Eur Child Adolesc Psychiatry (2012) 21:451–457
DOI 10.1007/s00787-012-0278-5

ORIGINAL CONTRIBUTION

Tourette syndrome in youth with and without obsessive compulsive disorder and attention deficit hyperactivity disorder

Eli R. Lebowitz · Maria G. Motlagh · Liliya Katsovich · Robert A. King · Paul J. Lombroso · Heidi Grantz · Haiqun Lin · Mary Jane Bentley · Donald L. Gilbert · Harvey S. Singer · Barbara J. Coffey · the Tourette Syndrome Study Group · Roger M. Kurlan · James F. Leckman

Received: 28 October 2011 / Accepted: 9 April 2012 / Published online: 28 April 2012

Abstract Chronic tic disorders (TD) are consistently found to have high rates of comorbidity with obsessive–compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD). The purpose of this study is to compare the severity of TD only to TD with comorbid OCD or ADHD based on severity of tics, measures of psychopathology and additional comorbid diagnoses. Baseline data from 158 youth with a chronic TD who participated in two longitudinal studies were examined. Fifty-three percent ($N = 85$) of the youth also met criteria for a diagnosis of OCD, 38.6 % ($n = 61$) met criteria for ADHD and 24.1 % ($N = 38$) met criteria for both. Measures of interest addressed severity of tics, symptoms of anxiety, depression, ADHD, psychosocial stress, global functioning and the presence of comorbid diagnoses. Youth with comorbid TD and OCD were characterized by more severe tics, increased levels of depressive and anxious symptoms, heightened psychosocial stress and poorer global functioning. Youth with comorbid TD and ADHD did not differ from those with TD alone on measures of tic severity, but experienced greater psychosocial stress and poorer global functioning. Subjects with comorbid TD and OCD had more internalizing disorders than those without OCD, while those with comorbid ADHD were more likely to meet criteria for oppositional defiant disorder. TD with OCD is a more severe subtype of TD than TD without OCD. TD with ADHD is associated with higher psychosocial stress and more externalizing behaviors. Further research is needed into the underlying relationships between these closely associated conditions.

Keywords Tourette's disorder · OCD ADHD · Comorbidity

E. R. Lebowitz and M. G. Motlagh contributed in equal measure to this study.

E. R. Lebowitz (✉) · M. G. Motlagh · L. Katsovich · R. A. King · P. J. Lombroso · H. Grantz · M. J. Bentley · J. F. Leckman
Yale Child Study Center, 230 South Frontage Rd, New Haven, CT 06520, USA
e-mail: eli.lebowitz@yale.edu

H. Lin
Yale University, 230 South Frontage Rd, New Haven, CT 06520, USA

D. L. Gilbert
Division of Neurology at the Cincinnati Children's Hospital Medical Center, University of Cincinnati Medical School, Cincinnati, OH, USA

H. S. Singer
Johns Hopkins University School of Medicine, Baltimore, MD, USA

B. J. Coffey
Child Study Center at the New York University School of Medicine, New York, NY, USA

R. M. Kurlan
Atlantic Neuroscience Institute, Overlook Hospital, Summit, NJ, USA

Introduction

Tic disorders (TD), including Tourette syndrome and chronic motor or vocal tic disorder, are consistently found to be linked to obsessive–compulsive disorder (OCD) [1, 2] and to attention deficit hyperactivity disorder (ADHD) [3–5] with significant bi-directional comorbidity. Indeed, the Diagnostic and Statistical Manual, fifth edition will likely include "tic-related" OCD as a subtype specific given the

strength of the clinical, genetic, neurobiological and treatment response data [6]. Brain imaging studies of TD, ADHD and childhood-onset OCD consistently point to involvement of cortico-striato-thalamocortico circuits in all three disorders [7–11]. Family genetic studies suggest there are likely shared genetic vulnerabilities between OCD and TS [12–17]. For example, O'Rourke et al. [18] reported that the presence of OCD or subclinical OCD in TS proband was associated with significantly increased risk of comorbid ADHD and TD in their first-degree relatives.

Some studies have addressed the clinical implications of having comorbid OCD or ADHD and compared tic severity and related psychopathology to cases of only TD. In the case of OCD, the results have been somewhat inconclusive. For example, one study of 61 adults with TD, OCD or TD + OCD demonstrated elevated levels of co-occurring psychopathologies in the TD + OCD condition [19]. A recently published study reporting on over 5,000 children with TD also found that the presence of comorbid OCD was associated with higher rates of additional comorbid diagnoses [20]. In contrast, a study of 306 youth did not find TD + OCD to have elevated rates of comorbid diagnoses [21], when compared with TD or OCD alone. Some studies have found greater tic severity in TD + OCD [22], supporting the hypothesis that the comorbid condition represents a more severe subtype of TD.

With regard to ADHD, the evidence so far points more toward the importance of the comorbid condition for disruptive and aggressive behaviors than for tic severity. Several studies have shown that TD youth without ADHD are less prone to angry outbursts, disruptive behaviors and social maladaptation than those with both conditions [23, 24]. Although comorbid ADHD seems to explain or in some way trigger many of the disruptive behaviors commonly reported in TD, strengthening the case for a related etiology, a study of the course of the combined condition over 4 years showed that the tic symptoms were considerably more likely to remit than symptoms of ADHD [25]. A large-scale study of children with TD also pointed to comorbid ADHD being associated with higher likelihood of internalizing disorders, particularly in younger children [26]. Tic severity has generally been found to be similar [23, 27, 28] across TD only and TD with ADHD, although at least one study found more severe phonic tics in youth with the comorbid condition [24].

The purpose of the current report is to present data from a large sample of youth with TD, with and without OCD and ADHD, and to identify associations between the presence of the comorbid disorders and the severity of tics and other symptoms, additional comorbidities, level of functioning and degree of psychosocial stress. Our a priori hypothesis was that individuals who had comorbid OCD or ADHD would present with more severe tics and greater psychosocial stress than those who had TD alone.

Method

Subjects

We present data from two multisite, prospective longitudinal studies undertaken by researchers affiliated with the Tourette Syndrome Study Group [29, 30]. In brief, both studies looked at longitudinal data collected over 25 months on children with TD. The aim of the original studies was to compare the course of illness of children who met the published diagnostic criteria for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) with those who did not [31]. Neither study provided evidence that exacerbations in tic or OC symptoms were linked with antecedent group A beta hemolytic streptococcal infections (GABHS) [29, 30].

In Study 1, a total of 40 case–control pairs matched for PANDAS status were recruited from ten sites across the USA [29]. In Study 2, 31 PANDAS cases and 53 non-PANDAS comparison cases were recruited from six sites, all of which also participated in Study 1 [30]. For the purpose of this analysis, only those individuals with a chronic TD were included. Inclusion criteria were as follows: (1) presence of OCD and/or a chronic tic disorder by DSM-IV criteria [32]; (2) age at onset between 3 and 14 years; (3) currently <16 years of age; and (4) informed consent provided by parent or guardian and assent provided by the subject. In both studies, PANDAS subjects were required to meet all five of the published diagnostic criteria for PANDAS [31].

Exclusion criteria included the following: (1) possible Sydenham chorea; (2) presence of mental retardation, pervasive developmental disorder, or a secondary tic disorder other than PANDAS (e.g., drug induced or neuroacanthocytosis); and (3) a psychiatric disorder other than OCD or chronic tics as the primary focus of treatment.

Procedures

At the initial visit, informed consent and/or assent were obtained. Recruitment rates for both studies were high, with over 90 % of patients queried agreeing to participate. A systematic clinical interview and examination were performed to ensure that the subject satisfied all of the enrollment criteria. In Study 1, a fully structured psychiatric interview, the Diagnostic Interview Schedule for Children-DSM-IV version (DISC-IV) [33], was used to verify that criteria for OCD or a chronic tic disorder were met. The DISC-IV was also used to determine the presence of any comorbid conditions. For eligible subjects, symptom severity was assessed with the following instruments: Yale Global Tic Severity Scale (YGTSS) for tics [34]; the Children's Yale-Brown Obsessive–Compulsive Scale (CY-BOCS) for OCD [35]. Ratings were also collected for

ADHD (Conners Abbreviated Symptom Questionnaire-Parent [ASQ-P]) [36], anxiety (Multidimensional Anxiety Scale for Children [MASC]) [37] and depression (Child Depression Inventory-Short Version [CDI SV]) [38]. In Study 2, the assessment methods were identical except that the diagnoses, including TD, OCD, and ADHD, were made after reviewing all available information including data from the Schedule for Affective Disorders and Schizophrenia for School-Age Children (SADS) [39].

In both studies, parents completed a rating of the level of perceived psychosocial stress at the baseline assessment (Perceived Stress Scale Parent—PSSP [40]). In both studies, the Child Global Assessment Scale for global functioning (C-GAS) was rated independently both by the site investigators and by the parents of each subject [41].

Data analysis

Analysis was carried out using PASW Statistics 18. A multivariate general linear model (MANCOVA) including both OCD and ADHD was used to test for their effects on tic severity (YGTSS), depression (CDI), anxiety (MASC), global functioning (C-GAS), and psychosocial stress (PSSP) and for potential interactions between the comorbid disorders. Meeting criteria for PANDAS and the study of origin were included in each analysis as a covariate. Binary logistic regression was used to model the effects of OCD and ADHD on the likelihood of additional comorbid diagnoses. All tests are two tailed with significance set at the 0.05 level.

Results

A total of 158 children, aged 6–14.5 years who met criteria for a chronic TD, were recruited from ten sites across the USA. The majority of these ($N = 143$, 90.5 %) met criteria for Tourette syndrome, and the minority for chronic motor ($N = 10$, 6.32 %) or vocal ($N = 1$, 0.6 %) tic disorders or tic disorder NOS ($N = 5$, 3.16 %). Eighty-five (53.8 %) of the 158 subjects with TD also met criteria for a diagnosis of OCD, and 61 (38.6 %) met criteria for ADHD. Thirty-eight subjects (24.1 %) met criteria for both OCD and ADHD and 50 (31.6 %) had neither ADHD nor OCD. These rates resemble those reported by others [42], although ADHD has usually been reported to be the more frequent comorbid condition [43]. Thirteen additional subjects did not meet criteria for a chronic TD and were not included in the current report. As presented in Table 1, the demographic

Table 1 Demographic and clinical characteristics for 158 children with tic disorders by sample of origin

	Study 1 [27] ($n = 76$)	Study 2 [28] ($n = 82$)
Age mean (SD)*	10.18 ± 1.8	11.2 ± 1.7
Male gender *N* (%)	77.6 (39 %)	73.1 (60 %)
Race (% Caucasian)	96.1 %	97 %
Parent education in years—mean (SD)	15.4 (2.5)	15.3 (2.8)
PANDAS percent (*N*)*	35.5 % (27)	51.2 % (42)
Clinical diagnosis—percent (*N*)		
OCD*	65.8 % (50)	42.6 % (35)
ADHD*	48.7 % (37)	29.2 % (24)
ODD	14.5 % (11)	13.4 % (11)
CD	2.6 % (2)	0 % (0)
General anxiety disorder	9.2 % (6)	7.3 % (6)
Separation anxiety	9.2 % (7)	18.2 % (15)
Specific phobia*	7.9 % (6)	23.1 % (19)
Major depression	9.2 % (7)	8.5 % (7)
Baseline severity measures—mean (SD)		
Yale Global Tic Severity Scale	17.8 (8.8)	16.8 (8.8)
Children's Yale-Brown Obsessive Compulsive Scale	7.9 (7.2)	8.7 (8.4)
Conners Abbreviated Symptom Questionnaire-Parent*	9.2 (7.5)	6.1 (5.6)
Children's Depression Inventory	5.5 (6.1)	2.0 (2.6)
Multidimensional Anxiety Scale for Children	46.4 (17.7)	47.2 (17.7)
Child Global Assessment Scale for Global Functioning-Clinician	77.0 (12.3)	73.5 (15.4)

PANDAS pediatric autoimmune disorders associated with streptococcal infections, *TD* tic disorder, *OCD* obsessive–compulsive disorder, *ODD* oppositional defiant disorder, *CD* conduct disorder

* $p < 0.05$

and clinical characteristics were similar across the two studies. Subjects in Study 1 were slightly older and had somewhat higher rates of psychiatric diagnoses (including OCD and ADHD) than those in Study 2. Study 2 included more subjects who met the criteria for PANDAS.

Tic severity

Youth with comorbid OCD had significantly more severe tics when compared with those without OCD, as measured by the YGTSS ($F_{(1)} = 14.6$, $p < 0.001$). Subjects with ADHD showed a non-significant trend to more severe tics compared with the non-ADHD subjects ($F_{(1)} = 1.5$, $p = 0.2$). The analyses did not reveal a significant interaction between the presence of OCD and ADHD with regard to tic severity ($p > 0.39$).

Related psychopathology

Comorbid OCD was also significantly associated with all the secondary measures of psychopathology, which included anxiety ($F_{(1)} = 5.33$, $p < 0.05$), depression ($F_{(1)} = 17.3$, $p < 0.001$), and psychosocial stress ($F_{(1)} = 16.1, p < 0.001$), as well a significant negative association with the overall global level of functioning as assessed by both parents ($F_{(1)} = 11.7$, $p < 0.005$) and clinicians ($F_{(1)} = 37.4$, $p < 0.001$). The presence of ADHD was significantly associated with the levels of stress ($F_{(1)} = 4.6$, $p < 0.05$) and global functioning as reported by parents ($F_{(1)} = 8.1$, $p < 0.01$) and clinicians ($F_{(1)} = 5.1, p < 0.05$), but not with specific measures of anxiety or depression. Table 2 summarizes the measures of tic severity and related psychopathology across conditions. No significant interactions were found between the effects of OCD and ADHD for any of these measures.

To investigate the consequences of having both comorbid disorders, we also conducted a multi-group analysis of variance comparing TD only, to TD + OCD, to TD + ADHD, and to TD + ADHD + OCD. In this analysis, only comparisons to the doubly comorbid condition were significant, implying that while OCD alone was considerably more significant than ADHD alone, the presence of both conditions posed more heightened risk for increased tics and related psychopathology than either condition does alone.

Table 2 Tic severity and related psychopathology in 158 youth with tics stratified by the presence of comorbid OCD and/or ADHD and by PANDAS status

Rating scale	TD Only ($N = 50$)		TD + OCD ($N = 85$)		TD + ADHD ($N = 61$)		TD + OCD + ADHD ($N = 38$)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
YGTSS								
PANDAS	15.6	8.5	20.4	9.6	18	9.8	21.2	8.7
Non-PANDAS	13.2	6.7	19.4	8.9	19.4	7.8	21.8	8.6
CDI SV								
PANDAS	0.85	1.8	2.5	2.6	2.8	2.9	3.1	3.2
Non-PANDAS	0.85	1.3	2.5	3	1.8	2.8	2.9	3.2
MASC								
PANDAS	39.7	12.3	50.4	16.3	47.9	15.2	48.4	15.8
Non-PANDAS	45	17.2	49.8	20.6	47.3	21.7	51.4	24.2
PSSP								
PANDAS	3.7	2.3	6.4	3.1	6.3	3.2	6.4	3.6
Non-PANDAS	4	3.1	6.7	3.2	6.4	3.2	7.5	3.2
CGAS Parent								
PANDAS	86.4	9.3	72.1	14.8	74.5	13.7	75.2	14.2
Non-PANDAS	87.4	7.7	77.8	12.7	76	12.3	72.4	12.3
CGAS Clinician								
PANDAS	83.7	11.8	69.3	14.8	69.8	13.9	68	14.8
Non-PANDAS	84.8	10.8	68.2	12.3	72.2	12.4	66	11.5

TD Tic disorder, *OCD* obsessive compulsive disorder, *ADHD* attention deficit hyperactivity disorder, *YGTSS* Yale Global Tic Severity Score, *CDI SV* Child Depression Inventory-Short Version, *PSSP* Perceived Stress Scale-Parent, *MASC* Multidimensional Anxiety Scale for Children, *CGAS* Children's Global Assessment Scale, *PANDAS/Non-PANDAS* refers to meeting published diagnostic criteria for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS)

Table 3 Binary logistic regression of anxiety disorders, oppositional defiant disorder, and depression in 158 youth with tic disorders as predicted by the presence of OCD or ADHD

	OCD			ADHD			H–L $\chi_{(2)}^2$	p
	β	Wald's $\chi_{(1)}^{2*}$	p	β	Wald's $\chi_{(1)}^2$	p		
Anxiety disorder	0.897	5.72	0.017	0.306	0.705	0.401	0.395	0.821
EXT	0.092	0.037	0.847	1.18	6.03	0.014	0.86	0.65
MDD	1.72	1.8	0.028	0.334	0.338	0.561	3.82	0.148

Anxiety disorder = at least one: separation anxiety, social phobia, specific phobia, agoraphobia, generalized anxiety, panic disorder

OCD obsessive compulsive disorder, *ADHD* attention deficit hyperactivity disorder, *EXT* externalizing disorder (i.e., oppositional defiant disorder and/or conduct disorder), *MDD* major depressive disorder; *H–L* χ^2 Hosmer and Lemeshow Chi-square goodness of fit

Comorbid diagnoses

The results of the logistic regression analyses showed that youth with OCD and/or ADHD were more likely to meet criteria for additional diagnoses compared to those without OCD or ADHD. Specifically, comorbid OCD significantly increased the likelihood of another internalizing disorder such as depression or an anxiety disorder, while ADHD increased the likelihood of additional externalizing disorders such as oppositional defiant disorder. Table 3 summarizes the impact of OCD and ADHD as predictors of additional diagnoses.

Impact of PANDAS

Meeting the published diagnostic criteria for PANDAS was included as a covariate in the GLM analyses of tic severity and related psychopathology. PANDAS status was not a significant variable in any of the analyses. PANDAS status was also not a significant predictor of comorbid conditions in the logistic regression models.

Discussion

This study reports on a large and well-characterized sample of pediatric patients diagnosed with a chronic TD and compares clinical features based on the presence or absence of a diagnosis of OCD or ADHD. The results highlight the impact that two frequently comorbid conditions can have on the severity and associated difficulties of youth with tic disorders. Consistent with our a priori hypothesis, pediatric patients with comorbid TD and OCD had more severe tics than children with TD who did not have OCD. This finding is in line with those reported by Coffey et al. [19] who found TD + OCD subjects to be characterized by more severe tics as measured by YGTSS. In contrast are the findings reported by Lewin et al. [21], who found no significant increase in tic severity in TD + OCD patients as measured by ADIS clinician severity rating (CSR). It is not certain to what extent this discrepancy may relate to the different assessment tool used in each study.

In addition to greater tic severity, subjects with comorbid OCD had greater severity on several measures of psychopathology including depression, anxiety, and levels of psychosocial stress as well as poorer global functioning. Interestingly, comorbid ADHD had a less pronounced impact on these variables. On average, youth with ADHD had only non-significantly more severe tics than those without ADHD, and the effect on other measures of psychopathology was limited to general measures such as psychosocial stress and global functioning but not tied to more severe specific symptoms such as anxiety or depression. These findings also reaffirm those reported by others who identified a greater effect of comorbid ADHD on stress and global functioning than on tic severity [28].

One way of understanding these results is to see OCD and ADHD as interacting in different ways with TD. Comorbid TD and OCD might represent a more severe subtype of TD, leading to increased symptoms relevant to both disorders. Comorbid ADHD may be better conceptualized as a separate problem complicating the presentation through added difficulties for the child and family. Earlier studies in adults have pointed to comorbid TD + OCD as a subtype of TD [19] and the relationship is likely to be recognized by the inclusion of a tic-related diagnosis of OCD in DSM V [6]. The current results within the pediatric population support this hypothesis. An alternative possibility that needs also to be considered is the potential for some compulsions to be characterized as tics, leading to greater tic severity ratings among youth with comorbid OCD. The similarities, and consequent ambiguous differences, between tics and compulsions, were described as long ago as by Pierre Janet [44] and more recently captured with the term "compultics" [45]. ADHD by comparison may be adding to the more general difficulty in functioning normally and adding considerable stress as demonstrated by the results of our investigation. The results of this study also support the strong link that has been reported elsewhere between disruptive behaviors in TD and the presence of ADHD [23, 24]. In fact, apart

from psychosocial stress and global functioning, the impact of ADHD was most prominent in increasing the likelihood of meeting criteria for a disruptive behavior disorder.

The findings should be interpreted in light of the studies limitations including the absence of OCD-only, ADHD-only and healthy control groups. Inclusion of these contrast groups would present a clearer picture and allow for better interpretation. Second, we relied on patients who had been referred to specialty TS clinics. This may have created an ascertainment bias. A potential limitation of the present study lies in the fact that the data analyzed were collected as part of an effort to investigate the relationship of streptococcal infections to the occurrence or exacerbation of TD and OCD. As such, the subjects were recruited because they either fit the published criteria for PANDAS or were matched to others who did, creating a potential bias that could in principle limit the ability to generalize these findings. However, the fact is that neither of the two studies showed a significant link between the PANDAS criteria and symptom severity. To further address this issue in the present study, PANDAS status was included as a covariate in the analyses. This variable was not found to be a significant factor in any of the results. Finally, the present study focuses on cross-sectional comparisons between subjects with and without OCD or ADHD, but presents only limited data addressing each of those conditions as one variable in a multivariate approach. This also presents a limitation on the interpretation of causal links explaining the associations reported.

Conclusion

Chronic TD with comorbid OCD, on average, is a more severe form of TD associated with more severe tics and internalizing psychopathology and poorer global functioning compared to youth with chronic TD and no OCD. In contrast, chronic TD with comorbid ADHD is associated with higher levels of psychosocial stress, poorer functioning, and increased risk for externalizing behavioral problems. However, the interactions between the two comorbid conditions need more research and an even larger sample size is necessary to properly investigate this multi-group model. Research needs to further investigate the links between TD, OCD, and ADHD as well as the genetic, epigenetic, and neurobiological factors contributing to these associations.

Acknowledgments Eli R. Lebowitz gratefully acknowledges the support of the Messer Anxiety Program at the Yale Child Study Center.

Conflict of interest None.

References

1. Ivarsson T, Melin K, Wallin L (2008) Categorical and dimensional aspects of co-morbidity in obsessive–compulsive disorder (OCD). Eur Child Adolesc Psychiatry 17(1):20–31
2. Hanna GL (1995) Demographic and clinical features of obsessive–compulsive disorder in children and adolescents. J Am Acad Child Adolesc Psychiatry 34(1):19–27
3. Apter A, Pauls DL, Bleich A, Zohar AH, Kron S, Ratzoni G, Dycian A, Kotler M, Weizman A, Gadot N (1993) An epidemiologic study of Gilles de la Tourette's syndrome in Israel. Arch Gen Psychiatry 50(9):734–738
4. Walkup JT, Scahill LD, Riddle MA (1995) Disruptive behavior, hyperactivity, and learning disabilities in children with Tourette's syndrome. Adv Neurol 65:259–272
5. Kurlan R, Como PG, Miller B, Palumbo D, Deeley C, Andresen EM, Eapen S, McDermott MP (2002) The behavioral spectrum of tic disorders: a community-based study. Neurology 59(3):414–420
6. Leckman JF, Denys D, Simpson HB, MataixCols D, Hollander E, Saxena S, Miguel EC, Rauch SL, Goodman WK, Phillips KA, Stein DJ (2010) Obsessive–compulsive disorder: a review of the diagnostic criteria and possible subtypes and dimensional specifiers for DSM-V. Depress Anxiety 27(6):507–527
7. Sheppard DM, Bradshaw JL, Purcell R, Pantelis C (1999) Tourette's and comorbid syndromes: obsessive compulsive and attention deficit hyperactivity disorder. A common etiology? Clin Psychol Rev 19(5):531–552
8. Albin RL, Mink JW (2006) Recent advances in Tourette syndrome research. Trends Neurosci 29(3):175–182
9. Cherkasova MV, Hechtman L (2009) Neuroimaging in attention–deficit hyperactivity disorder: beyond the frontostriatal circuitry. Can J Psychiatry 54(10):651–664
10. Sachdev PS, Malhi GS (2005) Obsessive–compulsive behaviour: a disorder of decision-making. Aust N Z J Psychiatry 39(9):757–763
11. Marsh R, Maia TV, Peterson BS (2009) Functional disturbances within frontostriatal circuits across multiple childhood psychopathologies. Am J Psychiatry 166(6):664–674
12. Grados MA (2010) The genetics of obsessive–compulsive disorder and Tourette syndrome: an epidemiological and pathway-based approach for gene discovery. J Am Acad Child Adolesc Psychiatry 49(8):810–819
13. Pauls DL (1992) The genetics of obsessive compulsive disorder and Gilles de la Tourette's syndrome. Psychiatr Clin North Am 15(4):759–766
14. Pauls DL, Towbin KE, Leckman JF, Zahner GE, Cohen DJ (1986) Gilles de la Tourette's syndrome and obsessive–compulsive disorder. Evidence supporting a genetic relationship. Arch Gen Psychiatry 43(12):1180–1182
15. Stewart SE, Illmann C, Geller DA, Leckman JF, King R, Pauls DL (2006) A controlled family study of attention-deficit/hyperactivity disorder and Tourette's disorder. J Am Acad Child Adolesc Psychiatry 45(11):1354–1362
16. Comings DE, Comings BG (1984) Tourette's syndrome and attention deficit disorder with hyperactivity: are they genetically related? J Am Acad Child Psychiatry 23(2):138–146
17. Pauls DL, Hurst CR, Kruger SD, Leckman JF, Kidd KK, Cohen DJ (1986) Gilles de la Tourette's syndrome and attention deficit disorder with hyperactivity. Evidence against a genetic relationship. Arch Gen Psychiatry 43(12):1177–1179
18. O'Rourke JA, Scharf JM, Platko J, Stewart SE, Illmann C, Geller DA, King RA, Leckman JF, Pauls DL (2011) The familial association of Tourette's disorder and ADHD: the impact of OCD symptoms. Am J Med Genet B Neuropsychiatr Genet 156(5):553–560

19. Coffey BJ, Miguel EC, Biederman J, Baer L, Rauch SL, O'Sullivan RL, Savage CR, Phillips K, Borgman A, Green-Leibovitz MI, Moore E, Park KS, Jenike MA (1998) Tourette's disorder with and without obsessive–compulsive disorder in adults: are they different? J Nerv Ment Dis 186(4):201–206
20. Wanderer S, Roessner V, Freeman R, Bock N, Rothenberger A, Becker A (2012) Relationship of obsessive–compulsive disorder to age-related comorbidity in children and adolescents with Tourette syndrome. J Dev Behav Pediatr 33(2):124–133
21. Lewin AB, Chang S, McCracken J, McQueen M, Piacentini J (2010) Comparison of clinical features among youth with tic disorders, obsessive–compulsive disorder (OCD), and both conditions. Psychiatry Res 178(2):317–322
22. Tukel R, Polat A, Ozdemir O, Aksut D, Turksoy N (2002) Comorbid conditions in obsessive–compulsive disorder. Compr Psychiatry 43(3):204–209
23. Sukhodolsky DG, Scahill L, Zhang H, Peterson BS, King RA, Lombroso PJ, Katsovich L, Findley D, Leckman JF (2003) Disruptive behavior in children with Tourette's syndrome: association with ADHD comorbidity, tic severity, and functional impairment. J Am Acad Child Adolesc Psychiatry 42(1):98–105
24. Carter AS, O'Donnell DA, Schultz RT, Scahill L, Leckman JF, Pauls DL (2000) Social and emotional adjustment in children affected with Gilles de la Tourette's syndrome: associations with ADHD and family functioning. J Child Psychol Psychiatry 41(2): 215–223
25. Spencer T, Biederman J, Coffey B, Geller D, Wilens T, Faraone S (1999) The 4-year course of tic disorders in boys with attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 56(9):842–847
26. Roessner V, Becker A, Banaschewski T, Freeman RD, Rothenberger A (2007) Developmental psychopathology of children and adolescents with Tourette syndrome–impact of ADHD. Eur Child Adolesc Psychiatry 16(Suppl 1):24–35. doi:10.1007/s00787-007-1004-6
27. Dykens E, Leckman J, Riddle M, Hardin M, Schwartz S, Cohen D (1990) Intellectual, academic, and adaptive functioning of Tourette syndrome children with and without attention deficit disorder. J Abnorm Child Psychol 18(6):607–615
28. Haddad ADM, Umoh G, Bhatia V, Robertson MM (2009) Adults with Tourette's syndrome with and without attention deficit hyperactivity disorder. Acta Psychiatr Scand 120(4):299–307
29. Leckman J, King R, Gilbert D, Coffey B, Singer H, Dure L, Grantz H, Katsovich L, Lin H, Lombroso P, Kawikova I, Johnson D, Kurlan R, Kaplan E (2011) Streptococcal upper respiratory tract infections and exacerbations of tic and obsessive–compulsive symptoms: a prospective longitudinal study. J Am Acad Child Adolesc Psychiatry 50(2):108–118
30. Kurlan R, Johnson D, Kaplan E (2008) Streptococcal infection and exacerbations of childhood tics and obsessive–compulsive symptoms: a prospective blinded cohort study. Pediatrics 121(6): 1188–1197
31. Swedo SE, Leonard HL, Garvey M, Mittleman B, Allen AJ, Perlmutter S, Lougee L, Dow S, Zamkoff J, Dubbert BK (1998) Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections: clinical description of the first 50 cases. Am J Psychiatry 155(2):264–271
32. American Psychiatric Association (2000) Diagnostic and statistical manual of mental disorders: DSM-IV-tr, 4th edn. American Psychiatric Association, Washington
33. Shaffer D, Fisher P, Lucas CP, Dulcan MK, Schwab-Stone ME (2000) NIMH diagnostic interview schedule for children version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. J Am Acad Child Adolesc Psychiatry 39(1):28–38
34. Leckman JF, Riddle MA, Hardin MT, Ort SI, Swartz KL, Stevenson J, Cohen DJ (1989) The Yale Global Tic Severity Scale: initial testing of a clinician-rated scale of tic severity. J Am Acad Child Adolesc Psychiatry 28(4):566–573
35. Scahill L, Riddle MA, McSwigginHardin M, Ort SI (1997) Children's Yale-Brown Obsessive Compulsive Scale: reliability and validity. J Am Acad Child Adolesc Psychiatry 36(6):844–852
36. DuPaul GJ (1991) Parent and teacher ratings of ADHD symptoms: psychometric properties in a community-based sample. J Clin Child Psychol 20(3):245–253
37. March J (1997) The multidimensional anxiety scale for children (MASC): factor structure, reliability, and validity. J Am Acad Child Adolesc Psychiatry 36(4):554–565
38. Kovacs M (1985) The Children's Depression Inventory (CDI). Psychopharmacol Bull 21(4):995–998
39. Kaufman J, Birmaher B, Brent D, Rao U, Flynn C, Moreci P, Williamson D, Ryan N (1997) Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL): initial reliability and validity data. J Am Acad Child Adolesc Psychiatry 36(7):980–988
40. Cohen S, Kamarck T, Mermelstein R (1983) A global measure of perceived stress. J Health Soc Behav 24(4):385–396
41. Shaffer D, Gould MS, Brasic J, Ambrosini P, Fisher P, Bird H, Aluwahlia S (1983) A Children's Global Assessment Scale (CGAS). Arch Gen Psychiatry 40(11):1228
42. Kadesjö B, Gillberg C (2000) Tourette's disorder: epidemiology and comorbidity in primary school children. J Am Acad Child Adolesc Psychiatry 39(5):548–555
43. Freeman RD (2000) An international perspective on Tourette syndrome: selected findings from 3,500 individuals in 22 countries. Dev Med Child Neurol 42(7):436–447
44. Pitman RK (1987) Pierre Janet on obsessive–compulsive disorder (1903). Review and commentary. Arch Gen Psychiatry 44(3): 226–232
45. Palumbo D, Kurlan R (2007) Complex obsessive compulsive and impulsive symptoms in Tourette's syndrome. Neuropsychiatr Dis Treat 3(5):687–693