Rage Attacks and Aggressive Symptoms in Japanese Adolescents with Tourette Syndrome

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ABSTRACT

Objective: This study was conducted to explore possible causes of rage attacks as well as clinically significant aggressive symptoms in Japanese adolescents with Tourette syndrome (TS).

Methods: The subjects included 29 adolescents (23 males, 6 females; mean age: 13.5±3.7 years). Eighteen subjects (62.1%) were diagnosed with TS only, 11 (37.9%) with TS and comorbidities, including attention-deficit/hyperactivity disorder and obsessive-compulsive disorder. Parents completed the Child Behavior Checklist. Clinically significant aggressive symptoms were assessed using two pilot tools, the Rage Screen and Questionnaire and the Clinical Rating of Aggression.

Results: Thirteen subjects (44.8%) were judged to have clinically significant aggressive symptoms, according to the Clinical Rating of Aggression. Twelve met criteria for recurrent rage attacks, according to the Rage Screen and Questionnaire. Between the 13 aggressive and 16 non-aggressive subjects, no significant differences were found in age, gender, psychiatric comorbidities, or concurrent medication. Child Behavior Checklist ratings to compare 11 aggressive and 12 non-aggressive subjects ≤16 years of age revealed elevated *t*-test scores on the anx-

Needs Assessment

Tourette syndrome (TS) is a neuropsychiatric disorder of childhood onset characterized by multiple motor and vocal tics that wax and wane in severity. Recurrent explosive outbursts ("rage attacks") and other aggressive symptoms in TS are a leading cause of morbidity for patients and their families. It seems that such symptoms are often secondary to comorbid psychiatric disorders in TS. There is a need to better recognize, characterize, and properly treat aggression in TS.

Learning Objectives

At the end of this activity, the participant should be able to:

- Identify explosive outbursts as a common symptom of impulsive aggression that occurs among clinical populations of children with Tourette syndrome (TS) worldwide.
- Recognize certain types of internalizing and externalizing behaviors that seem associated with explosive outbursts in Japanese adolescents with TS.
- Recognize that explosive outbursts and related behaviors as well as tics should be considered in treatment for TS.

Target Audience: Neurologists and psychiatrists

CME Accreditation Statement

This activity has been planned and implemented in accordance with the Essentials and Standards of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Mount Sinai School of Medicine and MBL Communications, Inc. The Mount Sinai School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

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This activity has been peer-reviewed and approved by Eric Hollander, MD, chair at the Mount Sinai School of Medicine. Review date: March 17, 2008. Dr. Hollander does not have an affiliation with or financial interest in any organization that might pose a conflict of interest.

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ious/depressed, thought problems, aggressive, internalizing, externalizing subscales, and total scale in the aggressive group versus the non-aggressive group.

Conclusion: Rage attacks and clinically significant aggressive symptoms are common problems in Japanese TS youth. Psychiatric morbidity appears associated with impulsive-aggressive symptoms. Treatment implications from these findings need to be explored further.

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INTRODUCTION

Tourette syndrome (TS) is defined as a chronic tic disorder with multiple motor tics and one or more vocal tics. TS has a high prevalence of psychiatric comorbidities, including obsessive-compulsive disorder (OCD), and attention-deficit/hyperactivity disorder (ADHD), and mood disorders.[1] "Rage attacks" or "recurrent explosive outbursts" are a type of impulsive-aggressive symptom that is common in TS and often contributes to social morbidity. Rage attacks are defined using modifications of the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition-Text Revision*[2] criteria for intermittent explosive disorder. Discrete episodes of failure to resist aggressive impulses that result in serious assaultive acts or destruction of property, with a degree of aggressiveness expressed during the episodes that is grossly out of proportion to any precipitating psychosocial stressors, qualify as rage attacks.[2-4]

Previous studies[3-5] have suggested that rage attacks in children with TS are associated with the presence of comorbid disorders, namely ADHD, OCD, and oppositional defiant disorder. One study of aggression in children with TS,[6] using the Child Behavior Checklist (CBCL), reported that the group with TS and comorbid ADHD or OCD was significantly more aggressive than the control group, but there were no differences in aggression between the TS-only and control groups.[7]

The current investigation was conducted to clarify the possible conditions associated with both clinically significant aggression and the specific type of impulsive aggression defined as "rage attacks" in Japanese youth with TS. Differences in clinical symptomatology and psychotropic medication usage between Japanese adolescents with TS who display these impulsive-aggressive symptoms and those without were compared.

METHODS

Adolescents diagnosed with TS were consecutively recruited as subjects for study from two Japanese specialty neuropsychiatric clinics. The assessment battery was used as a part of standard clinical evaluation. All subjects and their parents provided written informed consent for participation in the study and all study subjects provided oral or written assent. Patients with neurologic disorders or other known causes of aggression or who had experienced a change in psychotropic medication within 4 weeks were excluded from the study.

The study population consisted of 29 patients (23 males, 6 females; mean age: 13.5±3.7 years, range: 8–21 years of age) diagnosed with TS by two experienced child psychiatrists (YK, MO), according to *DSM-IV-TR* criteria.[2] Eighteen patients (62.1%) were diagnosed with TS only and 11 patients (37.9%) with TS and comorbid disorders. Of these, 11 patients with TS and psychiatric comorbidities; five patients (17.2%) with TS and ADHD; another five (17.2%) with TS and OCD; and one (3.4%) with TS, ADHD, and learning disorders (Table 1).

Data regarding clinical characteristics related to tics, including age of tic onset, type and severity of each tic symptom, as well as obsessive-compulsive symptoms, self-injurious behaviors, and impulsivity, was collected through clinical interviews with the patients and their parents by the two child psychiatrists (YK, MO) as well as from data obtained in patient medical records. Information concerning psychotropics was provided by treating physicians. Diagnoses of OCD, ADHD, or other psychiatric comorbidities were established based on clinical assessment and chart review using *DSM-IV-TR* criteria.

Two surveys, the Clinical Rating of Aggression (CRA) (Y. Kano, MD, PhD, and M. Ohta, MD, PhD, unpublished rating scale, 2002) and the Rage Screen and Questionnaire (RSQ),[4] were used for the screening and evaluation of impulsive aggression to assess current and past rage attacks.

The RSQ explores the presence of clinically significant rage attacks that have occurred in the

past week to month prior to evaluation. Rage symptoms must meet a designated threshold for frequency (ie, minimum of 3 episodes per week or ≥4 episodes during a 1-month period of time) and intensity (ie, degree of aggressiveness expressed during the episodes are grossly out of proportion to any precipitating psychosocial stressors or frustration) to be considered present. Although not yet validated, the RSQ was translated into Japanese for the purpose of studying rage phenomenology in Japanese youth with TS with the authors' permission.[4] The rage screen portion was adapted to also assess the presence of clinically significant recurrent rage attacks in the past 6 months, provided that there was at least one period of ≥3 episodes per week or a minimum of 4 episodes per month during this time period.

The rage questionnaire portion explores possible clinical features that are associated with rage symptoms in children and adults with TS.

The CRA was developed by Kano and Ohta to specifically assess clinically significant impulsive aggression phenomenology that occurred within the 1 month prior to initial consultation. The CRA is being used as a global assessment of impact of physically and verbally aggressive behaviors toward other individuals and property and focuses on impairment of daily life. It consists of a Likert scale, with scores ranging from 1 (none) to 5 (most severe):

1. None: No aggression or, if any, impairment of social adjustment;
2. Mild: A certain degree of aggression but not particularly noticeable, and slight impairment in some areas of daily life, such as family, school, and peer relationship;
3. Moderate: Slightly noticeable aggression affecting ≥1 areas of daily life (periodic distress and upheaval in the family, frequent teasing by peers or social avoidance, periodic interference in school);
4. Severe: Conspicuous aggression causing serious impairment of daily activities, including family life, school life, and peer relationship;
5. Most Severe: Extremely conspicuous aggression, making daily life very difficult.

The potential usefulness of the CRA was explored in this study to help acquire data regarding the clinical phenomenology of impulsive-aggressive symptoms in TS. However, the validity and reliability of neither the RSQ nor the CRA has been confirmed. Two experienced clinicians (YK, OH) had reached a high proficiency with RSQ and CRA ratings.

To assess a wide range of mental and behavioral problems in this study sample, the CBCL was completed by the subject's parents.[6] *t*-test scores of CBCL were calculated for subjects ≥16 years of age who completed this measure.

The Global Assessment of Functioning,[2] a standardized measure, was used to assess overall current social adjustment.

Overall tic severity was evaluated using the tic global severity rating of the Shapiro Tourette Syndrome Severity Scale (STSSS),[8] a 7-point rating scale of tic severity ranging from 0 (no tics) to 6 (extremely severe).

Statistical analysis used χ^2 test, Fisher's exact test, non-paired *t*-test, and Mann-Whitney test. Statistical significance was considered at $P<.05$.

TABLE 1.
Demographic Findings and Diagnoses in Aggressive and Non-aggressive Japanese Youth with TS

	Aggressive Group (n=13)	*Non-aggressive Group (n=16)*
Gender ratio (M:F)	10:3	13:3
Mean age (years)	13.5±3.4	13.4±4.1
TS only	7 (53.8%)	11 (68.8%)
TS+ADHD	3 (23.1%)	2 (12.5%)
TS+OCD	2 (15.4%)	3 (18.8%)
TS+ADHD+LD	1 (7.7%)	0 (0%)
CBCL data available	11	12

TS=Tourette syndrome; M=male; F=female; ADHD=attention-deficit/hyperactivity disorder; OCD=obsessive-compulsive disorder; LD=learning disorder; CBCL=Child Behavior Checklist.

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RESULTS

Global-behavioral Problems and Social Adjustment

To determine global-behavioral problems related to impulsive-aggressive symptoms, the CRA was first used to determine clinically significant aggression that causes distress and impairment that the clinician, patient, and/or family

view as worthy of intervention in 23 patients with available CBCL data. Eleven (47.8%) subjects were found to have clinically significant aggression and 12 (52.2%) did not. Both groups were then assessed by CBCL in order to compare long-term psychiatric morbidities associated with clinically significant impulsive-aggressive symptoms. *t*-test scores were then computed for both groups for the anxious/depressed, thought problems, aggression, internalizing, externalizing, and total problems subscales (Table 2). Scores were significantly higher in the aggressive group than in the non-aggressive group (*P*=.003, *P*=.002, *P*=.020, *P*=.031, *P*=.031, *P*=.013, respectively, *t*-test).

The Global Assessment of Functioning scores were lower in the aggressive group (mean: 49.7±8.2) than in the non-aggressive group (mean: 55.0±7.7), although this finding did not meet statistical significance (*P*=0.083, *t*-test).

Characteristics of Tourette Syndrome Patients Who Have Had Clinically Significant Rage Attacks in the Past Six Months

Using the RSQ to explore the clinical features and phenomenology of rage attacks over the past 6 months, it was found that of the 19 TS patients who were reported to have had recurrent rage attacks within the past 6 months, 14 (73.7%) felt guilty about their behaviors or regretted their actions afterward, of whom 6 (31.6%) always had a guilty conscience.

Sixteen patients (84.2%) reported verbal attacks or abuse during outbursts of anger, 14 (73.7%) physically attacked other people and/or property, and 12 (63.2%) had both verbal and physical attacks. Eighteen patients (94.7%) reported having attacks at home, followed by four (21.1%) patients having attacks at school, and three (15.8%) patients experiencing attacks at home and at school. Seventeen patients (89.5%) out of 19 directed the attacks toward their mothers, followed by 13 (68.4%) toward inanimate objects (Table 3). Eighteen (94.7%) claimed that their anger was precipitated by being told that they were wrong about something, followed by 15 (78.9%) when they felt they failed to have their way.

Characteristics of Tourette Syndrome Patients Who Have Had Clinically Significant Aggressive Symptoms in the Past Month

Two experienced child psychiatrists rated overall aggressive symptoms in these TS patients according to the guidelines for the CRA. They found 16 TS patients (55.2%) with no signs of aggression, 6 (20.7%) as mildly aggressive, and 7 (24.1%) as moderately aggressive, for a total of 13 (44.8%) aggressive subjects. Across all subjects, there were no significant differences in age, gender, or diagnoses (Table 1).

Of the 13 patients with clinical symptoms of aggression over the past 1 month prior to

TABLE 2.
CBCL Subscores in Aggressive and Non-aggressive Japanese Youths with TS

Scales	*Aggressive Group (n=11)*	*Non-aggressive Group (n=12)*	t	P
I. Withdrawn	59.5±10.1	56.0±5.5	–1.002	.332
II. Somatic	58.5±8.5	56.6±7.8	–0.551	.587
III. Anxious/Depressed	68.9±9.2	57.8±6.9	–3.321	.003
IV. Social	61.2±7.4	56.9±6.2	–1.501	.148
V. Thought	72.4±10.1	57.3±9.9	–3.596	.002
VI. Attention	65.5±9.9	61.2±6.9	–1.210	.240
VII. Delinquent	65.6±8.8	58.3±9.2	–1.963	.063
VIII. Aggressive	68.5±9.0	59.2±8.7	–2.318	.020
IX. Internal	66.6±10.9	58.1±6.1	–2.320	.031
X. External	69.2±9.6	58.3±10.6	–2.706	.013
Total CBCL Score	70.6±10.4	60.1±8.2	–2.716	.013

CBCL=Child Behavior Checklist; TS=Tourette syndrome.

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entry, 12 (92.3%) experienced symptoms that met RSQ criteria for rage attacks (Table 4). The parents of the remaining patient failed to report symptoms severe enough to meet required RSQ criteria for rage attacks, but described impulsive-aggressive symptoms that were judged to be clinically significant according to the CRA. Seven (43.8%) out of 16 without aggression also reported to have had at least one rage attack in the past 6 months but did not meet frequency or impairment criteria for clinically significant aggression. Additionally, seven patients (53.8%) out of 13 with aggression and none (0%) out from the non-aggressive group were reported to have had rage attacks within the week prior to assessment, indicating a significant difference between the two groups (P=.005, Fisher's exact test). This suggests that the presence and frequency of rage attacks within the past week may be the most meaningful criterion for distinguishing patients with significant impairment due to aggression from those without.

There were no significant differences between subjects in the mean age at onset of tics, coprolalia, and obsessive-compulsive symptoms between the TS patients with aggression and those without (Table 5). However, a significant difference (P=.011, Fisher's exact test) was noted between the two groups with respect to self-injurious behaviors, which were observed only in the aggressive group. Both the worst and current levels of tic severity were higher in the aggressive group than in non-aggressive group, although these findings did not meet statistical significance (P=.068, P=.092, Mann-Whitney test).

Of the 29 total subjects, 19 were taking psychotropics. Haloperidol was the most common and was being taken by 10 subjects. Seven subjects were on pimozide, six were on fluvoxamine, and three were on risperidone (Table 6). There were no statistically significant differences in presence, absence, or type of concomitant psychotropics between the aggressive group and the non-aggressive group.

TABLE 3.
Targets and Precipitants of Attacks

	Respondents (N=19)
Targets of Attacks	
Mother	17 (89.5%)
Objects/things	13 (68.4%)
Siblings	11 (58.9%)
Father	10 (52.6%)
Precipitants of Attacks	
Told they were wrong about something	18 (94.7%)
Failure to get their way	15 (78.9%)
Change in routine or schedule	14 (73.7%)
Felt sense of frustration	11 (58.9%)
Told to give up on a task	10 (52.6%)
Felt imperfection	8 (42.1%)
Had a possession taken away	7 (36.8%)

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Comparison of Rage Attacks and Aggression Among Three Groups by Diagnoses

Rage attacks, aggression, and related symptoms were compared among three groups (ie, TS only, TS+ADHD, and TS+OCD). *t*-test scores of withdrawn, attention, and total problems subscales in CBCL and the rates of obsessive-compulsive symptoms and self-injurious behaviors were significantly different among the three groups. However, no significant differences were found in rage attacks rated by RSQ and aggression rated by CRA.

DISCUSSION

The findings from this naturalistic study suggest that in this particular sample of TS patients represented at a Japanese specialty clinic, rage attacks appear to occur rather commonly. TS patients with rage attacks in this sample seemed to have more psychiatric comorbidity than TS patients without such symptoms, but the difference between these two groups was smaller than expected based on earlier reports.[3]

Tic severity and self-injurious behaviors appeared associated with clinically significant aggressive symptoms in TS. This finding in our current study is in agreement with recent studies[9] that correlated self-injurious behaviors and tic severity with the presence of episodic explosive outbursts/rage attacks.

Data from the RSQ which was translated into Japanese revealed that the majority of subjects with rage attacks targeted their anger at their mothers. Rage attacks were also found to occur

at home far more frequently than at school. In our current study, "teasing and embarrassment," "no reason at all," and "having to compete with others for attention" were reported as precipitants of rage attacks in ≤20% responses.

As expected, the aggression subscale score of the CBCL was significantly higher in the clinically significant impulsive-aggressive TS group. However, subscales for anxiety/depression and thought problems on the CBCL also reached pathological levels that were significantly higher for the clinically aggressive TS group than in the non-aggressive TS group.

This is a descriptive study of aggressive symptoms studied in a small sample of Japanese youth with TS who presented for treatment at a speciality clinic. Our findings are limited by the primarily naturalistic, descriptive nature of the assessment tools that relied mostly on both child and parent reports, since it is uncommon for rage attack symptoms to be witnessed in the clinician's office. The findings from this study are also compromised by potential referral bias, since it was conducted at a specialty psychiatric clinic and its findings may not be generalizable to TS patients in the community. The data exam-

TABLE 4.
Relationship Between RSQ and CRA

	Aggressive Group (n=13)	*Non-aggressive Group (n=16)*	P
≥1 rage attacks in the past 6 months	12 (92.3%)	7 (43.8%)	.073
≥1 rage attacks within 1 week	7 (53.8%)	0 (0%)	.005

RSQ=Rage Screen and Questionnaire; CRA=Clinical Rating of Aggression.

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TABLE 5.
Clinical Phenomenology in Aggressive and Non-aggressive Japanese Youth with TS

	Aggressive Group (n=13)	*Non-aggressive Group (n=16)*	P
Mean age at onset of tics (years)	6.1±2.3	6.4±2.5	.721
Mean age at first visit (years)	13.0±3.3	12.1±3.5	.466
Coprolalia	5 (38.5%)	5 (31.3%)	.684
OCS	5 (38.5%)	6 (37.5%)	.958
Self-injurious behaviors	5 (38.5%)	0 (0%)	.011
Worst ever STSSS rating			.068
2	0 (0%)	1 (6.3%)	
3	2 (15.4%)	7 (43.8%)	
4	5 (38.5%)	4 (25.0%)	
5	4 (30.8%)	3 (18.8%)	
6	2 (15.4%)	1 (6.3%)	
Current STSSS rating			.092
1	0 (0%)	2 (12.5%)	
2	3 (23.1%)	6 (31.3%)	
3	5 (38.5%)	7 (43.8%)	
4	3 (23.1%)	2 (12.5%)	
5	2 (15.4%)	0 (0%)	

TS=Tourette syndrome; OCS=obsessive-compulsive symptoms; STSSS=Shapiro Tourette Syndrome Severity Scale.

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ining potential differences in current comorbidities between the two groups must be viewed with caution since this is a relatively small, uncontrolled sample of patients and the psychiatric diagnoses were not established using standardized structured measures but instead relied on clinical assessments using *DSM-IV-TR* criteria. In addition, this sample reflected youth with TS whose overall symptoms were of sufficient severity to require specialty assessment and intervention.

While there appeared to be evidence supporting the impression that frequency (rather than impairment in daily life) of rage attacks may be the most significant clinical characteristic to distinguish clinically meaningful impulsive-aggressive symptoms in TS from those that are not, the results of this small, uncontrolled pilot study must be viewed as suggestive and further follow-up studies are necessary. The small sample size in this study may be related to some difference between our findings and previous North American studies.[3,4,6,10,11] In addition, there seem to be less recognition and treatment of TS and its psychiatric comorbidities in Japan, although this is improving.

Although none of the subjects in the study met *DSM-IV-TR* criteria for an anxiety or mood disorder, anxious and depressive symptoms were found to be closely associated with clinically significant aggressive symptoms on CBCL. This is of interest, since aggressive behavior is frequently observed in adolescents with major depression, regardless of gender.[12] Other investigators have pointed out that boys with aggression and ADHD develop depressive symptoms more frequently and have lower self-esteem than those without aggressive symptoms,[13] again emphasizing the possible association between depression and aggression. It would be important to attempt to study rage and other aggressive symptoms in Japanese youth with TS by using structured validated interviews and measures, such as the Kiddie-Schedule for Affective Disorders and Schizophrenia,[14] that can better evaluate current and lifetime mood and anxiety disorders. Although no significant difference was found in the rates of OCD and obsessive-compulsive symptoms between aggression and non-aggression groups, precipitants of rage attacks suggested close relationship to obsessive-compulsive symptoms. Obsessive-compulsive symptoms should be assessed more precisely using formal, standardized rating scales and then examined in Japanese TS youth with and without aggression in future studies.

This study highlights the common problem of significant impulsive-aggressive symptoms, including rage attacks, in youth with TS who present for treatment at a specialty clinic in Japan and contributes to the growing body of literature that suggests that aggressive symptoms in TS are considerable causes of morbidity in this population worldwide. The phenomenology of aggressive symptoms in TS, their clinical correlates, and potential diagnostic and treatment strategies requires further attention.

TABLE 6.
Medication Status in Aggressive and Non-aggressive Japanese Youth with TS

Medication	*Aggressive Group (n=13)*	*Non-aggressive Group (n=16)*
Receiving any psychotropic medication	10 (76.9%)	9 (56.3%)
Antipsychotics	9 (69.2%)	9 (56.3%)
Haloperidol	6 (46.1%)	4 (25%)
Pimozide	4 (30.8%)	3 (18.8%)
Risperidone	0 (0%)	3 (18.8%)
SSRIs	4 (30.8%)	4 (25%)
Fluvoxamine	3 (23.1%)	3 (18.8%)
Paroxetine	1 (7.7%)	1 (6.3%)
Clomipramine	0 (0%)	1 (6.3%)
Clonidine	1 (7.7%)	1 (6.3%)

TS=Tourette syndrome; SSRIs=selective serotonin reuptake inhibitors.

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CONCLUSION

In Japanese TS adolescents, no significant differences were found in age, gender, or comorbidities by the presence or absence of aggression within 1 month of clinical identification by experienced child psychiatrists. Tic severity and self-injurious behaviors appeared associated with clinical significant aggression. When global behavioral problems were evaluated by CBCL, *t*-test scores of anxious/depressed, thought problems and aggression were significantly higher in aggressive subjects than in non-aggressive subjects.

This study suggested that aggression was associated with psychiatric symptoms, especially anxiety and depression, in Japanese adolescents with TS. Relationship among these symptoms should be confirmed by more rigorous methods. ***CNS***

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