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ODD irritability is associated with obsessive–compulsive behavior and not ADHD in chronic tic disorders

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ABSTRACT

Gilles de la Tourette syndrome (TS) and chronic tic disorder (CT) are often associated with a variety of behavioral comorbidities including attention-deficit hyperactivity disorder (ADHD), obsessive–compulsive behavior (OCB), oppositional-defiant disorder (ODD) and temper outbursts. ODD is often associated with ADHD but its links to other symptoms of TS/CT is not as clear. This study examined whether the various symptoms of ODD were differentially linked to the various comorbidities in TS. A clinical sample of 135 children diagnosed with TS was evaluated through parent questionnaires and semi-structured interviews. Regressions and structural equation modeling confirmed that ODD is multidimensional in a TS/CT sample and showed that OCB was associated with the irritability symptoms of ODD whereas ADHD was associated with the Headstrong symptoms of ODD. Results suggest that increased attention to the different facets of ODD may help improve our understanding of emotional symptoms in TS/CT.

1. Introduction

Gilles de la Tourette syndrome (TS) and chronic tic disorder (CT) are characterized by repetitive and stereotyped tics with wax and wane in severity. In CT, either vocal or motor tics are present whereas in TS both types of tics are present. The prevalence of TS remains unclear partly because of symptom fluctuations but it is estimated that about 1–2% of the school age population is affected by TS and 3–6% if chronic tic disorders (CT) are included (Hornsey et al., 2001; Knight et al., 2012). In a majority of cases, TS is also associated with behavioral symptoms including obsessive–compulsive behavior (OCB), attention deficit hyperactivity disorder (ADHD) and temper outbursts (Spencer et al., 1998; Stephens and Sandor, 1999; Budman et al., 2000; Freeman et al., 2000; Kurlan et al., 2002; Bloch and Leckman, 2009; Cavanna et al., 2009; Grados and Mathews, 2009) while only about 8–25% of children with TS do not show any comorbidity (Freeman et al., 2000; Khalifa and von Knorring, 2005; Roessner et al., 2007; Robertson, 2012). Behavioral symptoms such as ADHD, OCB and temper outbursts are more related to the quality of life and adaptation of TS children than is the severity of tics (Bernard et al., 2003; Bloch and Leckman, 2009; Rizzo et al., 2012).

Oppositional defiant disorder (ODD) is also a frequent comorbidity in TS (Comings and Comings, 1987; Kurlan et al., 2002; Roessner et al., 2007; Robertson, 2012). ODD symptoms often have an impact on family functioning and social adaptation, especially in children with multiple symptoms such as TS children. ODD has often been considered as an ADHD-related comorbidity in TS, as a majority of TS children showing ODD also show ADHD (Spencer et al., 1998; Sukhodolsky et al., 2003; Roessner et al., 2007). However, some ODD symptoms show a clinical overlap with non-ADHD symptoms often present in TS such as irritability which is often observed in OCB.

There is evidence that some ODD symptoms are associated with emotional disorders such as mood disorders, anxiety disorders, OCB, and temper outbursts (Pierre et al., 1999; Stephens and Sandor, 1999; Burke et al., 2002; Greene et al., 2002; Maughan et al., 2004; Burke et al., 2005; Nock et al., 2007; Drabick et al., 2010; Sobanski et al., 2010). ODD symptoms can be an early indicator of risk of behavior problems, anxiety, or mood disorders (Speltz et al., 1999; Lavigne et al., 2001; Kim-Cohen et al., 2003; Burke et al., 2005; Boylan et al., 2007; Nock et al., 2007) and may

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contribute to the comorbidity between internalizing and externalizing symptoms (Burke et al., 2005). In TS, comorbid internalizing and externalizing symptoms are very frequent and thus ODD may also be associated with other symptoms than ADHD in this population.

Even though ODD symptoms are intercorrelated, ODD is increasingly viewed as a multifactorial disorder. Some ODD symptoms show a stronger association to emotional symptoms and others, a stronger association to ADHD (Stringaris and Goodman, 2009b; Burke et al., 2010; Rowe et al., 2010). In a community sample, ADHD was preferentially predicted by a portion of ODD symptoms (Headstrong component) whereas emotional disorders such as anxiety and depression were preferentially predicted by other ODD symptoms (Irritable component) and aggressive symptoms were predicted by a third set of ODD symptoms (Hurtful component) (Stringaris and Goodman, 2009b). In children with ADHD, the Irritable component of ODD was linked to emotional lability whereas the Headstrong component of ODD was not (Aebi et al., 2010). Also, there is evidence that the co-occurrence of ODD and generalized anxiety disorder (GAD) could not be explained by their joint co-occurrence with ADHD (Drabick et al., 2008).

Despite clear evidence for differential prediction of behavioral problems by different ODD symptoms, there have been several suggestions as to the number of interrelated components in ODD and which ODD symptoms are included in each component. For instance, Rowe et al. (2010) obtained a two-component model of ODD symptoms (Irritable and Headstrong), while Aebi et al. (2010) and Stringaris and Goodman (2009b) obtained three components. ODD-Irritable (temper outbursts, angriness, and touchiness) is identical in the three previous models, while the ODD-Headstrong and the ODD-Hurtful components vary. Rowe et al. (2010) include the five remaining ODD symptoms (argumentation, defiance, annoyance, blaming and spitefulness) in the ODD-Headstrong component whereas Stringaris and Goodman (2009b) and Aebi et al. (2010) combined these symptoms differently in ODD-Headstrong and ODD-Hurtful components. For Aebi et al. (2010), the criterion “annoys others” is included in the ODD-Hurtful component along with the spitefulness criteria, while for Stringaris and Goodman (2009b) the annoyance criterion is in the ODD-Headstrong component, leaving the ODD-Hurtful component with spitefulness as its only criterion.

A large majority of TS children in clinical samples show one or more behavioral comorbidities which have previously been linked to ODD. This makes this population particularly well suited to study ODD components and their links to other symptoms. In TS, ODD has traditionally been linked to ADHD only but the links between ODD and other symptoms need further investigation. The aim of the present study was to examine the factor structure of ODD symptoms in a clinical TS/CT sample and to explore the specific links between different ODD symptoms and behavioral comorbidities in TS/CT. We hypothesized that some components of ODD are preferentially linked to ADHD while others are preferentially linked to emotional symptoms like OCB.

2. Method

2.1. Participants

The present sample was composed of 135 children (118 boys) aged between 5 and 17 ($M=10.3$, S.D.$=2.6$) taking part in a large genetic study and diagnosed with TS ($N=129$) or CT ($N=6$) as defined by the Tourette Syndrome Classification Study Group (TSCSG, 1993): multiple motor tics and phonic tics (motor or phonic tics for CT) must be present at some time during the illness, although not necessarily concurrently; tics must occur many times a day, nearly every day, or intermittently throughout a period of more than 1 year; the anatomical location, number, frequency, type, complexity, or severity of tics must change over time; the onset must occur before the age of 21 years; involuntary movements and noises must not be explainable by other medical conditions; and tics must be witnessed directly or from video by a reliable examiner or concluded from clinical history. All affected individuals had four grand-parents of French Canadian descent. Families were recruited at the Tourette clinic of Sainte-Justine hospital. Patients (above 14 years) or their parents gave written and informed consent to the research coordinator which was not involved in their care. The research was approved by the institutional review board. Exclusion criteria were: a) inability to provide consent, b) a history of head injury or other neurological disorder which may cause tics, c) tics linked to drugs, d) a psychotic disorder, or e) a pervasive developmental disorder.

2.2. Measures

Parents first filled out questionnaires including the Parent Rating Scale (CPRS-L; Conners, 2003), as well as questionnaires on medical, obstetric, and developmental history for their children and for themselves. A clinical evaluation followed and consisted in multiple semi-structured interviews targeting tics using the Yale Global Tic Severity Scale (Y-GTSS; Leckman et al., 1989), as well as behavioral symptoms including OCB through the Yale-Brown Obsessive–Compulsive Scale (Y-BOCS; Goodman et al., 1989 and DSM-IV criteria; American Psychiatric Association, 2000), ADHD (DSM-IV criteria including age of onset, duration and interference; American Psychiatric Association, 2000) and ODD (DSM-IV criteria including duration and interference; American Psychiatric Association, 2000). Interviews were conducted by trained professionals including neurologists, neuropsychologists and psychiatrists, and all had previous experience with the Tourette syndrome population and with their specific evaluation. During interviews, professionals reviewed the questionnaires with the parents to ensure clarity and correspondence with the information shared during interviews. In interviews and questionnaires, parents were asked to consider the behavior of the child when no medication was taken.

The number of ODD symptoms was selected as the main measure of ODD because there is evidence that many children with fewer than the four criteria required for a clinical ODD diagnosis show significant functional impairment (Rowe et al., 2005). ODD criteria include: (1) loses temper, (2) argues with adults, (3) actively defies or refuses to comply with adults' requests, (4) deliberately does things that annoy other people, (5) blames others for his/her mistakes or misbehavior, (6) touchy or easily annoyed by others, (7) angry and resentful, (8) spiteful or vindictive. The main measure for ADHD was based on the number of DSM-IV criteria for ADHD met by the child. The criteria included inattention, hyperactivity and impulsivity related symptoms as detailed by the DSM-IV. If the participant showed 6 or more symptoms of either hyperactivity/impulsivity or inattention, a score of 3 was attributed (definite ADHD), for 5 symptoms a score of 2 was attributed (probable ADHD), for 4 symptoms a score of 1 was attributed (possible ADHD) and finally a score of 0 was attributed when less than 4 symptoms were documented (non-ADHD). As for OCB, the measure used was the total Y-BOCS score ranging from 0 to 40 since it is the most widely used measure of OCB severity (Deacon and Abramowitz, 2005). The Y-BOCS measure examines obsessions and compulsions which are presented as internalized symptoms (e.g., fear of harming others) as opposed to externalized or disruptive behaviors as in ODD. We selected this measure because TS/CT patients often have significant symptoms that may not meet the criteria for full-blown OCD on the level of distress and interference. Trained professionals evaluating OCB were aware of the array of tics of each patient before addressing OCB symptoms to ensure that the same symptoms were not counted as both tics and OCB. Compulsions were defined as clearly goal-directed behaviors to distinguish them from tics. The measures for tics, ODD, ADHD and OCB included in the analyses were all evaluations of the worst severity of symptoms in the patient's life.

2.3. Data analysis

The data were analyzed using the Statistical Package for Social Sciences (SPSS) 17.0. Pearson correlations were used to examine the associations between symptoms. Confirmatory factor analyses were used to determine the number of components which best accounted for the pattern of correlations between ODD criteria in our sample. Linear regressions were used to predict TS comorbidities with the two ODD components. The low multicollinearity assumption was respected since the Variance Inflation Factor (VIF) value was 1 for all regressions (less than 10) (Belseley et al., 1980). Some measures were statistically transformed to respect the normality assumption for linear regressions (i.e. OCB measure and ODD-Headstrong component). Structural equation models of the predictions of comorbidities by ODD components were tested using MXGui version 1.7.03. The following standard cut-offs were used as indications of an acceptable model: $RMR \leq 0.05$, $RMSEA \leq 0.06$ and $CFI \geq 0.95$ (Hu and Bentler, 1999).

3. Results

Table 1 shows clinical and demographic data for the sample. The proportion of boys was 87%. The sample reflected patients referred to a specialized TS clinic in that only 6.7% of the sample presented

none of the comorbidities examined, 80% of children were identified as having complex tics and 73% of children were currently taking medication. Clinical ODD was present in 54% of patients, whereas 86% showed at least one ODD symptom. Clinical ADHD was present in 59% of cases and 68% showed five or more ADHD symptoms. ODD was comorbid with ADHD in 73% of cases and with OCB in 74% of cases. The number of ODD symptoms was significantly correlated with the ADHD measure ($r=0.326$, $p<0.001$) and OCB measure ($r=0.278$, $p=0.002$). However, the ADHD measure was not significantly correlated with OCB measure ($r=0.022$, $p=0.81$). None of the clinical measures were significantly correlated with age, age of onset of tics and lifetime worst severity of tics.

Confirmatory factor analyses tested the factor structure of ODD in our sample. The model with only one ODD component was rejected ($\chi^2(20)=53.5$, $p<0.001$). The two-factor model of Rowe et al. (2010) (ODD-Irritable: angriness, temper, and touchiness; ODD-Headstrong: defiance, blaming, argumentation, spitefulness, and annoyance) was acceptable ($\chi^2(19)=25.8$, $p=0.137$) and provided a good fit ($RMR=0.048$, $RMSEA=0.052$, $CFI=0.981$). Also, the three component model of Aebi et al. (2010) (same ODD-Irritable component, but a third factor ODD-Hurtful measured by spitefulness and annoyance symptoms instead of being incorporated into ODD-Headstrong) was found to be acceptable ($\chi^2(17)=20.1$, $p=0.270$) ($RMR=0.054$, $RMSEA=0.037$, $CFI=0.992$) as was the Stringaris and Goodman (2009b) model in which the Hurtful component was identified with a single symptom (spitefulness) ($\chi^2(18)=23.7$, $p=0.165$) ($RMR=0.045$, $RMSEA=0.049$, $CFI=0.984$). A chi-square difference test confirmed that the difference between the two-component model of Rowe et al. (2010) and the three-component model of Aebi et al. (2010) was not significant ($p=0.06$) and thus, the more parsimonious two-component model was used in the structural equation modeling in the present data.

Table 1
Demographic and clinical data for children with TS/CT.

	TS/CT children
Proportion of boys	87.4%
Mean age (S.D.)	10.3 years (2.6)
Mean age of onset of tics (S.D.)	5.4 years (2.3)
ODD	54.1%
ADHD	59.3%
ODD+ADHD	72.8%
ADHD+ODD	66.3%
OCB	54.8%
OCB+ODD	62.2%
ODD+OCB	74.2%
ADHD+OCB	64.2%
TS without behavioral comorbidities	6.7%

Regressions examined which of the different components of ODD predicted the comorbidities measured. The OCB measure was significantly predicted [$F(1, 115)=9.0$, $p=0.003$; $R^2=0.07$] by the ODD-Irritable component ($\beta=0.27$, $p=0.003$), but not by the ODD-Headstrong component ($\beta=0.02$, $p=0.890$). Also, the ADHD measure was significantly predicted [$F(1, 133)=12.0$, $p=0.001$; $R^2=0.08$] by ODD-Headstrong ($\beta=0.29$, p=0.001), but not by ODD-Irritable ($\beta=0.05$, $p=0.647$). On this basis, we evaluated a structural equation model of the correlations between ODD components and comorbidities. The model postulates that ADHD is predicted by ODD-Headstrong and OCB is predicted by ODD-Irritable (see Fig. 1). This model was shown to be acceptable ($\chi^2(34)=38.9$, $p=0.259$) and also provided a good fit to the data ($RMR=0.052$, $RMSEA=0.033$, $CFI=0.987$).

4. Discussion

The present results confirm that ODD is not homogeneous in TS/CT as a multiple-factor structure of ODD was clearly more

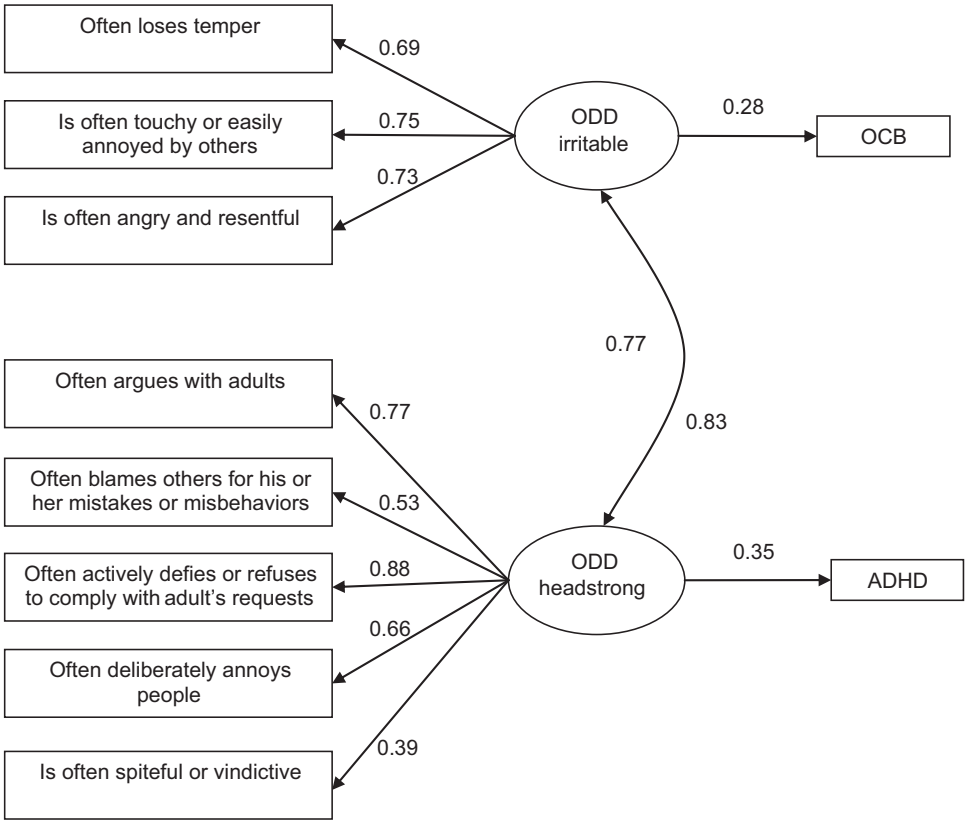

Fig. 1. Structural equation model of the prediction of Tourette syndrome comorbidities by ODD dimensions.

adequate than a single factor solution despite a strong overlap between ODD components. The results agree with previous analyses in other populations (Burke et al., 2005; Stringaris and Goodman, 2009b; Aebi et al., 2010; Rowe et al., 2010). They also suggest that in TS/CT, ODD cannot be assimilated to ADHD since ADHD was predicted by ODD-Headstrong symptoms only, while OCB was linked to ODD-Irritable symptoms.

The association of ADHD with ODD-Headstrong but not with ODD-Irritable was expected based on previous reports (Stringaris and Goodman, 2009b). One explanation may be that symptoms such as argumentation, defiance and blaming others may overlap the ADHD phenotype more than the more affective (irritable or vindictive) symptoms of ODD. The five symptoms of the ODD-Headstrong component can be viewed as more direct extensions of the impulsive behavior pattern of ADHD than the irritability symptom of ODD. Also, shared genetic and/or environmental influences may contribute to the high correlation between ODD-Headstrong and ADHD (Burt et al., 2005; Dick et al., 2005).

The link between ODD-Irritable and OCB observed here is coherent with previous data suggesting that this ODD component predicts anxiety and emotional problems in other populations (Stringaris and Goodman, 2009a, 2009b; Kolko and Pardini, 2010). In TS/CT, OCB is more frequent than in many other populations, and this could facilitate interactions between OCB and ODD irritability. It could be suggested that the associations observed here are linked to overlap between disorders and the difficulty of classifying symptoms as ODD, ADHD or OCB. However, there were no items related to irritability in the OCB measure and clinical interviews with professionals helped document examples of each type of disruptive behavior and whether it was context specific or generalized to many situations.

Our data suggest the presence of differential associations for different ODD components but a number of explanations could be proposed for these associations. One explanation is that ODD symptoms could serve as precursors to OCB or ADHD. It has been suggested that ODD may represent a heterogeneous common precursor to several externalizing and internalizing symptoms (Burke et al., 2010). ODD often precedes other symptoms including explosive outbursts, ADHD and OCB (Peterson et al., 2001; Burke et al., 2005; Nock et al., 2007; Bloch and Leckman, 2009) and a number of studies have suggested that preschoolers with ODD symptoms present an especially high risk for later ADHD, anxiety and mood disorders (Speltz et al., 1999; Lavigne et al., 2001; Boylan et al., 2007). However, the lack of correlation between ADHD and OCB symptoms in our sample suggests that ODD is not a monolithic precursor of ADHD and OCB and that ODD symptoms associated with ADHD are different from ODD symptoms associated with OCB.

A second explanation is that Headstrong and Irritable ODD symptoms may be differentially exacerbated by OCB and ADHD either at the level of brain pathology or symptoms. ADHD symptoms such as impulsivity, talkativeness and inattention may increase the probability of headstrong ODD symptoms in emotional arguments involving authority figures. In OCB, anxiety or frustration may increase the probability of irritability in social situations. In this explanation, ODD components would serve as early markers of ADHD and OCB.

A third possibility is that ODD may share common risk factors with other behavioral comorbidities. There is evidence that emotional dysregulation in early childhood predicts later disruptive behaviour and ODD symptoms (Keenan and Shaw, 2003; Stringaris et al., 2010). Several potential shared risk factors for ODD and anxiety disorders have been identified including temperament, information processing biases, parent-child processes, violence exposure and limbic and prefrontal dysfunction (Angold et al., 1999; Drabick et al., 2010).

The present data cannot help distinguish between different possible causal pathways between ODD components and TS/CT comorbidities. Future studies should examine longitudinal data to clarify the interactions between ODD and other symptoms in TS. However, the present results suggest that the presence of ODD-Irritable symptoms is linked to OCB symptoms in TS/CT. ODD components explained a very small proportion of variance in OCB and ADHD. This is probably linked to the strong genetic, epigenetic and developmental influences on these comorbidities which affect emotional and behavioral brain systems. Also, in TS/CT the presence of multiple comorbidities may increase the complexity of interactions between different influences.

Another possible component of ODD, ODD-Hurtful has previously been linked to conduct disorder (CD) (Stringaris and Goodman, 2009a; Kolko and Pardini, 2010). In the present study, this component was not retained because it did not add predictive value to the simpler two-component model. Also, the spitefulness criterion, a key measure in ODD-Hurtful, was very rarely fulfilled in our sample.

ODD may also be associated with other comorbidities in TS. For example, impulse control disorders such as intermittent explosive disorder (IED) and self-injurious behavior (SIB) are common in patients with TS (Frank et al., 2011; Wright et al., 2012). IED shows an obvious overlap with tantrum symptoms of ODD and was thus not examined here and we found no significant association between SIB and ODD components. However, the links between impulse control and irritability deserve further investigation. Also, the study did not address mood disorders as these data were not available for many patients. Future work will have to confirm the links between ODD-Irritable and mood disorders in the TS population.

There are several limitations to consider in the present study. First, parent reports were the main source of information for diagnoses even if they were confirmed by a clinician. The lack of data from educational or peer interaction settings may have contributed to an underestimation of severity for some symptoms. Parent reports have been shown to be good indicators of ODD symptoms (Aebi et al., 2010), but the severity of OCB and anxiety symptoms may be underestimated. Furthermore, there is evidence that parent reports provide valuable information for the evaluation of behavioral problems in children with TS (Termine et al., 2011). Also, our results were obtained from a restricted clinical sample of children with TS or chronic tics. The results may not generalize to community samples which often show lower symptom severity. Nonetheless, the use of a clinical sample allows the simultaneous investigation of several comorbidities and the examination of their links to different components of ODD.

The results may have several clinical implications. Clinicians and parents should become more attentive to ODD symptoms in TS/CT and to their specific expression as they are heterogenous. Interventions are usually guided by the detailed behavioral, cognitive and socioaffective profile of a child and ODD components might be helpful in specifying that profile. Hence, interventions should be adapted to the specific ODD profile of a child by considering which components of ODD are more present.

In conclusion, the results suggest that in TS/CT, ODD-Irritable symptoms are linked to OCB while ODD-Headstrong symptoms are linked to ADHD. Increased attention to the different facets of ODD may help increase our understanding of different subphenotypes in TS.

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