar relationship also holds true for external contextual factors. Youth with TD often have difficulty managing tics during certain activities and

situations (e.g., completing assignments or household chores, attending social functions; Capriotti et al., 2015; Himle et al., 2014; Storch et al., 2017). When tics are expressed during these activities, it can result in the disruption, early discontinuation, and/or eventual avoidance of these activities (e.g., tic severity increases during homework, so homework time is shortened by parents). Over time, as these activities are prematurely discontinued or avoided altogether, the expression of tics in these situations becomes unintentionally reinforced and results in heightened tic occurrence during these situations in the future (e.g., when homework attempted in the future, tic expression increases). Indeed, this can be further complicated by the common co-occurrence of anxiety, which can exacerbate tics in previously avoided activities and/or situations. Behavior therapy emphasizes decreasing environmental triggers for the tics, eliminating reinforcing social reactions to the tics, teaching the patient to become more aware of his or her premonitory urges, and then implementing competing responses contingent upon detection of tics to prevent further tic expression.

Despite its established efficacy, the precise mechanisms underlying behavior therapy are not fully explicated. While some evidence exists for habituation as a possible mechanism (Houghton et al., 2017; Verdellen et al., 2008), cognitive control represents another hypothesized mechanism that has received minimal investigation. Broadly, cognitive control refers to a system that modulates the operation of other cognitive and emotional systems in the service of goal-directed behavior (Insel et al., 2010). Cognitive control processes are typically engaged during contexts in which appropriate responses need to be selected from competing alternative responses. There are several cognitive control processes implicated in the behavioral treatment of TD: goal selection, response selection, inhibition/suppression, and performance monitoring. In behavior therapy for TD, goal selection is involved in attaining awareness to internal and external contexts that elicit tic expression. Meanwhile, response selection is implicated in the acquisition and selection of an appropriate behavioral response—tic suppression or competing responses—contingent upon awareness of internal and/or external contexts. Relatedly, inhibition/suppression is involved in the successful implementation of a behavioral response to prevent tic expression. Finally, performance monitoring is evident in adjustments in behavioral implementation based on the success/failure of inhibition suppression. Therefore, youth with TD exhibiting greater baseline cognitive control with respect to these processes would be anticipated to experience increased therapeutic benefit from behavior therapy.

To date, there have only been a handful of studies that have examined the relationship between neurocognitive processes of cognitive control (e.g., response inhibition) and behavior therapy outcomes. Deckersbach and colleagues (2006) found that greater baseline response inhibition on a visuospatial priming task predicted a positive treatment response among 30 adults with TD (Deckersbach et al., 2014). However in a large clinical trial of behavior therapy for adults with TD, the change in tic severity and treatment response to behavior therapy were not associated with baseline performance on neurocognitive tasks of inhibitory control (i.e., Go-No Go, Stroop Color-Word Test; Abramovitch et al., 2017). Finally, in a clinical trial of behavior therapy for youth with TD, Chang and colleagues (2018) found that baseline performance on neurocognitive tasks of inhibitory control were not predictive of reduction in tic severity and/or treatment response to behavior therapy (e.g.,

Stop Signal Task, Stroop Color-Word Test). Given the few studies, inconsistent findings, and developmental differences between youth and adults with TD, further research is critical to clarify the role of cognitive control in the behavioral treatment of TD. This line of research could elucidate neural mechanisms of treatment response to behavior therapy in youth with TD, inform strategies to optimize current behavioral treatments, and personalize treatment recommendations based on baseline cognitive control processes.

This study examined cognitive control processes in youth with TD and their relationship to behavior therapy treatment outcomes in a randomized controlled trial. The principle goal of this secondary outcome analysis was to determine whether baseline performance on tasks of cognitive control predicted reductions in symptom severity and treatment response to behavior therapy. As cognitive control processes may be separate from tic suppression abilities, our secondary goal was to examine whether baseline tic suppression capabilities predicted tic severity reductions and treatment response to behavior therapy. Finally, we explored whether baseline cognitive control processes improved over the course of behavior therapy.

METHODS

Participants

To participate in this randomized waitlist-controlled trial, youth with TD met the following inclusion criteria: (1) 9 to 14 years of age, (2) diagnostic criteria for a TD, (3) a Yale Global Tic Severity Scale (YGTSS) total tic score > 14 or >10 if only motor tics present (Leckman, Riddle, Hardin, & Ort, 1989), and (4) be fluent in English. Exclusion criteria included the following: (1) lifetime diagnosis of an autism spectrum disorder, mania, or psychotic disorder, (2) a psychiatric or psychosocial condition that requires immediate treatment not provided in the study (e.g., substance use, conduct disorder), (3) full scale intelligence quotient < 80, and (4) four or more prior behavior therapy sessions. Youth were required to be either medication free or taking a stable dose of psychiatric medication for at least six weeks prior to enrollment, with no planned changes for the duration of study participation.

Participants were 53 youth (M=10.93 years, SD=1.62 years, Range: 9–14 years) who met diagnostic criteria for Tourette's Disorder or a Chronic Motor Tic Disorder. Youth were predominantly non-Hispanic White (58.50%), male (71.70%), and had an average intelligence (M=107.37, SD=12.49). Common co-occurring psychiatric conditions included anxiety disorders (n=26, 49%), ADHD (n=19, 35.8%), obsessive-compulsive disorder (OCD; n=16, 30%), and depressive disorders (n=1, 1.8%). At the baseline assessment, youth had a moderate level of tic severity on the YGTSS total tic score (M=25.83, SD=6.19, Range: 15–43) and 5 youth (9.4%) were taking a tic influencing psychotropic medication (e.g., alpha-2 agonist, antipsychotic).

Measures

Psychiatric Diagnostic Interview.—Kiddie Schedule for Affective Disorders and Schizophrenia– Present and Lifetime version (K-SADS-PL) was used to assess psychiatric

diagnoses (Kaufman et al., 1997). The K-SADS is a structured psychiatric interview that is commonly used and has good psychometric properties.

Tic Severity and Impairment.—The Yale Global Tic Severity Scale (YGTSS) is a clinician-rated scale used to assess tic severity (Leckman et al., 1989). Motor and phonic tics are rated separately across five domains: number, frequency, intensity, complexity, and interference. Items are summed to produce a Total Tic Score (range: 0 – 50). Clinicians also rate impairment caused by tics using the Impairment Scale (range: 0 – 50). The YGTSS has good reliability and validity (Leckman et al., 1989; McGuire et al., 2018).

Treatment Response.—Signal detection analyses show that a 25%−35% reduction on the YGTSS Total Tic score corresponds with a positive treatment response (Jeon et al., 2013; Storch et al., 2011). Given the preliminary nature of these investigations, the higher benchmark of improvement (a 35% reduction on the YGTSS Total Tic score) was used to classify treatment responder status.

Premonitory Urge Severity.—The Premonitory Urge for Tics Scale (PUTS) is a 10-item scale that measures the severity of premonitory sensations that precede tics (Woods et al., 2005). Items are rated on a 4-point Likert scale (range: 1 – 4), and the first nine items are summed to produce a total urge severity score (Woods et al., 2005).

Cognitive Control Processes of Response Selection, Inhibition, and Suppression.—There were four assessments used to measure cognitive control processes: the Attention Network Task, the Stop Signal Task, the Go-No Go Task, and the Delis-Kaplan Executive Function System Color-Word Interference Test. The *Attention Network Task (ANT)* required subjects to respond by pressing the left or right mouse button that corresponded to the direction of a target arrow in the center of a visual display. The target arrow was flanked on both sides by cues that could be congruent (arrows of the same direction), incongruent (opposite direction), or neutral (dashes) to the target arrow (Eriksen & Eriksen, 1974). The ANT produces several scores, with the incongruent accuracy score percentage correct representing a measure of inhibitory control. The *Stop-Signal Task (SST)* required youth to perform a choice response time task on each trial, with responses withheld if an auditory beep was heard (Logan, Cowan, & Davis, 1984). Stop-signal reaction time (SSRT) is the amount of time needed to inhibit a response after presentation of the stop signal, and represents a measure of inhibitory control (Logan, Schachar, & Tannock, 1997). In the *Go-No Go (Go-No Go)* task, letters A through Z appeared on the screen one at a time and youth were required to press the space bar when any letter (“Go” trial) except the target letter “X” appeared (“NoGo” trial) (Serrien, Orth, Evans, Lees, & Brown, 2005). Errors of commission, or the percentage of “NoGo” trials that were incorrectly classified as “Go” trials represents a measure of inhibitory control and sustained attention (Abramovitch et al., 2017). Finally, the *Delis-Kaplan Executive Function System Color-Word Interference Test (D-KEFS CWIT)* is a Stroop-like task that consists of four parts: color naming, word reading, inhibition, and inhibition/switching (Delis, Kaplan, Kramer, Delis, & Kramer, 2001). The inhibition/switching scaled score represents a measure of inhibitory control.

Tic Suppression Task.—Prior to treatment assignment, youth completed a tic suppression task that included a 5-minute baseline condition (i.e., tic freely) and a 5-minute tic suppression condition (Himle & Woods, 2005; Woods & Himle, 2004). Participants were assigned to a counterbalanced order of baseline and tic suppression conditions generated by randomization. In the baseline condition, youth were prompted to "tic as much or as little as needed" and to try not to suppress tics. During the tic suppression condition, youth were verbally instructed to fixate on a dot for 5 minutes and try not to exhibit tics. Youth were informed that they could suppress tics in any way they wanted, as long as they remained seated in the chair and refrained from covering their face/head with their hands. In both conditions, youth were instructed to remain seated with their hands in their lap or on the armrests of the chair. After each condition, youth completed a questionnaire that asked if they actively tried to suppress tics during the condition. All youth reported that they did not try to suppress tics during the baseline condition, and actively tried to suppress tics during the suppression condition. Sessions were recorded and reviewed by research assistants masked to condition (i.e., tic freely or tic suppression). Research assistants were oriented to operational definitions of each participants' tics, which were initially generated by the independent evaluator based on tics identified during administration of the YGTSS. Research assistants independently coded tic occurrence during each 5-minute condition using Behavioral Observation Research Initiative Software version 7.9.7 (BORIS; Friard & Gamba, 2016). Interrater reliability for tic frequency ratings was calculated using an intraclass correlation coefficient (ICC) in SPSS 26.0, with good agreement observed (ICC = .84; Koo & Li, 2016).

Procedures

Study procedures were approved by the local institutional review board, and the trial was registered on ClinicalTrials.gov (NCT00675675). Recruitment took place at the University of California, Los Angeles between July 2007 and December 2011. After obtaining consent, participants completed a baseline assessment to characterize psychiatric diagnoses, tic severity (YGTSS), premonitory urges (PUTS), cognitive control processes (ANT, SST, Go-No Go, and D-KEFS CWIT), and tic suppression. Afterwards, youth were randomly assigned to receive 8 sessions of manualized behavior therapy over a period of 10 weeks (Piacentini et al., 2010; Woods et al., 2008) or a waitlist of equal duration to control for the waxing and waning nature of tic severity. Youth completed a post-treatment assessment after 10 weeks to determine change in tic severity and evaluate treatment response to study condition (YGTSS). All assessments were conducted by trained independent evaluators (IEs) masked to treatment condition. Youth who were randomized to the waitlist condition received 8 sessions of behavior therapy over 10 weeks and completed another assessment to determine change in tic severity and treatment response to behavior therapy (YGTSS).

Analytic Plan

An analysis of variance (ANOVA) and chi-square tests compared baseline group differences between the immediate treatment and waitlist conditions (see Table 1). For those youth in the waitlist condition, preliminary analyses compared 'waitlist' baseline and 'treatment' baseline characteristics of neurocognitive and behavioral outcomes (D-KEFS CWIT inhibition/switching, Go-No Go commission, SST reaction time, ANT incongruent, PUTS

total, YGTSS total score). A repeated measures ANOVA where visit ('waitlist' baseline, 'treatment' baseline) was entered as a predictor only found a small significant difference for YGTSS impairment (p=.04, η^2=.06). Meanwhile, all other comparisons were not statistically significant (p=.20–.96). As there were minimal differences between 'waitlist' and 'treatment' baselines, 'treatment' baselines was used as baseline for participants in the waitlist group because it was more representative of the participants functioning immediately prior to treatment.

For our primary aim to examine whether baseline performance on tasks of cognitive control predicted reductions in tic severity and treatment response, the active treatment and waitlist control groups were pooled in to a single behavior therapy group (N=53). Logistic regression was used to evaluate the influence of neurocognitive predictors (ANT incongruent accuracy, SST reaction time, Go-No Go commission errors, D-KEFS CWIT inhibition/switching condition) on YGTSS responder status (responder/non-responder) at post-treatment. Multiple linear regression was used to evaluate the influence of neurocognitive predictors on post-treatment YGTSS total score, controlling for treatment baseline YGTSS total score.

For our secondary aim to determine if baseline tic suppressibility predicted treatment response, first a tic suppressibility score was calculated using the following formula [baseline tic frequency – suppression tic frequency)/BL tic frequency*100] used in prior research (Conelea et al., 2018). Then a logistic regression analysis was used and included baseline PUTS total score and tic suppressibility score as predictors of YGTSS responder status at post-treatment. Finally, a multiple linear regression was used to evaluate the influence of baseline PUTS total score and tic suppressibility on YGTSS total score post-treatment, controlling for pre-treatment YGTSS total score.

Finally for our exploratory aim to determine whether changes in cognitive control processes occurred over the course of treatment, multiple mixed effects regression models were used. Models included time and treatment response as predictors with a random intercept. The dependent outcome was the post-treatment performance on the cognitive control task (ANT incongruent accuracy, SST reaction time, Go-No Go commission errors, D-KEFS CWIT inhibition/switching condition).

Results

Treatment Response and Efficacy of Behavior Therapy

When examining the efficacy of behavior therapy during treatment, a repeated measures ANOVA found a significant effect of time, F(1,48)=37.55, p<.001, η^2=.44, where marginal means indicate a significant reduction in YGTSS tic severity ($M_{TXbaseline}$=24.67, SE=.83; $M_{TXendpoint}$=17.26, SE=.86, see Supplemental Table 1). Twenty-two youth (41.5%) exhibited a treatment response to behavior therapy. When examining changes in tic-related impairment, a repeated measures ANOVA found a significant effect of time, F(1,45)=45.79, p<.001, η^2=.50, where the marginal means indicate a significant reduction in YGTSS Impairment score ($M_{TXbaseline}$=22.52, SE=.1.05; $M_{TXendpoint}$=12.05, SE=1.09, Supplemental Table 1).

Cognitive Control Processes Predicting Behavior Therapy Outcomes

Baseline cognitive control processes did not significantly predict treatment response status at post-treatment (n=37; D-KEFS CWIT inhibition/switching z=0.64, p=0.52; Go-No Go commission z=−0.69, p=0.49; SST reaction time z=−0.22, p=0.82; ANT incongruent accuracy z=−0.60, p=.55, see Supplemental Table 2). When using a dimensional therapeutic improvement outcome (YGTSS total tic score; n=37), there was one notable distinction (see Supplemental Table 3). When controlling for baseline YGTSS total tic score (t=2.00, p=0.054), D-KEFS CWIT inhibition/switching score was the only cognitive control indicator to significantly predict tic severity at post-treatment. A measure of inhibition/switching, a higher D-KEFS CWIT inhibition/switching score at baseline was predictive of lower YGTSS severity post-treatment (β=−0.36, t=−2.35, p=.025, η^2 =0.15). Meanwhile, none of the other cognitive control predictors in the model predicted YGTSS total tic score at post-treatment (Go-No Go commission z=−0.29, p=0.78; SST reaction time z=−.52, p=0.60; ANT incongruent accuracy z=−0.72, p=0.48, see Supplemental Table 3).

Tic Suppression Abilities Predicting Behavior Therapy Outcomes

A logistic regression model (n=16) indicated that neither tic suppressibility (OR=1.01, z=−0.77, p=0.44) nor PUTS total score (OR=0.95, z=−0.55, p=0.58) predicted treatment response status at post-treatment (see Supplemental Table 4). When controlling for pre-treatment YGTSS total score (t=1.91, p=0.08), the PUTS total score (t=−0.56, p=0.58) and tic suppressibility (t=−1.07, p=0.30) did not predict YGTSS total tic score at post-treatment (see Supplemental Table 5).

Exploring the Effect of Behavior Therapy on Cognitive Control Processes

Mixed-effect regression models found no significant change in cognitive control processes on neurocognitive tasks (D-KEFS CWIT inhibition/switching, b=−.009, p>.05, treatment response, b=−.44, p>.05; Go-No Go commission, b=−.07, p>.05, treatment response, b=.20, p>.05; SST reaction time b=−1.90, p>.05, treatment response, b=−3.95, p>.05; and ANT incongruent accuracy b=−.097, p>.05, treatment response, b=−1.68, p>.05, see Supplemental Table 6). As shown in Table 2, the enhancing effects of behavior therapy on cognitive control processes were relatively small for both responders (d = 0.04 – 0.38) and non-responders (d = 0.04 – 0.22).

Discussion

This study examined the relationship between cognitive control processes and behavior therapy outcomes in a randomized controlled trial of youth with TD. Findings revealed that cognitive control processes related to inhibition/switching performance (D-KEFS CWIT inhibition/switching score) predicted reductions in tic severity on the YGTSS. This is the second report to find a neurocognitive predictor of behavior therapy in TD (e.g., visuo-spatial priming task; Deckersbach, Rauch, Buhlmann, & Wilhelm, 2006). Recent meta-analytic work also suggests that inhibitory control is impaired among patients with TD (e.g., verbal inhibition, Stroop CW Interference score; Morand-Beaulieu et al., 2017). While Chang and colleagues (2018) found that baseline performance on neurocognitive tasks of inhibitory control was not predictive of tic severity reductions or treatment response

to behavior therapy (e.g., Stop Signal Task, Stroop Color-Word Test), there are some noted distinctions between the D-KEFS CWIT and Stroop Color-Word test tasks. Specifically, during the Stroop task, participants are required to name the color of the ink instead of the word (i.e., a less automated task) and inhibit the interference arising from the more automated task (i.e., reading the word). In contrast, during the D-KEFS CWIT task, participants must switch back and forth between reading the word and naming the color of the ink. The D-KEFS CWIT task is more cognitively demanding and requires both suppression/inhibition and set shifting/cognitive flexibility to perform well. Increased cognitive demand may also explain why the visuo-spatial priming task that requires four categories and inhibition predicts behavior therapy outcomes in TD (Deckersbach et al., 2006), whereas more simplistic Go-No Go and Stop Signal tasks that have only two response categories do not. Given that both the visuo-spatial priming task and the D-KEFS CWIT task also capture aspects of cognitive flexibility, this particular facet of executive functioning paired with inhibition may be an important baseline factor in the treatment of TD. Unfortunately, executive functioning in TD has received minimal examination and may warrant further investigation.

No predictive relationship for other neurocognitive markers of cognitive control was found for behavior therapy outcomes. This is consistent with prior studies and suggests that inhibitory control performance on tasks such as the Go/No-Go or Stop-Signal Task is not related to treatment processes (Abramovitch et al., 2017; Chang et al., 2018; Morand-Beaulieu et al., 2017). Given that some youth with TD are reported to have difficulties with neurocognitive performance, these findings are promising and suggest these youth can still benefit from behavior therapy. Behavior therapy can reduce tic severity and does not diminish cognitive functioning among youth with TD (Chang et al., 2018). This further supports the recommendation of behavior therapy as a first line treatment for all youth with TD, regardless of neurocognitive performance. Although our single-site sample size is smaller than prior multisite clinical trials (e.g., Piacentini et al., 2010), behavior therapy reduced tic severity and impairment with therapeutic effects comparable to other child treatment studies. Beyond providing further support that behavior therapy reduces tic severity, this suggests that the findings observed here are generalizable to definitive large-scale, multisite, clinical trials.

Interestingly, baseline tic suppression did not predict treatment outcome. For this task, youth were verbally prompted to suppress tics. Reliance on a verbal request to suppress tics is in contrast to the added analysis of contingency management and/or contingent reinforcement (e.g., providing tokens for periods in which youth did not tic) used in prior tic suppression studies (Greene et al., 2015; Himle, Woods, & Bunaciu, 2008; Woods & Himle, 2004; Conelea et al., 2018). Although limited by a small sample size, there are two implications. First, youth with TD who have difficulty suppressing tics at baseline would still likely benefit from behavior therapy. Youth who had difficulty suppressing tics still exhibited reductions in tic severity after behavior therapy, and may be more motivated to consistently implement behavior therapy strategies to reduce tic severity (instead of relying in part on tic suppression abilities). Second, contingency management and/or reward learning may likely play a critical role in tic suppression in addition to the cognitive control process of inhibition/suppression (Conelea et al., 2018). Indeed, contingencies and rewards

are implicated in the neurobehavioral model that underlies behavior therapy (e.g., social rewards for inhibiting tics during social interactions, relief from premonitory urges; Himle et al., 2014; Houghton et al., 2017). Thus, future research should compare the role of tic suppression both with and without contingency management and/or reinforcement learning in behavioral treatment outcome. Furthermore, when examining tic suppression in future research, it will be important to consider that some youth may be more (or less) experienced implementing tic suppression as a tic management strategy. Future studies should consider prior experience utilizing tic suppression, and explore the possible benefit of 'tic suppression training sessions' to determine whether performance relates to a lack of tic suppression capabilities or rather a lack of knowledge of how to engage in tic suppression. Finally when exploring the effects of behavior therapy on cognitive control processes, there were only small non-significant changes in cognitive control processes. This preliminary finding suggests that the effects of behavior therapy are largely tic specific (i.e., reductions in tic severity on the YGTSS) and do not generalize to the broad domain of cognitive control. However, the exploratory nature and small sample size warrant careful consideration before over interpretation of this finding.

Despite the numerous strengths of this study (e.g., clinical trial methodology, raters masked to treatment condition), a few limitations exist. First, this study selected a priori aspects of cognitive control hypothesized to be relevant to behavior therapy for TD. As such, there are other facets of cognitive control that were not fully examined and warrant further investigation. Second, no data imputation strategies were applied to address missing data. Although data were missing at random (Little's MCAR, $p > .05$), imputation of missing neurocognitive performance and tic suppressibility were not applied due to the limited information about imputation on these constructs at baseline and post-treatment. However, we did examine different approaches when data on tic severity outcomes were inferred using post-baseline observations carried forward. Given that findings regarding neurocognitive predictors were not notably different, the more conservative findings are presented here.

These limitations notwithstanding, there are clear clinical and research implications for these findings. From a clinical perspective, the D-KEFS CWIT task is relatively quick to administer and could be completed during a clinical evaluation to assess the generalizability of these findings to clinical care. If it continued to predict treatment response to behavior therapy, this information could help effectively allocate scarce therapeutic resources of trained behavior therapy providers (Woods, Conelea, & Himle, 2010). Meanwhile from a research perspective, these findings offer the possibility of a new treatment target to improve treatment response rates to behavior therapy. For instance, cognitive strategies and pharmacological interventions that enhanced inhibition/suppression performance on the D-KEFS CWIT task may result in improved behavior therapy outcomes for TD.

In summary, this study found that baseline inhibition/suppression predicted treatment response to behavior therapy in youth with TD. While these findings are promising and highlight the contribution of cognitive control processes to behavior therapy outcomes, there are numerous other related constructs (e.g., executive functioning) and learning processes (e.g., associative learning, reinforcement/reward learning) that remain largely unexamined in the context of behavior therapy. Thus, considerable more research is needed to both

replicate and extend these findings on cognitive control processes before drawing definitive conclusions. Specifically, given the multiple mechanisms that are involved over the course of behavioral treatment, it is important to further understand these hypothesized processes and their interactions to determine the optimal approach to enhance behavior therapy outcomes in TD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Comparison of Baseline Characteristics Between Treatment Groups (N = 53)

	Entire Sample (*N* = 53)	Behavior Therapy (*n* = 25)	Waitlist Condition (*n* = 28)		
	N (%)	N (%)	N (%)	χ^2	p-value
Demographics					
Age	10.93 (1.62)	10.80 (1.85)	11.05 (1.41)	0.31	.58
Male	38 (71.7%)	18 (72%)	20 (71.4%)	.002	0.96
Non-Hispanic White	32 (60.38%)	14 (56%)	18 (64%)	0.38	0.54
Psychiatric Diagnosis					
Anxiety Disorders[1]	26	14	12	0.91	0.34
ADHD	19	11	8	1.16	0.28
OCD	16	8	8	0.03	0.85
Depressive Disorders[2]	1	1	0	1.14	0.29
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	***F***	**p-value**
Clinical Characteristics					
YGTSS Total Tic Score	25.83 (6.19)	26.36 (5.71)	25.36 (6.67)	.34	0.56
YGTSS Impairment Score	25.04 (8.55)	27.70 (8.96)	22.78 (7.64)	4.39	0.04
PUTS Total Score	23.17 (5.36)	23.56 (5.36)	22.82 (5.44)	0.25	0.62
Cognitive Control Processes					
ANT Incongruent Accuracy	39.62 (8.64)	39.48 (8.94)	39.74 (8.52)	0.01	0.91
SST Reaction Time	303.83 (102.96)	296.38 (102.47)	310.63 (105.23)	0.21	0.65
Go-No Go Commission Errors	22.96 (7.62)	24.42 (7.42)	21.71 (7.70)	1.65	0.21
D-KEFS Color-Word Interference	10.71 (2.78)	11 (2.87)	10.46 (2.73)	0.47	0.49
Tic Suppression					
Tic Suppression Score	42.94 (42.72)	52.35 (42.94)	37.15 (43.25)	0.52	0.48

Note: ADHD = Attention Deficit Hyperactivity Disorder, OCD = Obsessive Compulsive Disorder, YGTSS = Yale Global Tic Severity Scale, PUTS = Premonitory Urge to Tic Scale, SWAN = Strengths and Weaknesses of ADHD Symptoms and Normal Behavior, ANT = Attention Network Task, SST = Stop-signal task, D-KEFS = Delis-Kaplan Executive Function System

[1]Anxiety Disorders included the following conditions: Social phobia, separation anxiety, generalized anxiety, specific phobia

[2]Depressive Disorders included the following conditions: major depressive disorder, dysthymia, depressive disorder NOS

Table 2.

Baseline and Post-Treatment Neurocognitive Performance by Treatment Response Status

	Non-Responder			Responder		
	Baseline	**Post-Treatment**	**Effect Size[a]**	**Baseline**	**Post-Treatment**	**Effect Size[a]**
	Mean (SD)	**Mean (SD)**		**Mean (SD)**	**Mean (SD)**	
ANT Incongruent Accuracy	41.5 (4.75)	40.91 (7.06)	0.07	40.33 (10.55)	38.94 (7.14)	0.16
SST Reaction Time	277.19 (113.06)	270.06 (103.04)	0.07	275.26 (81.91)	260.20 (72.34)	0.15
Go-No Go Commission Errors	23.80 (6.66)	22.14 (6.57)	0.22	23.00 (7.36)	23.21 (7.71)	0.03
D-KEFS Color-Word Interference	11.27 (2.81)	11.39 (3.12)	0.04	11.18 (3.24)	10.55 (2.48)	0.38

Note: ANT = Attention Network Task, SST = Stop-signal task, D-KEFS = Delis-Kaplan Executive Function System

[a]Effect size calculated by difference in means between baseline and post-treatment, divided by the standard deviation for the entire sample at baseline