The Tourette's Disorder Scale (TODS): Development, Reliability, and Validity

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The Tourette's Disorder Scale (TODS)

Development, Reliability, and Validity

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To address the lack of a simple and standardized instrument to assess overall illness severity of Tourette's disorder (TD), the authors developed and tested a 15-item scale to measure a broad range of common symptoms including tics, inattention, hyperactivity, obsessions, compulsions, aggression, and emotional symptoms. Independent investigators used the 15-item Tourette's Disorder Scale (TODS) to assess 60 TD patients who were taking part in a double-blind placebo-controlled multicenter 8-week treatment study. Interrater reliability, internal consistency, convergent and discriminant validity, and sensitivity to change were examined. The TODS was associated with good interrater reliability, excellent internal consistency, and favorable levels of validity and sensitivity to change. Individual TODS items showed good convergent and discriminant validity against other measures. The TODS is a simple, efficient way for clinicians and parents to rate the severity of multiple symptoms commonly found in patients with Tourette's disorder.

Keywords: Tourette's Disorder Scale; validation; reliability; illness severity

Although motor and vocal tics are a defining symptom of Tourette's disorder (TD), many patients with TD also display other neuropsychiatric features including obsessive compulsive symptoms (Pauls, Towbin, Leckman, Zahner, & Cohen, 1986), inattention, hyperactivity, impulsivity (Comings, 1994; Comings & Comings, 1990a), emotional liability, and anxiety (Coffey, Biederman, Geller, et al., 2000; Coffey, Biederman, Smoller, et al., 2000; Coffey, Frazier, & Chen, 1992; Coffey & Park, 1997; Comings & Comings, 1990b). Extreme temper or "rage attacks" also occur in approximately 30% of patients (Budman, Bruun, Park, Lesser, & Olson, 2000; Budman, Bruun, Park, & Olson, 1998b; Riddle, Hardin, Ort, Leckman, & Cohen, 1988; Stefl, Bornstein, & Hammond, 1988; Stephens & Sandor, 1999).

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For children and adolescents with TD, the behavioral and emotional symptoms (BESs) are often more troublesome clinically than the tics (Budman, Bruun, Park, & Olson, 1998a; Nolan, Sverd, Gadow, Sprafkin, & Ezor, 1996; Singer & Rosenberg, 1989a; Spencer et al., 1998; Stephens & Sandor, 1999; Stokes, Bawden, Camfield, Backman, & Dooley, 1991; Wodrich, Benjamin, & Lachar, 1997). For example, Wand, Matazow, Shady, Furer, and Staley (1993) found that mood swings, temper control, and aggression where among the most disabling features of TD, in those 6 to 17 years old. Similarly, Dooley, Brna, and Gordon (1999) found that parents of TD patients considered attention deficit and learning difficulties to be the most significant symptoms, whereas motor and vocal tics were considered least important.

Historically, two positions have been taken by TD researchers about the relationship between tics and the BESs. One position holds that BESs are secondary to, or independent of, the tic disorder. Related to this position is the notion that BESs are elevated in clinical samples of tic disorder patients because individuals with multiple problems are more likely to be referred for medical evaluation. This potential confounding variable is known as "ascertainment bias." The second position holds that BESs are an integral part of the TD diathesis. Although evidence exists for both positions (Coffey, Biederman, Geller, et al., 2000; Coffey, Miguel, Savage, & Rauch, 1994; Coffey & Park, 1997; Nolan et al., 1996; Robertson, 2000; Spencer et al., 1998), more recent evidence favors the latter position. For example, Kurlan et al. (2002) found that obsessive-compulsive disorder (OCD); attention deficit hyperactivity disorder (ADHD); and various anxiety, mood, and behavioral disorders were more commonly found in children with tics than those without. Because these data were derived from a community-based sample of 1,500 children, the possibility of ascertainment bias was eliminated. In an analysis of 29 tic-related symptoms in 85 TD individuals, Alsobrook and Pauls (2002) identified four significant factors: (1) aggressive phenomena, (2) motor and vocal tic phenomena, (3) compulsive phenomena, and (4) tapping phenomena. These four factors accounted for 61% of the phenotypic variance in Tourette probands and their first-degree relatives. Overall, the findings from these two recent studies strongly support an etiological relationship between BESs and tic disorders.

It is becoming clear that the BESs have profound effects on quality-of-life (QOL) measures in TD patients not only in childhood but even into adulthood. Using the Quality of Life Assessment Schedule, Elstner, Selai, Trimble, and Robertson (2001) interviewed 103 adult TD outpatients and found that in addition to tic severity, factors influencing QOL domains were obsessive-compulsive behavior and depression and anxiety.

Whereas the severity of non-OCD anxiety and tic severity are closely related (Coffey, Biederman, Smoller, et al., 2000), more severe symptoms of mood instability, depression, and rage often occur in TD patients with only mild tic severity (Berthier, Kulisevsky, & Campos, 1998; Budman et al., 1998b; Stephens & Sandor, 1999). For example, Berthier et al. (1998) found that one third of their clinically referred adult TD patients had comorbid bipolar disorder, which was mainly associated with mild tic severity. Similarly, Coffey et al. (2000) recently found that the comorbid presence of a mood disorder, such as major depression or bipolar disorder, strongly predicted past psychiatric hospitalization, whereas tic severity was only a slightly significant predictor. These findings suggest that the severity of illness is not necessarily associated with tic severity in patients with TD, particularly those who are referred to psychiatric clinics.

In clinical practice, the usual approach is to address the most obvious symptoms (Gadow, 1991). Because tics are important symptoms of TD, most traditional treatment outcome studies have focused mainly on treating the tic symptoms of the disorder (Shapiro et al., 1989). However, clinical experience and empirical evidence suggests that families are more concerned about the associated BESs than the tics themselves (Dooley et al., 1999; Sheehan, Shytle, Newman, Sanberg, & Silver, 1999). Targeting these BESs is paramount, because treatment of tics alone will often not address these symptoms and may even make them worse (Coffey, Biederman, Geller, et al., 2000; Gadow, 1991). This is particularly unfortunate for those children and adolescents whose BESs cause the greatest impairment. This limitation along with unclear diagnostic boundaries may help to explain why only two medications are approved for TD.

Although excellent tic-specific measures are available for use in clinical drug trials (Shytle, Silver, & Sanberg, 1995), a simple and standardized instrument to assess overall Tourette's illness severity does not exist. Therefore, we developed and evaluated a brief clinician and parent rating scale for this purpose—the Tourette's Disorder Scale (TODS). Our hypothesis was that the TODS would serve as a better measure of illness severity than scales currently available for TD.

STUDY 1

Scale Development

Because current TD scales focus primarily on tic symptoms, we decided to develop a scale based on symptom information received from parents of TD children as well as on scale properties that have been sensitive in discriminat-

ing drug from placebo in adult psychopharmacology studies (Sheehan, Harnett-Sheehan, & Raj, 1996). To gather this information, we conducted an Internet survey of parents of children and adolescents with TD (Sheehan et al., 1999). The survey, which was based on the methods developed previously (Bonson & Murphy, 1996), was sent to a Tourette's syndrome e-mail list and the newsgroup. First, we asked parents about the occurrence and relative importance of 32 behavioral and emotional symptoms (BESs), representing three dimensions of psychopathology (i.e., aggression, anxiety, and mood), which have been frequently described in the TD literature (Budman, Bruun, Park, & Olson, in press; Budman et al., 1998a, 2000; Coffey, Biederman, Geller, et al., 2000; Coffey et al., 1994; Coffey & Park, 1997; Comings, 1994; Comings & Comings, 1990a, 1990b; Nolan et al., 1996; Robertson, 2000; Singer & Rosenberg, 1989b; Spencer et al., 1998; Stephens & Sandor, 1999; Stokes et al., 1991; Wand et al., 1993; Wodrich et al., 1997). Parents reviewed the list of BESs and were asked, "During the past month, please indicate how often the following symptoms have caused significant impairment in your child's daily life." Frequency of each symptom disturbance was measured on a scale from 0 to 3 (*never*, *sometimes*, *often*, or *always*). Parents were then asked to select the "10 most problem symptoms" from the list. Finally, parents were asked to weigh the relative importance of these BESs against their child's tics by having them indicate which end of the spectrum their child fits on a visual-analogue scale, the Tourette's Symptom Importance Scale (TSIS) shown in Figure 1.

Thirty-five parents responded to the survey. As shown in Table 1, 80% of parents stated that during the past month, the BESs caused more problems (defined as a TSIS score > 1) in their child's daily life than the tics (BESs > Tic Group). This finding is consistent with our own experience where most of the patients with Tourette's disorder referred to our clinic report primary impairment from symptoms other than tics.

Those items that met the following "key symptom" criteria: (1) on average, caused significant problems more than "sometimes" and (2) were rated as a "top 10" problem by more than 25% of the group were used in the construction of the TODS, as shown in the appendix (Sheehan et al., 1999).

To perform an initial psychometric evaluation, the TODS was included as an outcome measure in a recent multicenter treatment study in TD patients.

STUDY 2

The purpose of the psychometric evaluation was to assess the interrater reliability of the TODS-CR, to evaluate its internal consistency, and to examine its convergent and discriminant validity vis-à-vis expert opinion and other standard instruments. We also wanted to evaluate its sensitivity to change in the course of treatment.

METHOD

Sites and Participants

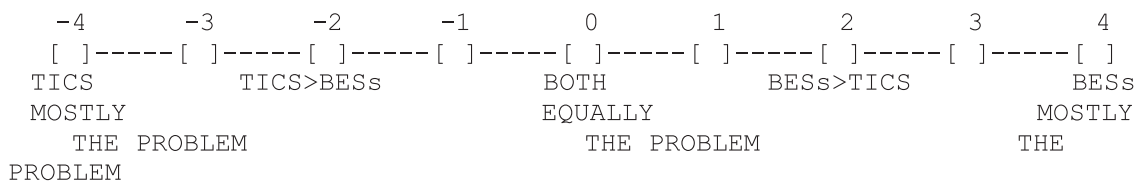
Participants ($N = 60$) were recruited from patients who were participating in a multicenter double-blind placebo-controlled safety and exploratory study of mecamylamine (Inversine®) for TD (Silver et al., 2001). Twelve research centers from various regions of the United States participated in the trial. All patients had to be between the ages of 8 and 17 years and had to have a principal *DSM-IV* diagnosis of TD, as determined by the MINI-KID, a child and adolescent version of the MINI International Neuropsychiatric Interview (MINI) for *DSM-IV* (Sheehan et al., 1998). Because we hypothesized that the treatment medication under investigation would have a greater effect on BESs than tics, a predominance of behavioral and emotional symptom impairment over tic impairment (TSIS score of > 1) was required for inclusion into the study (Silver et al., 2001). Patients with a history or presence of any psychotic disorder, organic dementia, drug or alcohol dependence, those who would be unable to follow the study protocol, or those with significant medical problems or significant abnormalities on laboratory testing were excluded. All patients and their parents signed statements giving informed consent for the treatment study, including consent for assessment interviews. Patients who met the study criteria were randomly assigned to treatment with mecamylamine or placebo.

Measures

A list of the instruments used in the study and the schedule of administration are provided in Table 2.

TODS. As indicated, two versions of the TODS, one rated by the parent (TODS-PR) and the other rated by the clinician (TODS-CR) were administered. The parent was asked to base his or her rating on recalled observations of the patient's Tourette's spectrum symptoms during the past week. The clinician based his or her rating on information gathered from both the parent and the patient concerning the patient's symptoms occurring in the same time frame. Thus, the clinician-rated version is a semistructured interview conducted with both parent and child, whereas the parent-rated version is a pencil-and-paper assessment based on the participant's behavior. On both scales, the se-

FIGURE 1
Tourette Symptom Importance Scale (TSIS)



NOTE: BESs = behavioral and emotional symptoms.

TABLE 1
Relative Importance of Symptoms for Parents of Children and Adolescents with Tourette's Disorder

	Group		
	BESs > Tics	*Tics > BESs*	*Total Sample*
Number of patients	28	7	35
% of patients	80	20	100
Mean age ± *SEM*	11 ± 0.5	11 ± 0.7	11 ± 0.5
Mean TSIS score ± *SEM*	3.4 ± 0.2	–1.3 ± 0.8	2.4 ± 0.4

NOTE: BESs = behavioral and emotional symptoms; > = more Important (i.e., causes greater impairment); TSIS = Tourette's Symptom Importance Scale.

TABLE 2
Assessment Procedures

Day	*–7 (Screen)*	*0 (Baseline)*	*Weeks 1-8*
Diagnostic Interview (MINI-KID)	[CHAR]		
USF Personal Data Inventory (USFPDI)	[CHAR]		
Tourette Disorder Scale–Clinician Rated (TODS-CR)	[CHAR][a]	[CHAR]	[CHAR]
Tourette Disorder Scale–Parent Rated (TODS-PR)	[CHAR]	[CHAR]	[CHAR]
Yale Global Tic Severity Scale (YGTSS)		[CHAR]	[CHAR][b]
Child/Adolescent Inventory (C/ASI-4)		[CHAR]	[CHAR][b]
Sheehan Disability Scale (SDS)		[CHAR]	[CHAR][b]
Conners Parent Rating Scale (CPRS)		[CHAR]	[CHAR][b]
Family Impact Scale (FIS)		[CHAR]	[CHAR][b]

NOTE: MINI-KID = a child and adolescent version of the MINI International Neuropsychiatric Interview; USF = University of South Florida.
a. To examine interrater reliability, two interviewers rated the same patient using the TODS-CR on this day.
b. These scales were administered only at Weeks 1, 4, and 8.

verity ratings for each item used a scale ranging from 0 to 10 (0 = *not at all* and 10 = *extremely*). An overall total score was calculated by summing the item scores (minimum score = 0, maximum score = 150).

Other instruments. The following additional scales, which were administered as part of the treatment study, were used in the validation component of the psychometric evaluation: The Yale Global Tic Severity Study (YGTSS) provides an evaluation of the number, frequency, intensity, complexity, and interference of motor and phonic symptoms and is currently the most frequently used primary efficacy measure for assessing treatment effects on tic symptoms in patients with a tic disorder. The available evidence suggests that the instrument is reliable and has appropriate construct, convergent, and discriminant validity for measurement of tic symptoms (Leckman et al., 1989). The Conners Parent Rating Scale (CPRS), which has excellent psychometric properties, has been used for many years to assess child psychopathology, particularly ADHD symptoms, from the parent's perspective (Goyette, Conners, & Ulrich, 1978). The Child Symptom Inventory-4 (CSI-4) is a parent rating scale that screens for *DSM-IV* emotional and behavioral disorders in children between 5 and 12 years old, and the Adolescent Symptom Inventory-4 (ASI-4) screens for these disorders in adolescents. The CSI-4 and ASI-4 can be scored to derive symptom count scores (diagnostic model) or symptom severity scores (normative data model) (Gadow & Sprafkin, 1997). For the purposes of this study, symptom severity scores on certain items (Obsessions, Compulsions, and Depression) from both children (CSI-4) and adolescents (ASI-4) were combined (C/ASI-4). The Sheehan Disability Scale (SDS) uses visual-spatial, numeric, and verbal descriptive anchors to assess disability across three domains: school, social life, and family life (Sheehan et al., 1996). The psychometric properties of the Disability Scale are characterized with high internal consistency, reliability, and construct validity (Leon, Olfson, Portera, Farber, & Sheehan,

1997). The Family Impact Scale (FIS) uses visual-spatial, numeric, and verbal descriptive anchors and is currently under development to assess the impact of having a neuropsychiatric disorder on family functioning. The psychometric properties of the FIS are characterized with high internal consistency and high face and construct validity, but interrater reliability and convergent and divergent validity have yet to be assessed (Wilkinson et al., 2000). The University of South Florida Personal Data Inventory (USFPDI) has been used primarily to gather demographic information from individuals who participate in research conducted at the USF Institute for Research in Psychiatry. This instrument was used to gather appropriate demographic information, and two items relating to academic and social performance during the past 3 years were also used in assessing the validity of the TODS relative to other measures. For the latter two items, a decline in performance was reflected as a decrease in score from 0 to negative 3.

Procedure

Raters. The TODS-CR, the YGTSS, and the MINI-KID were completed by trained clinical interviewers with previous experience working with children and adolescents who have TD. All clinical interviewers were provided with a training packet to facilitate familiarity with the format of the TODS-CR. The TODS-PR and all of the other instruments used in this study were rated by the participants' parents.

Interview/scale administration procedures. At screen, all participants were administered the MINI-KID to determine the presence of TD and to assess whether any comorbid disorders were present. Participants were interviewed with only one parent present. The TODS-CR followed by the TODS-PR were administered at screen, baseline (medication free), and each week for 8 weeks by experienced clinicians and by the participants' parent (see Table 2). For the TODS-CR rating, all questions were addressed by the clinician to the subject first. The parent was then asked for his or her comment on the response. In the event of a discrepancy in response between participant and parent, the interviewer invited further discussion and pursued the questioning by asking for examples until satisfied that the rating chosen reflected the expression of that symptom or sign. At each of the study visits, the parent subsequently completed the TODS-PR blind to the TODS-CR rating.

At screen, a subset of 54 participants had a second TODS-CR assessment performed by a second clinical interviewer blind to the results of the TODS-CR administered by the first interviewer. This second assessment was performed to evaluate the interrater reliability of the TODS-CR.

Sample comparison. Because the sample used in the TODS validation study was drawn from TD participants whose parents stated that the behavioral and emotional symptoms caused more impairment than the tics, it was important to examine parameters of TODS scores obtained from an independent sample of participants. TODS-PR scores from 99 TD participants who participated in a mail survey (TSA survey sample) were compared with the 60 TD participants used in the validation study (validation sample). The purpose of the mail survey was to examine the impact of TD on the family (Wilkinson et al., 2000). However, for this TSA survey sample, parents were not asked to rate whether their child's behavioral and emotional symptoms caused more impairment than the tics. Two hundred and seventy-three packets of surveys, each containing a TODS-PR, were mailed to Florida Chapter of the Tourette's Syndrome Association members who had a child between the ages of 7 and 17 with TD. Of the 273, 99 completed questionnaires were returned (Wilkinson et al., 2000).

Statistical Analyses

The interrater reliability of the TODS was assessed using Pearson's correlation coefficients and Bland-Altman plots (Bland & Altman, 1986). The internal consistency of the TODS was analyzed by employing Cronbach's alpha. Mean scores and standard deviations for individual items and the total score on all scales were calculated for all participants. The validity of the TODS-CR vis-à-vis expert opinion and vis-à vis other scales was analyzed using Pearson's correlation coefficients. The sensitivity to change of the TODS-CR and YGTSS were analyzed by using a time-by-group analysis of variance (time: baseline, week 8; group: responder, nonresponder). For these analyses, responders were defined as having a week-8 Clinical Global Improvement Score of 5 or greater on a 21-point scale with positive values 1 to 10 for improvement, 0 for no change, and negative values 1 to 10 for worsening of symptoms.

RESULTS

Demographic and Clinical Measures

Table 3 displays the demographic characteristics of the study participants used to evaluate the psychometric properties of the TODS as well as the descriptive statistics for the pretreatment (baseline) clinical outcome measures

TABLE 3
Demographic Characteristics of the Study Patients and Clinical Measures at Baseline

	n	M	SD	%
Age	60	11.3	2.1	
Age first symptom	60	5.3	2.5	
Age first psychiatric medication	60	6.6	3.1	
Sex				
Male	54			89
Female	6			11
Race				
White	59			98.5
Black	1			1.5
Scales				
TODS-CR	60	71.8	32.7	
TODS-PR	60	75.2	34.1	
YGTSS				
Total motor tic score	60	13.3	3.9	
Total phonic tic score	60	9.7	5.6	
Overall impairment from tics	60	25.2	10.4	
Global severity score	60	48.2	16.4	
CPRS				
Conduct	60	10.9	5.9	
Learning	60	7.7	3.9	
Psychosomatic	60	2.5	2.5	
Impulse	60	7.5	3.1	
Anxiety	60	3.7	2.9	
Hyperactivity	60	16.4	6.3	
Disability				
Work/school	60	5.9	2.9	
Family	60	6.1	2.4	
Social	60	6	0.2	
TSIS	60	2.8	0.96	
FIS	60	106	75.2	

NOTE: TODS-CR = Tourette's Disorder Scale–Clinician Rated; TODS-PR = Tourette's Disorder Scale–Parent Rated; YGTSS = Yale Global Tic Severity Study; CPRS = Conners Parent Rating Scale; TSIS = Tourette's Symptom Importance Scale; FIS = Family Impact Scale.

used in the validity component of the study. Table 4 displays the percentages of comorbid *DSM-IV* psychiatric disorders found in the sample.

Reliability

Interrater reliability for the TODS-CR for the 12 pairs of separate assessments at each site ranged from .70 to .94 ($p < .001$). For the total sample, interrater reliability on individual scale items ranged from .53 (item 4: sudden mood changes) to .79 (item 2: motor tics) ($p < .001$). The correlation coefficient for parent (TODS-PR) and clinician (TODS-CR) ratings was .88 ($p < .001$).

To further substantiate the interrater reliability between the two clinician raters, a Bland-Altman (Bland & Altman, 1986) scatter plot was performed using data from all centers combined. The scatter plot provided error assessment of the measurement between the two raters. The difference between the raters was plotted against the mean TODS total score of the two raters. Because there was a decrease in variability of the differences between raters as the TODS total score increased, the ratios of the measurements were then plotted instead of the differences as recommended by Bland and Altman (1986). The distribution of data was then determined using two standard deviations (*SD*s) as limits of acceptability. Interrater scatter plots demonstrated that all but one rating were within two *SD*s of acceptable levels of agreement, indicating adequate interrater reliability (Bland & Altman, 1986).

TABLE 4
Comorbid *DSM-IV* Psychiatric Disorders

MINI-KID Diagnoses	n	%
Attention deficit hyperactivity disorder	35	58
Oppositional defiant disorder	35	58
Obsessive compulsive disorder	17	28
Major depression	14	23
Hypomania (past)	11	18
Hypomania (current)	10	17
Suicidality	9	15
Agoraphobia	8	13
Separation anxiety	7	12
Social phobia	7	12
Generalized anxiety	6	10
Dysthymia	5	8
Panic disorder (current)	5	8
Specific phobia	4	7
Panic disorder (past)	1	2
Adjustment disorder	1	2

Internal Consistency

For the entire study group, the internal consistency (Cronbach's alpha) of the total score on the TODS-PR was .92. Item analysis of the TODS-CR yielded very similar findings with a Cronbach's alpha of .93.

Sample Comparison and Factor Analysis

The TODS-PR from the TSA survey sample was characterized with excellent internal consistency, with a Cronbach's alpha of .94. Sample comparisons with ANOVA revealed that the validation sample had a significantly higher score for the irritability item than the TSA survey sample (Table 5). Moreover, a principal components factor analysis with varimax rotation of the TODS-PR scores from the TSA survey sample yielded a four-factor solution with nearly identical item loading and structure as the factor analysis for the TODS-PR from the validation study (data not shown). Because an optimal factor analysis requires at least 10 scores per item (150 TODS scores), the two samples were combined ($n = 159$) in a factor analysis revealing a four-factor solution that explained

TABLE 5
Mean Item and Total Score Comparisons of the TODS-PR From Two Independent Samples

TODS-PR Items	Sample: Validation (n = 60)	Sample: Survey (n = 99)	ANOVA: F
Irritable	6.6	4.8	12*
Motor tics	5.4	4.6	2.5
Argumentative	6.6	5.4	4.9
Sudden mood changes	5.7	4.2	7.5
Demands attention	5.2	4.7	0.64
Hot temper	6.0	4.6	5.9
Vocal tics	4.1	3.5	0.89
Obsessions	3.7	3.2	0.71
Difficulty paying attention	5.3	4.8	0.75
Loud or talkative	5.1	4.6	0.77
Restless or "hyper"	5.2	4.7	0.57
Compulsions	3.9	2.9	2.6
Tense, anxious, or nervous	4.8	4.2	1.3
Depressed or uninterested in most things	2.6	2.3	0.31
Impulsive	4.8	4.5	0.28
Total score	74.7	63.2	4.07

NOTE: TODS-PR = Tourette's Disorder Scale–Parent Rated. Bonferroni corrected alpha: *$p < .002$.

99% of the rotated variance. As shown in Table 6, the four factors were named Aggression, ADHD, OCD, and Tics, accounting for 39%, 27%, 21%, and 13% of the variance, respectively. The factor subscores from the TODS-PR were also used in the validation analyses. Results from a similar factor analysis of the TODS-CR from the validation sample are also shown in Table 6. Although the factor structures were similar, the distribution of variance was different. The four factors were ADHD, Aggression, OCD, and Tics, accounting for 34%, 33%, 19%, and 14% of the variance, respectively.

Convergent and Divergent Validity

Table 7 presents the correlations of the item and total scores on the TODS-CR with scores on the YGTSS, the CPRS, and the C/ASI-4. To reduce the chance of Type I error, only clinically relevant correlations are shown across all measures. For example, to demonstrate both convergent and divergent validity, correlations for both the "Motor Tics" and "Vocal Tics" items of the TODS are shown across all measures. Thus, TODS-CR items "Motor Tics" and "Vocal Tics" were strongly correlated with the motor and vocal tic subscores of the YGTSS, but not with other subfactors of other scales such as conduct, learning problem, and psychosomatic subfactors of the CPRS, nor with the obsession and compulsion subfactors of the C/ASI. The TODS-CR total score was correlated significantly

TABLE 6
Factor Analysis Results for Both the TODS-PR and TODS-CR

TODS-PR Items (n = 159)	Tentative Factor Names: Aggression	ADHD	OCD	Tics	Item Communalities
Irritable	*–0.85*	0.20	–0.18	–0.18	0.83
Motor tics	–0.17	0.26	–0.19	*–0.46*	0.35
Argumentative	*–0.79*	0.22	–0.18	–0.21	0.76
Sudden mood changes	*–0.79*	0.21	–0.19	–0.25	0.77
Demands attention	*–0.59*	0.35	–0.18	–0.33	0.61
Hot temper	*–0.84*	0.28	–0.23	–0.08	0.85
Vocal tics	–0.26	0.25	–0.15	*–0.62*	0.53
Obsessions	–0.25	0.20	*–0.80*	–0.17	0.77
Difficulty paying attention	–0.13	*0.67*	–0.21	–0.17	0.54
Loud or talkative	–0.29	*0.71*	–0.14	*–0.43*	0.79
Restless or "hyper"	–0.37	*0.68*	–0.24	–0.22	0.71
Compulsions	–0.15	0.28	*–0.76*	–0.11	0.70
Tense, anxious, or nervous	–0.25	*0.49*	–0.35	–0.23	0.48
Depressed or uninterested in most things	–0.26	0.21	*–0.42*	–0.29	0.37
Impulsive	–0.33	*0.58*	–0.32	–0.15	0.57
Variance explained %	38.48	27.28	20.74	13.46	
Eigenvalues	3.70	2.60	2.00	1.30	

TODS-CR Items (n = 60)	Tentative Factor Names: ADHD	Aggression	OCD	Tics	Item Communalities
Irritable	–0.21	*–0.71*	–0.26	–0.37	0.75
Motor tics	*–0.50*	–0.18	0.01	*–0.42*	0.46
Argumentative	–0.34	*–0.78*	–0.20	–0.17	0.79
Sudden mood	–0.24	*–0.80*	–0.25	–0.24	0.82
Demands attention	*–0.55*	*–0.44*	–0.26	–0.06	0.56
Hot temper	–0.26	*–0.88*	–0.11	–0.08	0.86
Vocal tics	–0.16	–0.30	–0.17	*–0.53*	0.42
Obsessions	–0.17	–0.27	*–0.78*	–0.07	0.71
Inattention	*–0.70*	–0.18	–0.08	–0.18	0.56
Loud/talkative	*–0.73*	–0.20	–0.28	–0.26	0.72
Restless	*–0.70*	–0.28	–0.10	–0.27	0.65
Compulsions	–0.13	–0.23	*–0.86*	–0.33	0.91
Tense, anxious, nervous	*–0.54*	–0.04	–0.33	*–0.47*	0.62
Depressed or uninterested in most things	–0.32	–0.14	–0.22	*–0.47*	0.39
Impulsive	*–0.78*	–0.38	–0.08	–0.05	0.77
Variance explained %	34.21	32.76	18.77	14.11	
Eigenvalues	3.40	3.30	1.80	1.40	

NOTE: Numbers in italics indicate statistically significant correlation. TODS-PR = Tourette's Disorder Scale–Parent Rated; TODS-CR = Tourette's Disorder Scale–Clinician Rated; ADHD = attention deficit hyperactivity disorder; OCD = obsessive-compulsive disorder.

TABLE 7
Convergent Validity: Correlations of the Item and Total Scores on the TODS-CR With YGTSS, CPRS, and C/ASI-4

	Yale Global Tic Severity Scale (YGTSS)				*Conners Parent Rating Scale (CPRS)*						*Child/Adolescent Symptom Inventory (C/ASI-4)*		
TODS-CR Items	*Motor Tics*	*Phonic Tics*	*Overall Impairment*	*Global Severity*	*Conduct*	*Learning Problem*	*Psychosomatic*	*Impulsive*	*Anxiety*	*Hyperactivity*	*Obsessions*	*Compulsions*	*Depression*
Irritable					0.30		*0.40**						*0.52**
Motor tics	*0.47**	0.15	*0.42**	*0.43**	0.11	0.25	0.20	*0.43**	0.24	*0.37**	0.13	0.16	0.22
Argumentative					*0.45**								
Sudden mood changes					0.34		0.35						*0.61**
Demands attention					*0.46**			*0.55**		0.32			
Hot temper					*0.45**								
Vocal tics	*0.39**	*0.74**	*0.49**	*0.66**	0.21	0.11	0.12	0.26	*0.36**	*0.30**	0.28	0.31	*0.41**
Obsessions									*0.36**		*0.47**	*0.47**	
Difficulty paying attention						*0.48**		*0.57**		*0.61**			
Loud or talkative					0.28			*0.60**		*0.55**			
Restless or “hyper”					0.28			*0.70**		*0.62**			
Compulsions									*0.46**		*0.44**	*0.51**	
Tense, anxious, or nervous	0.23	0.24	*0.35**	*0.36**					*0.49**				
Depressed or Uninterested in most things					*0.44**		0.25		*0.39**				*0.60**
Impulsive					*0.39**			*0.66**		*0.63**			
TODS total score	*0.36**	*0.49**	*0.37**	*0.49**	*0.44**	0.27	0.24	*0.61**	*0.33**	*0.65**	0.33	0.29	*0.59**

NOTE: Numbers in italics indicate statistically significant correlation. TODS-CR = Tourette’s Disorder Scale–Clinician Rated.
Bonferroni corrected alphas: YGTSS = *$p < .003$, CPRS = *$p < .001$, and C/ASI-4 = *$p < .003$.

with the YGTSS Global Severity score ($r = .49$, $p < .005$). However, in support of divergent validity of the TODS, the TODS-CR total score was not correlated with psychosomatic and learning disorder subfactors of the CPRS.

The TODS-CR total score was correlated significantly ($p < .005$) with the Impulsive and Hyperactivity factors of the CPRS ($r = .61$ and $r = .65$, respectively). TODS-CR items associated with ADHD (i.e., "Difficulty paying attention," "Loud or talkative," "Restless or hyper," and "Impulsive") were correlated with similar symptom factors of the CPRS (e.g., Impulsive and Hyperactive). Furthermore, TODS-CR items "Tense, anxious, or nervous"; "Obsessions"; and "Compulsions" for the most part only correlated significantly with items of the CPRS Anxiety factor.

For the Child and Adolescent Symptom Inventory, TODS-CR items measuring "Obsessions" and "Compulsions" exhibited significant correlations with the "Obsessions" and "Compulsions" items measured on the Child and Adolescent Symptom Inventory. TODS-CR items "Sudden mood changes" and "Depressed or uninterested in most things" were strongly correlated ($r = .61$ and $r = .60$, $p < .005$) with the "Depression" item on the Child and Adolescent Symptom Inventory.

As shown in Table 8, correlations of the item, total, and factor subscores on the TODS-PR with scores on the YGTSS, the CPRS, and the C/ASI-4 were very similar to those found with the TODS-CR. Moreover, TODS-PR subfactors (Aggression, Obsessive/Compulsive, ADHD, and Tics) had significant correlations with matched items on the other measures.

Table 9 displays the correlations between the TODS-CR and TODS-PR total scores with total scores on the YGTSS, FIS, and Disability scales. Significant correlations were found between the total scores on the TODS and the YGTSS, FIS, and Disability scales. In contrast, the tic-specific measure, the YGTSS, had no significant correlation with the FIS, and the correlation with the Disability scale was lower for the YGTSS than for either of the TODS scales.

Table 10 shows the relationship between declines in school and social performance and total scores on the TODS scales and other scales. Of all of the measures employed, only the TODS-CR and the Depression Severity measure from the C/ASI were significantly correlated with measures of academic and social decline during the past 3 years.

Sensitivity to Change

As shown in Figure 2, for those participants who completed the trial, 18 were classified as responders (Week 8 Clinical Global Improvement [CGI] scores > 5) and 20 were classified as nonresponders (Week 8 CGI scores < 5). The sensitivity to change of the TODS-CR and YGTSS were analyzed by using a time-by-group analysis of variance (time: baseline, week 8; group: responder, nonresponder). For the TODS, both main effects and the interaction effect were statistically significant, group: $F(1, 36) = 11.2$, $p = .002$; time: $F(1, 36) = 26$, $p < .0001$; interaction: $F(1, 36) = 18.4$, $p = .0001$.

However, for the YGTSS, only the main effect of time and the interaction effect were statistically significant, group: $F(1, 36) = 1.9$, $p = 0.18$; time: $F(1, 36) = 50$, $p < .0001$; interaction: $F(1, 36) = 11.7$, $p = .002$. Classification of a participant as a responder or nonresponder does not necessarily mean that he or she responded to the study medication but rather that he or she demonstrated clinical improvement over time as defined by the CGI. Differences between active treatment and placebo are not reported here and have been published elsewhere.

DISCUSSION

The TODS is a 15-item, interview-based scale for assessing multidimensional symptom severity of TD. The results reported here indicate that the scale has acceptable interrater reliability and excellent internal consistency when administered by experienced clinicians. The findings also provide initial support for the concurrent and discriminant validity of the scale.

Although the total scores from both the TODS-CR and YGTSS were sensitive to clinically meaningful change at end point, the TODS-CR appeared to be superior at discriminating responders from nonresponders. The TODS-CR and PR also demonstrated higher correlations with measures of family impact and disability than did the YGTSS. Moreover, the TODS-CR and the Depression Severity measure from the C/ASI, but not the YGTSS, were significantly correlated with measures of academic and social decline during the past 3 years. Preliminary factor analyses of the TODS revealed a four-factor solution (Aggression, ADHD, OCD, and Tics) accounting for 99% of the variance.

Overall, these findings strongly support the hypothesis that tics are only partly responsible for overall impairment in Tourette's patients (Alsobrook & Pauls, 2002; Coffey, Biederman, Geller, et al., 2000; Kurlan et al., 2002) and that the TODS captures a broader range of symptoms that collectively play a larger role in illness severity for the child and his or her family.

TABLE 8
Convergent Validity: Correlations of the Item, Total, and Factor Subscores on the TODS-PR With YGTSS, CPRS, and C/ASI-4

	Yale Global Tic Severity Scale (YGTSS)				*Conners Parent Rating Scale (CPRS)*						*Child/Adolescent Symptom Inventory (C/ASI-4)*		
TODS-CR Items	*Motor Tics*	*Phonic Tics*	*Overall Impairment*	*Global Severity*	*Conduct*	*Learning Problem*	*Psychosomatic*	*Impulsive*	*Anxiety*	*Hyperactivity*	*Obsessions*	*Compulsions*	*Depression*
Irritable					0.30		0.26						*0.50**
Motor tics	*0.54**	0.20	*0.41**	*0.45**	0.10	0.23	0.15	0.31	0.26	0.32	0.12	0.09	0.27
Argumentative					*0.38**								
Sudden mood changes					*0.40**		0.31						*0.50**
Demands attention					*0.42**			*0.40**					
Hot temper					*0.42**								
Vocal tics	0.25	*0.59**	*0.47**	*0.56**	0.23	0.14	0.05	0.25	*0.35**	0.25	0.28	0.29	*0.48**
Obsessions											*0.42**	*0.50**	
Difficulty paying attention					*0.47**		*0.49**		*0.58**				
Loud or talkative					0.30			*0.57**		*0.57**			
Restless or “hyper”					0.34			*0.68**		*0.62**			
Compulsions									*0.26*		*0.39**	*0.45**	
Tense, anxious, or nervous	0.31	0.32	*0.39**	*0.42**					*0.49**				
Depressed or uninterested in most things			*0.53**		0.30		0.31				*0.52**		
Impulsive					0.33			*0.61**		*0.57**			
TODS total score	0.33	*0.51**	0.35	*0.47**	*0.44**	0.27	0.24	*0.89**	0.33	*0.65**	0.27	0.24	*0.55**
TODS factors													
Aggression					*0.44**		0.30						*0.54**
ADHD					*0.43**	*0.39**		*0.72**		*0.73**			
Obsessive/ Compulsive Tics	*0.45**	*0.54**	*0.51**	*0.64**					*0.43**		*0.41**	*0.49**	

NOTE: Numbers in italics indicate statistically significant correlation. TODS-PR = Tourette’s Disorder Scale–Parent Rated; ADHD = attention deficit hyperactivity disorder.
Bonferroni corrected alphas: YGTSS = *$p < .003$, CPRS = *$p < .001$, C/ASI-4 = *$p < .003$.

TABLE 9
Correlations of Total TODS Scores With Total Scores From Other Tourette Disorder Outcome Measures

Convergent Measures	*TODS-CR*	*TODS-PR*	*YGTSS*
YGTSS	*.49**	*.47**	
Disability Scale	*.62**	*.65**	*.40**
Family Impact Scale	*.50**	*.59**	.26

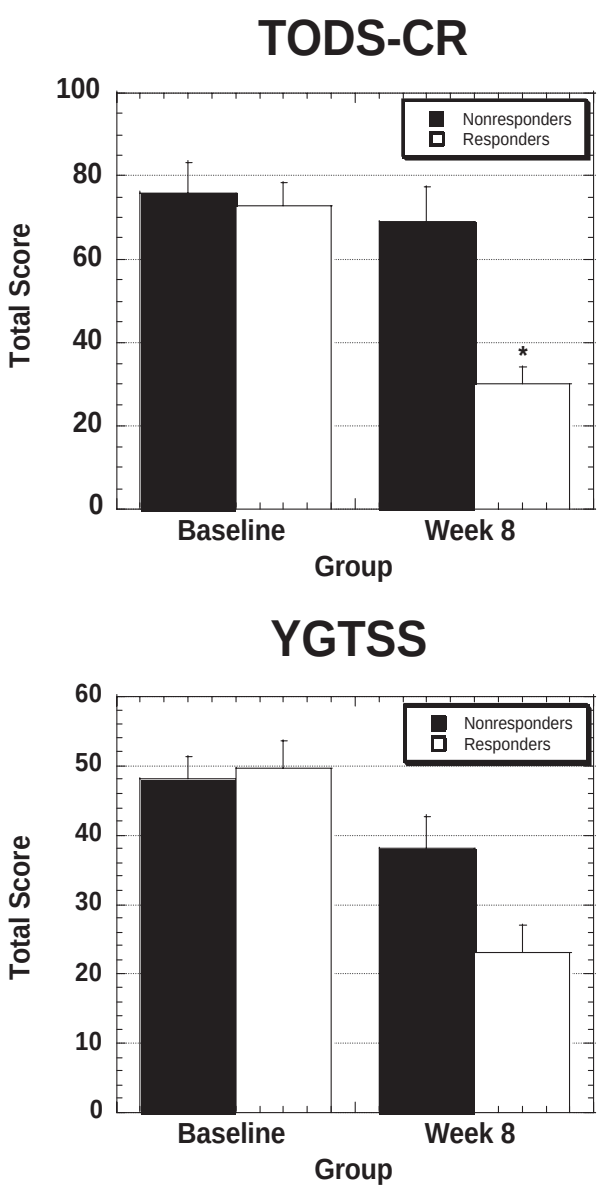
NOTE: Numbers in italics indicate statistically significant correlation. TODS-CR = Tourette's Disorder Scale–Clinician Rated; TODS-PR = Tourette's Disorder Scale–Parent Rated; YGTSS = Yale Global Tic Severity Scale.
Bonferroni corrected alpha: *$p < .006$.

TABLE 10
Relationship Between Academic/Social Function and Total Scores on the TODS and Other Scales

	Decline in Past 3 Years (USFPDI)	
N = *60*	*School Performance*	*Social Interactions*
TODS-CR	*–.39**	*–.33**
YGTSS	–.15	–.19
Depression (C/ASI)	*–.49**	*–.37**

NOTE: Numbers in italics indicate statistically significant correlation. TODS = Tourette's Disorder Scale; USFPDI = University of South Florida Personal Data Inventory; TODS-CR = Tourette's Disorder Scale–Clinician Rated; YGTSS = Yale Global Tic Severity Scale; Depression (C/ASI) = depression item from Child/Adolescent Symptom Inventory.
Bonferronni corrected alpha: *$p < .008$.

FIGURE 2
Sensitivity to Clinically Meaningful Change (CGI defined) Over Time (error bars = *SEM*) for Both the TODS-CR and YGTSS



NOTE: TODS-CR = Tourette's Disorder Scale–Clinician Rated; YGTSS = Yale Global Tic Severity Study; CGI = Clinical Global Improvement.
* Significant main effect for responder versus nonresponder.

Limitations

It should be noted that the high interrater reliability (r = .88) between parent (TODS-PR) and clinician (TODS-CR) ratings was likely confounded because each parent was questioned about their child's symptoms during the TODS-CR assessment.

Given the nature of the study group, the present results supporting the reliability, internal consistency, and validity of the TODS have to be regarded with caution. Specifically, the inclusion criteria for enrollment into the multicenter treatment study included (1) a predominance of behavioral and emotional symptom impairment over tic impairment, (2) a willingness to discontinue any preexisting medication regimens, and (3) a willingness to be randomly assigned to treatment conditions involving drug and placebo therapy. Accordingly, the study selection procedures would have been expected to impose a range restriction for some TD features. Although appropriate for a medication trial, the study selection procedures could have conceivably affected the psychometric behavior of some of the scale items being evaluated. To address this issue, TODS-PR scores from 99 TD patients who participated in a mail survey (TSA survey sample) were compared with the 60 TD patients used in the validation study (validation sample). The TODS-PR from the TSA survey sample was characterized with excellent internal consistency. Com-

parisons of item means revealed that the validation sample only had a significantly higher irritability score than the TSA survey sample. Moreover, a factor analysis of the TODS scores from the TSA survey sample yielded a four-factor solution with nearly identical item loading and structure as the factor analysis for the TODS-PR from the validation study. Furthermore, the proportions of participants who meet *DSM-IV* criteria for common psychiatric disorders (e.g. ADHD and OCD) associated with TD were similar to those reported previously in other study samples (Coffey & Park, 1997). Because the mean YGTSS score at baseline in this study was similar to that reported in other studies (Sallee et al., 2000), it appears that participants in this study had comparable levels of tic severity, despite the predominance of impairment caused by BESs. Therefore, the present sample appears to be adequate for the initial evaluation of the psychometric properties of the TODS. Nevertheless, future research should examine the psychometric properties of the TODS in more diverse groups of patients with TD.

Conclusions

It could be asked: Why use the TODS when TD severity can be assessed in other ways? Unfortunately, few controlled medication trials for Food and Drug Administration (FDA) approval have been conducted to investigate the efficacy of medication across the broad spectrum of TD symptoms in children and adolescents. A major obstacle to such studies is the lack of efficacy measures that adequately address the BESs of TD. To resolve this problem, investigators have in the past used scales developed for comorbid disorders in an effort to measure the BESs (Shytle et al., 1995). However, because these scales do not include measures of tic symptoms, they cannot be used as primary efficacy measures in controlled medication trials seeking FDA-approved indication for TD. Moreover, the practice of using different scales with different psychometric properties for such studies limits and further complicates interpretations regarding the relationship between various symptoms and their individual response to treatment. We believe the more pragmatic approach was to design a single scale that covers both tics and the key BESs that cause the greatest impairment for the patient and his or her family. This general rationale for treatment has been advocated by others in the field of child and adolescent psychopharmacological studies (Gadow, 1991).

It could be argued that individual items on the TODS simply measure symptoms of common comorbid disorders of TD (e.g., ADHD) and therefore do not reflect the true symptoms of TD. We take the position that the diagnostic boundaries of TD are still unclear and that it may take some time before the TD phenotype(s) is fully defined and characterized. What is clear from our findings and those from others is that for the majority of patients who seek medical treatment, the BESs cause as much or greater impairment than the tics themselves. This is consistent with recent symptom prevalence information from more than 3,500 TD patients worldwide, where only about 12% of patients suffer from tics alone (Freeman et al., 2000).

With the exception of Orap® and Haldol®, both approved many years ago for the treatment of tics only, no medications have been approved by the FDA for the treatment of TD. Thus, the physician is often faced with the risks of treating these patients with combinations of medications "off label" in order to treat the BESs.

The TODS provides a simple and efficient way to monitor TD's severity in patients in research and clinical settings for whom a diagnosis has been established. The TODS provides a convenient way for tracking progress over time, particularly for those patients who are being treated with multiple medications. Future employment of the TODS as a valid and sensitive measure of treatment effects in TD may open the door to identifying novel medications that are effective for more than one dimension of this neuropsychiatric disorder.

APPENDIX
Tourette's Disorder Scale (TODS)

Rated by:

Clinician Parent

IN THE PAST WEEK, how much has this patient been bothered by the following symptoms?

Not at all		*A little*			*Moderately*			*Markedly*		*Extremely*	
1	0	1	2	3	4	5	6	7	8	9	10	Irritable
2	0	1	2	3	4	5	6	7	8	9	10	Motor Tics
3	0	1	2	3	4	5	6	7	8	9	10	Argumentative
4	0	1	2	3	4	5	6	7	8	9	10	Sudden Mood Changes
5	0	1	2	3	4	5	6	7	8	9	10	Demands Attention
6	0	1	2	3	4	5	6	7	8	9	10	Hot Temper
7	0	1	2	3	4	5	6	7	8	9	10	Vocal Tics
8	0	1	2	3	4	5	6	7	8	9	10	Obsessions*
9	0	1	2	3	4	5	6	7	8	9	10	Inattention
10	0	1	2	3	4	5	6	7	8	9	10	Loud/talkative
11	0	1	2	3	4	5	6	7	8	9	10	Restless
12	0	1	2	3	4	5	6	7	8	9	10	Compulsions*
13	0	1	2	3	4	5	6	7	8	9	10	Tense, Anxious, Nervous
14	0	1	2	3	4	5	6	7	8	9	10	Depressed or uninterested in most things
15	0	1	2	3	4	5	6	7	8	9	10	Impulsive

Obsessions*

In the past week, has the patient been bothered by recurrent unwanted thoughts that kept coming into his/her mind that (s)he couldn't get rid of: like bad thoughts or urges; or nasty pictures? For example, did (s)he think about hurting somebody even though (s)he knew (s)he didn't want to? Was (s)he afraid (s)he or someone would get hurt because of some little thing (s)he did or didn't do? Was (s)he afraid that (s)he would do something really shocking? Does (s)he feel that things need to be "just right."

(NOTE: DO NOT INCLUDE SIMPLE EXCESSIVE WORRIES ABOUT REAL LIFE PROBLEMS. DO NOT INCLUDE OBSESSIONS DIRECTLY RELATED TO EATING DISORDERS, SEXUAL BEHAVIOR, OR ALCOHOL OR DRUG ABUSE BECAUSE THE PATIENT MAY DERIVE PLEASURE FROM THE ACTIVITY AND MAY WANT TO RESIST IT ONLY BECAUSE OF ITS NEGATIVE CONSEQUENCES)

Compulsions*

In the past week, has the patient performed tasks or certain acts over and over without being able to stop doing it, like checking, counting, touching, washing, or organizing things over and over; or saying or doing something over and over until it feels "just right."

REFERENCES

Alsobrook, J. P., II, & Pauls, D. L. (2002). A factor analysis of tic symptoms in Gilles de la Tourette's syndrome. *American Journal of Psychiatry, 159*(2), 291-296.

Berthier, M. L., Kulisevsky, J., & Campos, V. M. (1998). Bipolar disorder in adult patients with Tourette's syndrome: A clinical study. *Biological Psychiatry, 43*(5), 364-370.

Bland, J. M., & Altman, D. G. (1986). Statistical method for assessing agreement between two methods of clinical measurement. *The Lancet, 1*, 307-310.

Bonson, K. R., & Murphy, D. L. (1996). Alterations in responses to LSD in humans associated with chronic administration of tricyclic antidepressants, monoamine oxidase inhibitors or lithium. *Behavioural Brain Research, 73*(1-2), 229-233.

Budman, C. L., Bruun, R. D., Park, K. S., Lesser, M., & Olson, M. (2000). Explosive outbursts in children with Tourette's disorder [In Process Citation]. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*(10), 1270-1276.

Budman, C. L., Bruun, R. D., Park, K. S., & Olson, M. E. (1998a). Rage attacks in children and adolescents with Tourette's disorder: A pilot study. *Journal of Clinical Psychiatry, 59*(11), 576-580.

Budman, C. L., Bruun, R. D., Park, K. S., & Olson, M. E. (1998b). Rage attacks in children and adolescents with Tourette's disorder: A pilot study [In Process Citation]. *Journal of Clinical Psychiatry, 59*(11), 576-580.

Budman, C. L., Bruun, R. D., Park, K. S., & Olson, M. E. (in press). Rage attacks in children and adolescents with Tourette syndrome: A pilot study. *Journal of Clinical Psychiatry.*

Coffey, B., Frazier, J., & Chen, S. (1992). Comorbidity, tourette syndrome, and anxiety disorders. *Advances in Neurology, 58*, 95-104.

Coffey, B. J., Biederman, J., Geller, D. A., Spencer, T. J., Kim, G. S., Bellordre, C. A., et al. (2000). Distinguishing illness severity from tic severity in children and adolescents with Tourette's disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*(5), 556-561.

Coffey, B. J., Biederman, J., Smoller, J. W., Geller, D. A., Sarin, P., Schwartz, S., et al. (2000). Anxiety disorders and tic severity in juve-

niles with Tourette's disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*(5), 562-568.

Coffey, B. J., Miguel, E. C., Savage, C. R., & Rauch, S. L. (1994). Tourette's disorder and related problems: A review and update. *Harvard Review of Psychiatry, 2*(3), 121-132.

Coffey, B. J., & Park, K. S. (1997). Behavioral and emotional aspects of Tourette syndrome. *Neurologic Clinics, 15*(2), 277-289.

Comings, D. E. (1994). Tourette syndrome: A hereditary neuropsychiatric spectrum disorder. *Annals of Clinical Psychiatry, 6*(4), 235-247.

Comings, D. E., & Comings, B. G. (1990a). A controlled family history study of Tourette's syndrome, I: Attention-deficit hyperactivity disorder and learning disorders. *Journal of Clinical Psychiatry, 51*(7), 275-280.

Comings, D. E., & Comings, B. G. (1990b). A controlled family history study of Tourette's syndrome, III: Affective and other disorders. *Journal of Clinical Psychiatry, 51*(7), 288-291.

Dooley, J. M., Brna, P. M., & Gordon, K. E. (1999). Parent perceptions of symptom severity in Tourette's syndrome. *Archives of Disease in Childhood, 81*(5), 440-441.

Elstner, K., Selai, C. E., Trimble, M. R., & Robertson, M. M. (2001). Quality of Life (QOL) of patients with Gilles de la Tourette's syndrome. *Acta Psychiatrica Scandinavica, 103*(1), 52-59.

Freeman, R. D., Fast, D. K., Burd, L., Kerbeshian, J., Robertson, M. M., & Sandor, P. (2000). An international perspective on Tourette syndrome: Selected findings from 3,500 individuals in 22 countries [In Process Citation]. *Developmental Medicine and Child Neurolology, 42*(7), 436-447.

Gadow, K. D. (1991). Clinical issues in child and adolescent psychopharmacology. *Journal of Consulting and Clinical Psychology, 59*(6), 842-852.

Gadow, K. D., & Sprafkin, J. (1997). *Child and Adolescent Symptom Inventory 4: Norms manuals*. Stony Brook , NY: Checkmate Plus.

Goyette, C. H., Conners, C. K., & Ulrich, R. F. (1978). Normative data on revised Conners Parent and Teacher Rating Scales. *Journal of Abnormal Child Psychology, 6*(2), 221-236.

Kurlan, R., Como, P. G., Miller, B., Palumbo, D., Deeley, C., Andresen, E. M., et al. (2002). The behavioral spectrum of tic disorders: A community-based study. *Neurology, 59*(3), 414-420.

Leckman, J. F., Riddle, M. A., Hardin, M. T., Ort, S. I., Swartz, K. L., Stevenson, J., et al. (1989). The Yale Global Tic Severity Scale: Initial testing of a clinician-rated scale of tic severity. *Journal of the American Academy of Child and Adolescent Psychiatry, 28*(4), 566-573.

Leon, A. C., Olfson, M., Portera, L., Farber, L., & Sheehan, D. V. (1997). Assessing psychiatric impairment in primary care with the Sheehan Disability Scale. *International Journal of Psychiatry in Medicine, 27*(2), 93-105.

Nolan, E. E., Sverd, J., Gadow, K. D., Sprafkin, J., & Ezor, S. N. (1996). Associated psychopathology in children with both ADHD and chronic tic disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 35*(12), 1622-1630.

Pauls, D. L., Towbin, K. E., Leckman, J. F., Zahner, G. E., & Cohen, D. J. (1986). Gilles de la Tourette's syndrome and obsessive-compulsive disorder. Evidence supporting a genetic relationship. *Archives of General Psychiatry, 43*(12), 1180-1182.

Riddle, M. A., Hardin, M. T., Ort, S. I., Leckman, J. F., & Cohen, D. J. (1988). Behavioral symptoms in Tourette's syndrome. In D. J. Cohen, R. D. Bruun, & J. F. Leckman (Eds.), *Tourette's syndrome and tic disorders: Clinical understanding and treatment* (pp. 151-162). New York: John Wiley.

Robertson, M. M. (2000). Tourette syndrome, associated conditions and the complexities of treatment. *Brain, 123*, 425-462.

Sallee, F. R., Kurlan, R., Goetz, C. G., Singer, H., Scahill, L., Law, G., et al. (2000). Ziprasidone treatment of children and adolescents with Tourette's syndrome: A pilot study. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*(3), 292-299.

Shapiro, E. S., Shapiro, A. K., Fulop, G., Hubbard, M., Mandeli, J., Nordie, J., et al. (1989). Controlled study of haloperidol, pimozide, and placebo for the treatment of Gilles de la Tourette's syndrome. *Archives of General Psychiatry, 46*, 722-730.

Sheehan, D., Shytle, R., Newman, M., Sanberg, P., & Silver, A. (1999, July). *Development of the Tourette Disorder Scale (TODS)*. Paper presented at the 39th annual meeting of the New Clinical Drug Evaluation Unit Program (NCDEU), Boca Raton, Fl.

Sheehan, D. V., Harnett-Sheehan, K., & Raj, B. A. (1996). The measurement of disability. *International Clinical Psychopharmacology, 11*(Suppl. 3), 89-95.

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., et al. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and ICD-10. *Journal of Clinical Psychiatry, 59*(Suppl. 20), 22-33, quiz 34-57.

Shytle, R. D., Silver, A. A., & Sanberg, P. R. (1995). Clinical assessment of motor abnormalities in Tourette's syndrome. In P. R. Sanberg, K. P. Ossenkopp, & M. Kavaliers (Eds.), *Motor activity and movement disorders: Research issues and applications* (pp. 343-364). Totowa, NJ: Humana.

Silver, A. A., Shytle, R. D., Sheehan, K. H., Sheehan, D. V., Ramos, A., & Sanberg, P. R. (2001). Multi-center double blind placebo controlled study of mecamylamine monotherapy for Tourette's disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*(9), 1103-1110.

Singer, H. S., & Rosenberg, L. A. (1989a). Development of behavioral and emotional problems in Tourette syndrome. *Pediatric Neurology, 5*(1), 41-44.

Singer, H. S., & Rosenberg, L. A. (1989b). Development of behavioral and emotional problems in Tourette syndrome. *Pediatric Neurology, 5*(1), 41-44.

Spencer, T., Biederman, J., Harding, M., O'Donnell, D., Wilens, T., Faraone, S., et al. (1998). Disentangling the overlap between Tourette's disorder and ADHD. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 39*(7), 1037-1044.

Stefl, M. E., Bornstein, R. A., & Hammond, L. (1988). *A survey of Tourette syndrome patients and their families: The 1987 Ohio Tourette Survey*. Cincinnati: Ohio Tourette Syndrome Association.

Stephens, R. J., & Sandor, P. (1999). Aggressive behaviour in children with Tourette syndrome and comorbid attention-deficit hyperactivity disorder and obsessive-compulsive disorder. *Canadian Journal of Psychiatry, 44*(10), 1036-1042.

Stokes, A., Bawden, H. N., Camfield, P. R., Backman, J. E., & Dooley, J. M. (1991). Peer problems in Tourette's disorder. *Pediatrics, 87*(6), 936-942.

Wand, R. R., Matazow, G. S., Shady, G. A., Furer, P., & Staley, D. (1993). Tourette syndrome: Associated symptoms and most disabling features. *Neuroscience and Behavioral Reviews, 17*, 271-275.

Wilkinson, B., Newman, M., Shytle, R., Silver, A., Sheehan, D., & Sanberg, P. (2000). Family Impact of Tourette's syndrome. *Journal of Child and Family Studies, 10*(4), 477-483.

Wodrich, D. L., Benjamin, E., & Lachar, D. (1997). Tourette's syndrome and psychopathology in a child psychiatry setting. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*(11), 1618-1624.

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