



# A cluster analysis of tic symptoms in children and adults with Tourette syndrome: Clinical correlates and treatment outcome



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## ABSTRACT

Cluster analytic methods have examined the symptom presentation of chronic tic disorders (CTDs), with limited agreement across studies. The present study investigated patterns, clinical correlates, and treatment outcome of tic symptoms. 239 youth and adults with CTDs completed a battery of assessments at baseline to determine diagnoses, tic severity, and clinical characteristics. Participants were randomly assigned to receive either a comprehensive behavioral intervention for tics (CBIT) or psychoeducation and supportive therapy (PST). A cluster analysis was conducted on the baseline Yale Global Tic Severity Scale (YGTSS) symptom checklist to identify the constellations of tic symptoms. Four tic clusters were identified: Impulse Control and Complex Phonic Tics; Complex Motor Tics; Simple Head Motor/Vocal Tics; and Primarily Simple Motor Tics. Frequencies of tic symptoms showed few differences across youth and adults. Tic clusters had small associations with clinical characteristics and showed no associations to the presence of coexisting psychiatric conditions. Cluster membership scores did not predict treatment response to CBIT or tic severity reductions. Tic symptoms distinctly cluster with little difference across youth and adults, or coexisting conditions. This study, which is the first to examine tic clusters and response to treatment, suggested that tic symptom profiles respond equally well to CBIT. Clinical trials. gov. identifiers: NCT00218777; NCT00231985.

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## 1. Introduction

Tics are sudden motor movements or vocalizations that begin in childhood and may persist into adulthood (Leckman, 2002). Transient tics are common in school-age children affecting as many as 24% in this age group (Snider et al., 2002). Chronic tic disorders are delineated by tic type (motor, phonic or both) and duration. For example, Persistent (Chronic) Motor Tic Disorder is defined by the presence of a single or multiple motor tics that persist for more than a year. The diagnosis of Tourette Syndrome (TS) requires both multiple motor and one or more phonic tics (not necessarily concurrently) that last more than a year (American Psychiatric Association, 2013). The estimated prevalence of TS

ranges from three to eight per 1000 in children (Centers for Disease Control, 2009). In community and clinical samples, chronic tic disorders are associated with a wide range of behavioral and emotional difficulties (Sukhodolsky et al., 2003; Storch et al., 2007; Centers for Disease Control, 2009; Specht et al., 2011; Kraft et al., 2012).

Tic disorders have a heterogeneous presentation, with tics varying across and within individuals according to type (motor or phonic), anatomical location, and complexity (number of muscle groups involved) (Leckman et al., 2006). Tics in individuals with TS often begin with eye blinking and movements of the face and head region. Motor tics usually precede phonic tics and simple tics precede more complex tics (Leckman, et al., 2006; Bloch and Leckman, 2009). Simple tics include brief, repetitive movements such as eye blinking, grimacing, head jerks, shrugging or vocalizations such as throat clearing, grunting. Complex motor tics involve larger muscle groups and

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appear more goal-directed in character (e.g., arm thrusts, gyrating, bending). Vocalizations such as words or short phrases (e.g., “oh boy”, “you bet”) can also occur. Although often believed to be prototypic of TS, coprolalia, or bouts of uncontrolled cursing, affects only an estimated 18.5% of patients (Freeman et al., 2009). Many individuals with TS experience premonitory urges associated with tics, with some difficulty in urge recognition among youth under 10 years of age (Woods et al., 2005). Although tic severity ranges from mild to severe across individuals, most cases exhibit a fluctuating course with peaks in symptom severity that stabilize over a period of weeks (Lin et al., 2002). Following the onset of tics in early school-age years, tics often increase in number, type and frequency into early adolescence and often subside in early adulthood (Bloch and Leckman, 2009). Nonetheless, tic symptoms and impairment may persist into adulthood, resulting in a diminished quality of life (Bloch and Leckman, 2009; Gorman et al., 2010). Although the cause of TS is unknown, available evidence suggests that dysregulation of cortical and subcortical motor circuits underlie tic symptoms (see Leckman et al., 2010 for a review).

Beyond the broad categories of simple and complex tics, there is little consensus regarding the existence and organization of symptom subtypes within tic disorders (Walkup et al., 2010). This lack of consensus may be due to differences in sample selection, assessment methods, and nomenclature used in prior studies. For instance, a tic could be classified as a “facial grimace” on one measure, but as a “mouth/jaw movement” or a “facial tic” on another measure. In an attempt to circumvent measurement variability, several studies have relied upon factor and/or cluster analytic techniques (Alsobrook and Pauls, 2002; Mathews et al., 2007; Robertson and Cavanna, 2007; Robertson et al., 2008; Kircanski et al., 2010;). Collectively, these four studies have produced two consistent findings. First, tic symptoms cluster by complexity (simple versus complex) (Mathews et al., 2007; Robertson et al., 2008; Kircanski et al., 2010). Second, compulsive tic behaviors (e.g., touching, repetitive behaviors, echolalia) cluster separately from other tic symptoms (e.g., head movements, leg movements, coprolalia) (Alsobrook and Pauls, 2002; Robertson et al., 2008).

Kircanski and colleagues used agglomerative cluster analysis to examine clusters of tic symptoms from the Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989) and their clinical correlates in 99 children (Kircanski et al., 2010). The YGTSS is a reliable and valid clinician-rated instrument that is commonly used in clinical trials to measure tic severity (Leckman et al., 1989; Storch et al., 2005). Kircanski et al. (2010) identified four overlapping clusters; predominantly complex tics, simple head/face tics, simple body tics, and simple vocal/facial tics. Associations were reported between specific symptom clusters and symptom severity, age, and premonitory urge ratings (Kircanski et al., 2010). To date, no cluster analytic study has explored associations between tic clusters and treatment outcome.

In the present study, data were compiled from two multicenter, randomized clinical trials (RCTs) comparing the Comprehensive Behavioral Intervention for Tics (CBIT; Woods et al., 2008) to a structured psychoeducation and supportive therapy intervention (PST) in children (Piacentini et al., 2010) and adults (Wilhelm et al., 2012) with chronic tic disorders. The two RCTs employed identical designs and assessment methods, which included study participation lasting 10 weeks in duration, and blinded assessments of the YGTSS conducted at baseline, mid-point (Week 5) and endpoint (Week 10). The first RCT included 126 youth ages 9–17 years (Piacentini et al., 2010); the second RCT included 122 participants between 16 and 69 years of age (Wilhelm et al., 2012). Similar to Kircanski et al. (2010), we used an agglomerative cluster analysis to identify tic symptom

clusters based on the YGTSS and examined associations of clinical characteristics and tic clusters. In addition, the present study also examined the association between specific tic clusters and response to CBIT.

## 2. Method

### 2.1. Participants

To be eligible, participants had to have a chronic tic disorder of at least moderate severity, and be fluent in English. Moderate severity was defined as having a CGI-Severity (CGI-S) rating of “moderately ill” (4) or greater (Guy, 1976). In the child CBIT trial, the YGTSS Total Tic score had to be greater than 13 (participants with only motor or vocal tics required a YGTSS score greater than 9). In the adult CBIT trial, the YGTSS Total Tic score had to be greater than 14 (participants with only motor or vocal tics requires a YGTSS score greater than 10). Cases with severe tics (greater than 30 on the YGTSS Total Tic score) were reviewed by a cross-site panel to confirm appropriateness for study participation.

A current or lifetime diagnoses of major depression, anxiety disorders (including obsessive compulsive disorder; OCD), and/or attention deficit hyperactivity disorder (ADHD) were acceptable for enrollment if the coexisting disorder was stable and did not necessitate immediate treatment. Participants on psychotropic medication (including tic medication) could enter the trial if the medication was stable for at least six weeks prior to the baseline assessment and there was no expected dose change during the 10-week trial. Exclusion criteria included: IQ less than 80; current diagnosis of substance abuse or substance dependence; lifetime diagnosis of pervasive developmental disorder, mania or psychotic disorder; or previously receiving four or more sessions of habit reversal training for tics.

Six youths and three adults were excluded from the collective sample ( $N=248$ ) due to missing or illegible YGTSS symptom checklist data. The final sample included 239 participants (171 males and 68 females) ranging in age from 9–69 years ( $M_{\text{years}}=21.67$ ,  $S.D._{\text{years}}=14.10$ ). Most participants were diagnosed with Tourette Disorder ( $n=212$ ). Twenty-five participants met criteria for Chronic Motor Tic Disorder and two participants were diagnosed with Chronic Vocal Tic Disorder. Sample characteristics are presented in Table 1. Additional sample details can be found in Piacentini et al. (2010) and Wilhelm et al. (2012).

### 2.2. Measures

#### 2.2.1. Diagnostic interviews

Age appropriate structured diagnostic interviews were used to assess current diagnoses. For participants in the child CBIT study, the Anxiety Disorders Interview Schedule for DSM-IV-TR: Child Version (ADIS; Silverman and Albano, 1996) with a supplementary tic module, were administered to parents and youth. The ADIS is a structured clinical interview that assesses current episodes of Axis I disorders, and differential diagnoses based on DSM-IV criteria. The ADIS has consistently demonstrated strong psychometric properties, including test-retest reliability, inter-rater reliability, and concurrent validity (Silverman et al., 2001; Wood et al., 2002). For participants in the adult CBIT trial, the Structured Clinical Interview for DSM-IV (SCID; First et al., 2002) was administered to participants. The SCID-Patient version is a semi-structured interview that assess current episodes of Axis I disorders. Additionally for adult CBIT participants, a supplementary tic and ADHD interview were administered.

#### 2.2.2. Tic symptoms and severity

The presence and severity of tics among participants was assessed using the Yale Global Tic Severity Scale (YGTSS; Leckman et al., 1989). The YGTSS is a clinician-rated scale with demonstrated reliability and validity designed to measure tic severity over the previous week (Leckman et al., 1989; Storch et al., 2005). The initial section of the YGTSS consists of a checklist of 40 possible tics separately categorized as simple motor, complex motor, simple vocal and complex vocal. Different types of simple vocal tics (e.g., coughing, throat clearing, sniffing, grunting, animal noises) are subsumed under a single category titled “any simple phonic tic.” Inter-rater reliability of the symptom YGTSS symptom checklist has not been evaluated. Tics noted as present in the past week are then globally rated on a series of 5-point subscales (number, frequency, intensity, complexity, and inference) with motor and vocal tics rated separately. The YGTSS yields three tic severity scores: Total Motor (0–25); Total Phonic (0–25) and the combined Total Tic Score (0–50). Additionally, the YGTSS also includes an Impairment scale scored from 0 to 50.

#### 2.2.3. Premonitory urge ratings

Across participants, ratings of premonitory urges were assessed using the Premonitory Urge for Tics Scale (PUTS; Woods et al., 2005). The PUTS is a 9-item, self-report questionnaire designed to establish the presence and current degree of

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