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Neurocognitive predictors of treatment response to randomized treatment in adults with tic disorders

Amitai Abramovitch [a,b,c,*], Lauren S. Hallion [b,c,d,e], Hannah E. Reese [b,c,f], Douglas W. Woods [g], Alan Peterson [h], John T. Walkup [i], John Piacentini [j], Lawrence Scahill [k,l], Thilo Deckersbach [b,c,1], Sabine Wilhelm [b,c,1]

[a] Department of Psychology, Texas State University, San Marcos, TX, USA
[b] Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA
[c] Department of Psychiatry, Harvard Medical School, Boston, MA, USA
[d] Department of Psychology, University of Pittsburgh, Pittsburgh, PA, USA
[e] Anxiety Disorders Center, Institute of Living, Hartford, CT, USA
[f] Department of Psychology, Bowdoin College, Brunswick, ME, USA
[g] Department of Psychology, Marquette University, Milwaukee, WI, USA
[h] The University of Texas Health Science Center at San Antonio, San Antonio, TX, USA
[i] Department of Psychiatry, Weill Cornell Medical College, New York, NY, USA
[j] Department of Psychiatry and Biobehavioral Sciences, University of California Los Angles, Los Angeles, CA, USA
[k] Department of Psychiatry, Yale University, New Haven, CT, USA
[l] Department of Pediatrics, Emory University, Atlanta, GA, USA

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ABSTRACT

Tourette's disorder (TS) and chronic tic disorder (CTD) are neurodevelopmental disorders characterized by involuntary vocal and motor tics. Consequently, TS/CTD have been conceptualized as disorders of cognitive and motor inhibitory control. However, most neurocognitive studies have found comparable or superior inhibitory capacity among individuals with TS/CTD relative to healthy controls. These findings have led to the hypothesis that individuals with TS/CTD develop increased inhibitory control due to the constant need to inhibit tics. However, the role of cognitive control in TS/CTD is not yet understood, particularly in adults. To examine the role of inhibitory control in TS/CTD, the present study investigated this association by assessing the relationship between inhibitory control and treatment response in a large sample of adults with TS/CTD. As part of a large randomized trial comparing behavior therapy versus supportive psychotherapy for TS/CTD, a battery of tests, including tests of inhibitory control was administered to 122 adults with TS/CTD at baseline. We assessed the association between neuropsychological test performance and change in symptom severity, as well as compared the performance of treatment responders and non-responders as defined by the Clinical Global Impression Scale. Results indicated that change in symptoms, and treatment response were not associated with neuropsychological performance on tests of inhibitory control, intellectual ability, or motor function, regardless of type of treatment. The finding that significant change in symptom severity of TS/CTD patients is not associated with impairment or change in inhibitory control regardless of treatment type suggests that inhibitory control may not be a clinically relevant facet of these disorders in adults.

1. Introduction

Tourette's disorder (TS) and persistent (chronic) motor or vocal tic disorder (CTD), are neurodevelopmental disorders characterized by multiple vocal and motor tics (American Psychiatric Association, 2013). The worldwide prevalence of tic disorders in children is estimated at 0.8%, with higher prevalence in boys (1.1%), whereas the prevalence of tic disorders in adults is estimated at 1:2000 (Knight et al., 2012). Tic disorders usually onset in childhood and their severity tend to decrease with age. However, it has been estimated that 11% of individuals with tic disorders continue to experience moderate to severe tics resulting in daily life functional impairments into adulthood (Bloch et al., 2006; Leckman et al., 1998).

Compared to controls, individuals diagnosed with tic disorders exhibit different patterns of brain activity in the cortico-striato-thalamo-cortical (CSTC) neural circuitry (Leckman et al., 2010). The prominent role of the CSTC system in executive and inhibitory functions, together with the clinical presentation of tics, led to the hypothesis that tic disorders are disorders of motor disinhibition, wherein patients experience

* Corresponding author at: Department of Psychology, Texas State University, San Marcos, TX 78666, USA.
E-mail address: abramovitch@txstate.edu (A. Abramovitch).
[1] Denotes equal contribution.

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difficulties suppressing tics (Jung et al., 2013). Indeed, imaging studies reveal increased activation of the CSTC network in patients with tic disorders during attempts to inhibit eye blinking (Mazzone et al., 2010).

1.1. Inhibitory control in tic disorders

Studies investigating executive function in tic disorders, particularly tasks of inhibitory control (including response inhibition, response suppression, and interference control), reveal mixed results (Kalsi et al., 2015). In fact, the majority of studies utilizing the gold standard tests of inhibitory control have revealed intact performance among adults with tic disorders. These include research utilizing Go/No-Go tasks (GNG; Serrien et al., 2005; Thomalla et al., 2014; Watkins et al., 2005) and the Stroop task (Eddy and Cavanna, 2014; Thibault et al., 2009). Very few studies found underperformance on tasks of behavioral inhibition in adults with TS/CTD (Jackson et al., 2015), but these results were found on tasks such as Sentence Completion, or the Simon task (Dursun et al., 2000; Georgiou et al., 1995). In addition, it has been argued that such studies tend to include participants with comorbid disorders such as Attention Deficit/Hyperactivity Disorder (ADHD) and OCD, and that inhibitory deficits may be found mainly in individuals diagnosed with tic disorders concomitant with OCD and/or ADHD (Jung et al., 2013). Notably, recent reviews of the literature highlight findings indicating a paradoxical *superior* behavioral control among adolescents and adults diagnosed with tic disorders compared to controls—hypothetically due to years of experience attempting to inhibit tics (Jackson et al., 2015; Jung et al., 2013). However, more research is required to support this notion, and the role of behavioral inhibition in adult TS/CTD remains unclear.

1.2. Neuropsychological functions and treatment response in tic disorders

Behavioral interventions for tic disorders, such as Habit Reversal Therapy (HRT) and its newer version called Comprehensive Behavioral Intervention for Tics (CBIT), are found to be effective for the treatment of tic disorders, (Piacentini et al., 2010; Wilhelm et al., 2012) yielding large effect sizes in adult samples (McGuire et al., 2014). However, very little is known about predictors of treatment response to behavior therapy for tic disorders. Neuropsychological predictors of treatment response may be important in informing treatment selection, as well as informing treatment development. To our knowledge, there are only three studies that examined changes in cognitive function following cognitive behavioral therapy (CBT) for adult TS/CTD. Lavoie et al. (2011) reported improved performance on the Purdue Pegboard Test following treatment. However, this test assesses basic motor functions, and the authors did not include executive function or other neuropsychological tests in their study. In another study (Deckersbach et al., 2006) the authors compared a small sample of individuals diagnosed with TS receiving Habit Reversal Therapy (n = 15) to a sample (n = 15) receiving supportive psychotherapy. The authors found that aspects of performance on a visuospatial priming task had predictive value for treatment response. Notably, the authors used this task to assess response inhibition, although the task was visuospatial in nature which poses difficulties in differentiating between the predictive value of visuospatial function versus response inhibition. In a recent study, however, Morand-Beaulieu et al. (2015) employed a stimulus-response compatibility inhibition task in a sample of 20 TS/CTD adult patients and 20 controls and found no performance difference between pre- and post-treatment. Thus, the goal of this study was to utilize gold standard tasks of inhibitory control—namely, the Go/No-Go (GNG) test assessing response inhibition, and the Stroop test, assessing interference control—to predict treatment response to CBIT among adults with TS and CTD. In light of the mixed literature and the novelty of this study, our investigation is exploratory.

2. Materials and methods

2.1. Study design

Participants were recruited as part of a large-scale, randomized controlled trial comparing 10 weeks (8 sessions) of Comprehensive Behavioral Intervention for Tics (CBIT) to psychoeducation and supportive therapy (PST). See Wilhelm et al. (2012) for a detailed description of the study procedures. Neuropsychological measures were administered at baseline. Clinical severity was assessed by an independent evaluator (a clinician blind to treatment condition) at baseline and at post-treatment.

Participants were recruited at three sites: Massachusetts General Hospital/Harvard Medical School, Yale University, and University of Texas Health Science Center at San Antonio.

2.2. Participants

Adult participants (n = 122) were included in the present study. Inclusion criteria were age ≥ 16 years, a diagnosis of TS or CTD of moderate severity or greater based on the Clinical Global Impression-Severity Score (CGI-S ≥ 4), and a Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) total score ≥ 14 (>10 for those with only motor or vocal tics). Additional inclusion criteria were fluency in English, IQ > 80 on a standardized intelligence test, no history of schizophrenia or pervasive developmental disorder, and no current substance use disorder. Other comorbidities (bipolar disorder, depression, anxiety and related disorders, and ADHD) were permitted provided that the co-occurring disorder was stable and not of sufficient severity to require clinical attention. Participants were excluded if they previously completed a course (>4 sessions) of CBT for tics. Medications for tics were permitted provided the dose was stable for at least 6 weeks with no planned changes for the duration of the study. Fifty-one participants (41.8%) were medicated—out of which 8 participants were on tic medication only (e.g., alpha agonists, neuroleptics), 23 were on other medications in addition to tic medication, and 20 participants were on non-tic medication only (e.g., SSRIs).

2.3. Treatments

A comprehensive description of the study treatments can be found elsewhere (Wilhelm et al., 2012). Briefly, both treatments consisted of eight 60–90 min sessions administered over 10 weeks. CBIT comprised psychoeducation, tic awareness training, competing response training, relaxation training, and functional analysis. PST comprised disorder-specific psychoeducation and supportive therapy. Therapists had at least a master's degree in clinical psychology, followed detailed treatment manuals, and were specifically trained on both treatments for this study. Treatment sessions were videotaped and randomly selected for fidelity ratings. Fidelity was good or better for 75.7% of CBIT tapes and 87.7% of PST tapes.

2.4. Measures

2.4.1. Clinical measures

Structured Clinical Interview for DSM-IV Patient Version (SCID-P): Diagnostic status was assessed via the SCID-P (First et al., 2002), a widely-used and well-validated semi-structured interview developed to establish past and current DSM-IV diagnoses.

Clinical Global Impression-Improvement Scale (CGI-I): The CGI-I (Guy and Bonato, 1970) is a single-item standard global assessment used to assess changes in severity of the target disorder. The CGI-I scores range between 1 (very much improved) and 7 (very much worse). Positive response to treatment in the present study was defined as a score of 2