Prevalence and clinical correlates of explosive outbursts in Tourette Syndrome

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ABSTRACT

The aim of this study was to examine the prevalence and clinical correlates of explosive outbursts in two large samples of individuals with Tourette Syndrome (TS), including one collected primarily from non-clinical sources. Participants included 218 TS-affected individuals who were part of a genetic study (N=104 from Costa Rica (CR) and N=114 from the US). The relationships between explosive outbursts and comorbid attention deficit hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), tic severity, and prenatal and perinatal complications were examined using regression analyses. Twenty percent of participants had explosive outbursts, with no significant differences in prevalence between the CR (non-clinical) and the US (primarily clinical) samples. In the overall sample, ADHD, greater tic severity, and lower age of tic onset were strongly associated with explosive outbursts. ADHD, prenatal exposure to tobacco, and male gender were significantly associated with explosive outbursts in the US sample. Lower age of onset and greater severity of tics were significantly associated with explosive outbursts in the CR sample. This study confirms previous studies that suggest that clinically significant explosive outbursts are common in TS and associated with ADHD and tic severity. An additional potential risk factor, prenatal exposure to tobacco, was also identified.

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1. Introduction

Explosive outbursts (also referred to as “rage attacks”) are sudden, dramatic, repetitive episodes of verbal and/or physical aggression that are developmentally age-inappropriate and disproportionate to the putative trigger (Budman et al., 1998). These symptoms can be classified under the DSM-IV-TR diagnostic category of intermittent explosive disorder (IED) as an independent disorder, but have also been described in a variety of neuropsychiatric conditions, including obsessive-compulsive disorder (OCD), mood disorders, non-OCD anxiety disorders, and disruptive behavioral disorders such as oppositional defiant disorder (American Psychiatric Association, 1994; Kessler et al., 2006; Storch et al., 2012). Data from the National Comorbidity Survey Replication Adolescent Supplement indicated that two-thirds of adolescents experience significant anger attacks; of these, 7.8% met DSM-IV criteria for lifetime IED. In this study, 6.2% of all adolescent respondents met 12-month criteria for IED with a mean age of onset at 12 years (McLaughlin et al., 2012).

According to the NCS, 81% of participants with explosive outbursts in the general population have been diagnosed with at least one other DSM-IV disorder, most commonly mood disorders (37.4%), anxiety disorders (58.1%), impulse control disorders (44.9%), and substance abuse disorders (35.1%) (Kessler et al., 2006). Explosive outbursts have been reported to occur with significant frequency in Tourette Syndrome (TS), a phenomenologically heterogeneous disorder characterized by the childhood onset of chronic multiple motor and vocal tics (American Psychiatric Association, 1994). Previous studies among clinically referred samples suggest that approximately 25–70% of...
TS-affected individuals report problems with explosive anger and that, when present, such symptoms are a leading cause of morbidity (Budman et al., 1998, 2000, 2008; Stephens and Sandor, 1999; Zhu et al., 2006; Cavanna et al., 2011, Kano et al., 2008, Wright et al., 2012). However, the relationship, if any, between explosive outbursts and the underlying tic diathesis has been difficult to untangle (Goodman et al., 2006; Wright et al., 2012).

Previous clinical studies have reported a strong association between the presence of explosive outbursts in TS and comorbid obsessive-compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD) (Budman et al., 2000; Freeman et al., 2000; Sukhodolsky et al., 2003; Mol Debes et al., 2008; Cavanna et al., 2011; Wright et al., 2012). However, confirmation of these associations, further exploration and clarification of the possible relationship of explosive outbursts in TS with demographic characteristics such as gender, socioeconomic status and ethnicity, as well as clinical characteristics such as tic severity, tic type, and severity of obsessions and compulsions, are needed. Earlier clinical studies of explosive outbursts in TS were limited by relatively small sample sizes and sample composition, consisting of patients recruited primarily from TS specialty clinics (Budman et al., 1998; Stephens and Sandor, 1999, 2000, 2003; Kano et al., 2008). Therefore, in this study we examined the prevalence and demographic and clinical correlates (including potential pre- and perinatal risk factors, tic severity, and obsessive-compulsive symptom severity) of explosive outbursts in two separate populations of individuals with TS who were initially recruited for participation in TS genetic studies. The first study sample included individuals with TS who were living in the United States (US) and who were recruited primarily from TS specialty clinics. The second sample was derived from individuals with TS living in Costa Rica and who, in most cases, were recruited from the community rather than from clinics. The aim of this investigation was to first examine the prevalence of explosive outbursts in this large (combined) sample of individuals with TS and compare it to previously reported rates. We then sought to identify specific characteristics highly correlated with explosive outbursts in the overall sample. Next, we examined the prevalence and clinical characteristics of explosive outbursts in each of the two samples separately. We hypothesized that the prevalence of explosive outbursts would be at the lower end of the previously reported range of frequencies, and that explosive outbursts would, as previously described, be associated with comorbid OCD and/or ADHD (Budman et al., 1998; Stephens and Sandor, 1999; Cavanna et al., 2011; Wright et al., 2012). However, we also hypothesized that pre- or perinatal risk factors such as maternal tobacco or alcohol use during pregnancy or hypoxia at birth would be associated with increased rates of explosive outbursts in TS-affected individuals, based partly on our previous findings relating these risk factors to increased risk for OCD (Mathews et al., 2006).

2. Methods

2.1. Participants

The study sample consisted of 218 individuals diagnosed with TS (ages 5–75 years) recruited for genetic studies between 1996 and 2009, including a genetic study of individuals with TS from the genetically isolated Central Valley of Costa Rica (N = 104) and a genetic study among individuals of Ashkenazi Jewish descent in the US (N = 114). Costa Rican (CR) participants were ethnically Hispanic; US participants were Caucasian. 85% of participants were under 18 at the time of interview, and 21% of participants were female. Participants from the US were recruited primarily from TS specialty clinics and by referral from the National Tourette Syndrome Association (TSA). CR participants were recruited from healthcare professionals, media advertisements, elementary schools, and friends or family members. Written informed consent (and assent, for children between 5 and 17 years) was obtained for all participants, and all studies were approved by the relevant Institutional Review Boards.

2.2. Diagnostic assessments

Diagnostic information was systematically gathered using structured instruments administered by two psychiatrists (CAM and LDH) who were blinded to IED diagnosis. Lifetime symptom prevalence and worst-ever symptom severity were assessed in all cases. Interviews were videotaped for confirmation of tics. Information about explosive outbursts was elicited using a questionnaire that probed for the diagnostic criteria for IED according to the DSM-IV (APA DSM-IV, 1994; Budman et al., 2000). The Yale Global Tic Severity Scale (YGTS) was used to assess worst-ever lifetime severity (Leckman et al., 1989). Socioeconomic status was measured using the Hollingshead scale, a five point scale assessing parental income, education, and profession, with one being the lowest socioeconomic class and five being the highest (Hollingshead, 1975). Other demographic, medical, social, and clinical characteristics, including pre- and perinatal history, developmental and school performance, medical history, and family history of tics and obsessive-compulsive symptoms (OCS), were assessed using a semi-structured clinical interview.

Information about motor and vocal tics, OCD, obsessive-compulsive symptoms (OCS), ADHD, and self-injurious behavior (SIB) was elicited using a self-report questionnaire that was designed for genetic studies of TS and in use generally for genetic and other etiological studies (TSACG, 1999, 2007). For all child cases and for 43% of the adult cases in Costa Rica and 10% of the adult cases in the US (74% of total, 91% CR group, 58% US group), parents were present during the interview, allowing for confirmation of childhood symptoms, and providing detailed information on prenatal, perinatal and early childhood history. When parents were not present for the interview, adult participants were asked to confirm their prenatal, perinatal, and childhood history with their parents, if still living. Additionally, when possible, this information was confirmed by the research staff via telephone. Diagnoses of TS, OCD, and ADHD were made according to DSM-IV criteria by experienced clinicians using a best-estimate consensus diagnosis approach (CAM, VIR, TLL, and NW) (Leckman et al., 1982). The inter-rater agreement was 95% for TS (k = 0.62), 94% for OCD (k = 0.88), and 91% for ADHD (k = 0.82).

2.3. Outcome and predictor variables

The primary outcome measure was presence or absence of clinically significant explosive outbursts, defined as meeting full symptom criteria for IED. Predictor variables included gender, ethnicity (Costa Rican/Hispanic or US/Caucasian), age at interview, comorbid diagnoses of OCD and ADHD, and presence of moderate or severe SIB. Moderate SIB was defined as behaviors that resulted in moderate tissue damage, such as skin picking that led to profuse bleeding, scarring, or infections requiring treatment. Severe SIB was defined as extreme behaviors that had permanent potentially impairing outcomes such as self-cutting, or deliberate eye enucleation (Mathews et al., 2004). Other predictor variables included YGTS scores (motor and phonic tics), age of onset of tics, family history of tics, socioeconomic status, referral source, birth weight, prenatal problems, perinatal problems, medication exposure in utero, and perinatal maternal smoking. Perinatal problems included history of traumatic birth, fetal respiratory distress, nuchal cord, forceps or suction delivery, hypoxia at birth, jaundice, emergency or unplanned cesarean section, premature delivery (greater than two weeks pre-term), or twin births. Prenatal problems included pre-eclampsia, hyperemesis of pregnancy, threatened abortion, and gestational diabetes. Information was also obtained about medication use (prescribed and over the counter), tobacco (any regular or repeated but episodic cigarette or tobacco use during pregnancy), regular alcohol (≥ 5 glasses of wine or equivalent during pregnancy) or any illicit drug exposure in utero. Medication use included assessment of the use of putoin and fenoterol, as well as fertility drugs. Referral sources included referral into the study by the National TSA, health care providers (including TS specialists), newspaper or other media advertisements, school screening for TS, or referral by family members or friends. For the purposes of the analysis, referral source was grouped into referral by a medical professional versus community (or other) referral.

2.4. Analyses

Statistical analyses were generated using Stata 11.0 (Statistical Software: Release 11 [program] 2010). Univariate analyses were conducted for each predictor and potential confounder variable and presence or absence of explosive outbursts using either chi square analyses (for categorical variables) or t-tests (for continuous variables). These analyses were done separately for the CR and US groups as well as for the overall sample. Variables with positive associations (p < 0.10) with explosive outbursts were then entered into a logistic regression separately for each ethnic group, as the CR and US groups had significant differences in baseline characteristics. For the overall sample, any variable with a positive association in either the CR or the US sample was included in a logistic
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