Tic-Related Versus Tic-Free Obsessive-Compulsive Disorder: Clinical Picture and 2-Year Natural Course

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ABSTRACT

Objective: The tic-related subtype of obsessive-compulsive disorder (OCD) has a distinct clinical profile. The course of tic-related OCD has previously been investigated in treatment studies, with inconclusive results. This study aimed to compare clinical profiles between tic-related and tic-free OCD patients and to establish the influence of tics on the 2-year natural course in adult OCD patients.

Methods: Within the Netherlands OCD Association cohort, 377 patients with a current *DSM-IV* diagnosis of OCD were divided into a tic-related group (28%) and a tic-free group and compared on clinical variables with *t* tests or χ^2 tests. Linear mixed-model analyses were used to compare the 2-year course between the groups, with the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) as primary outcome measure. Data were collected from 2005 to 2007 and from 2007 to 2009.

Results: Compared to patients with tic-free OCD, those with tic-related OCD reported earlier disease onset ($P = .009$) and more symmetry/ordering symptoms ($P = .002$). Overall symptom severity was similar in both groups. Patients with tic-related OCD reported increased traits of attention-deficit hyperactivity ($P < .001$) and autism ($P = .005$) compared to the tic-free OCD group. Clinical improvement at 2-year follow-up (mean = 5.3-point decrease on the Y-BOCS, $P < .001$, 95% CI = 4.3 to 6.3) was not significantly moderated by tic status ($P = .24$). This remained unchanged after correcting for baseline differences.

Conclusions: Tics do not critically affect the 2-year course of adult OCD, but tic-related OCD shows differences from tic-free OCD, such as early onset and increased autism and ADHD traits, that may indicate a neurodevelopmental subtype.

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Obsessive-compulsive disorder (OCD) is a disabling disorder that often runs a chronic course.[1–3] Although OCD is considered as a single disease entity, its phenotypical expression is heterogeneous, and lifetime comorbidity with other psychiatric disorders including affective and anxiety disorders is 80%–90%.[4,5] Tic disorders are reported in 17%–29% of adult OCD patients.[2,6,7] A further characterization of the heterogeneity in OCD is important, as identification of more homogeneous subphenotypes may aid in identifying genes involved in its pathophysiology and lead to more tailored treatment strategies. One proposed subtype is tic-related OCD,[8] which is now included in *DSM-5*.

Previous reports have suggested that OCD patients with a lifetime history of tics may differ in clinical presentation, comorbidity patterns, neurobiological and genetic underpinnings, and treatment responsiveness. Tic-related OCD occurs more frequently in men,[6,9,10] more often has an early onset,[6,9,11,12] and is highly familial.[13] Patients with tic-related OCD report more sensory phenomena and higher rates of symmetry/ordering symptoms[14,15] and autistic traits.[16] Furthermore, elevated rates of attention-deficit/hyperactivity disorder (ADHD) in OCD[17] may be attributed to the tic-related subtype since ADHD is associated with tic disorders.[18]

Treatment studies have shown less effectiveness of selective serotonin reuptake inhibitors (SSRIs) in tic-related pediatric OCD.[19,20] A retrospective case-control study[21] in 66 adult patients indicated a less favorable response to fluvoxamine in tic-related versus tic-free OCD. However, more recent studies[12,22–24] have reported no critical effect of tics on treatment response, suggesting that tic relatedness has no effect on OCD treatment outcome in adults (Table 1). Male gender and early age at onset, both associated with tic-related OCD, were previously shown to decrease the likelihood of remission in OCD[25] and could mediate an unfavorable course. Few long-term follow-up data from treatment studies are available to clarify this issue, and to date, no naturalistic studies have investigated the influence of comorbid tics on clinical outcome. The ongoing Netherlands OCD association (NOCDA) study is the largest cohort to date, with 419 adult OCD patients with systematic natural follow-up.[26]

The first goal of this study was to characterize the clinical profile of tic-related OCD compared with tic-free OCD, extending previous findings by including data on comorbidity with ADHD and autism spectrum disorders. The second aim was to compare the 2-year course of OCD between tic-related and tic-free patients.

METHODS

Sample

Data were obtained from the NOCDA study, of which the details have been described elsewhere.[26] In brief, NOCDA is an ongoing 6-year

Clinical Points

- Tic-related and tic-free obsessive-compulsive disorders (OCD) have a different clinical presentation, but both subtypes run a similar natural course in adult patients.
- Clinicians should pay attention to features of other neurodevelopmental disorders in tic-related OCD that could lead to changes in treatment strategies.

naturalistic cohort study aiming to establish the course of OCD and determinants of long-term outcome. Over a period of 4 years, 687 adult OCD patients were invited to participate in the study during intake assessments. In total, 419 patients (60.9%) with a lifetime diagnosis of OCD were included. All participants signed informed consent forms, and the study was approved by the medical ethics committee of the VU University Medical Center, Amsterdam, the Netherlands (October 2005). The Supplementary Methods contains additional information on NOCDA. Five participants were excluded because tic screening was missing, and 37 participants were excluded because they did not have a current (1-month) diagnosis of OCD. The remaining sample consisted of 377 OCD patients. Data collected at baseline (from 2005 to 2007) and 2-year follow-up measurements (from 2007 to 2009) were used for this report.

Power Considerations

To calculate what effect sizes could reliably be detected with the included number of participants, a sensitivity analysis for between-within effects of repeated measures analysis was performed using G-Power,[27] with an α set to .05 and a β of .2 (power of 80%). The current sample size was sensitive to detect a small size effect of tics on the course of OCD ($f = 0.14$, equaling Cohen $d = 0.28$).

Assessments at Baseline

Demographic characteristics (age, gender, and education level), use of medication, and the presence of OCD or tic disorders in first-degree relatives were recorded. Lifetime and current *DSM-IV* diagnoses (including OCD) were assessed with the Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders-Research Version, Patient Edition.[28] The age at which patients first fulfilled *DSM-IV* criteria for OCD was marked as the age at onset. Early onset was defined as onset before the age of 20 years, based on previously reported admixture analyses in the same cohort.[29] A life chart interview[30] was used to assess retrospective OCD symptoms, and *chronicity* was defined as the presence of moderate to severe OCD symptoms during the 2 years prior to the baseline interview.[31] An 80-item adapted, self-report version of the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) symptom checklist[32] (see Supplementary Methods for details on the adaptation) was used to establish the presence of 4 OCD symptom dimensions[33]: aggression/checking (20 items), symmetry/ordering (10 items), contamination/washing (9 items), and hoarding (2 items). The interview version of the 10-item Y-BOCS severity scale (0–40) was used to measure obsessive-compulsive symptom severity.

Patients with lifetime tics were included in the tic-related group. Tics were evaluated with a 10-item tic screener (Supplementary Methods), followed by a complete tic interview when the screen was positive (the Yale Global Tic Severity Scale [Y-GTSS][34]). The 18-item ADHD Rating Scale-IV[35] is an interview based on *DSM-IV* criteria for ADHD (9 items on inattention and 9 items on hyperactivity-impulsivity). A version translated and validated in an adult Dutch population[36] was used to establish the presence of ADHD traits.

Autistic traits were rated using the 50-item Autism-Spectrum Quotient[37] (range, 50–200). Second, each item

Table 1. Overview of Treatment Studies That Compare Tic-Related OCD and Tic-Free OCD in Adults

Study	Treatment	No. of Participants	Mean age, y	Outcome Measure	Follow-Up	Results
McDougle et al (1993)[21]	Retrospective medication case-control study	33 with tics 33 without tics	30	Y-BOCS and CGI	No long-term follow-up	Tic-related OCD showed more unfavorable response to fluvoxamine than tic-free OCD
Rosario-Campos et al (2001)[12]	12-wk medication trial	21 early vs 21 late onset Percentage of tics not reported	32	>40% decrease in Y-BOCS	No long-term follow-up	No effect of tics on treatment response Early onset associated with more severe illness and tics
Shavitt et al (2006)[23]	14-wk medication trial	41 34% tics	31	Y-BOCS decrease	No long-term follow-up	No effect of tics on treatment response Presence of sensory phenomena associated with better response
Husted et al (2007)[24]	8-wk open-label medication trial	74 18% tics	34	>25% decrease in Y-BOCS and Y-BOCS <16 and CGI 1 or 2	No long-term follow-up	No differences between tic-related and tic-free OCD
Jakubovski et al (2013)[22]	Medication vs CBT trial	88 CBT 108 SSRI	34	Response: >35% decrease in Y-BOCS Remission: Y-BOCS <9	Naturalistic follow-up every 3–6 mo until 2 y (75 patients)	Family history of tics associated with higher Y-BOCS, between 18-mo and 2-y follow-up No effect of tic disorders on outcome

Abbreviations: CBT = cognitive-behavioral therapy, CGI = Clinical Global Impressions, OCD = obsessive-compulsive disorder, SSRI = selective serotonin reuptake inhibitor, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

Table 2. Demographic and Clinical Characteristics of Tic-Related and Tic-Free OCD and Group Differences at Baseline

Characteristic	OCD Without Tics (n = 270, 72%)	OCD With Tics (n = 107, 28%)	*t*	*df*	*P* Value	95% CI of the Difference
Demographic measures						
Age, mean (SD), y	37 (10.8)	35 (11.3)	1.2	375	.24	−1.0 to 3.9
Gender, n (%)						
Female	161 (60)	52 (49)	3.8[a]	1	.05	NA
Male	109	55				
Education (no. of years), mean (SD)	13 (3.1)	12 (3.4)	3.3	374	.001	0.5 to 1.9
Clinical measures						
Late-onset diagnosis (> 19 y), n (%)[b]	101 (42)	27 (27)	6.9[a]	1	.009	NA
Age at OCD onset, mean (SD), y	19 (9.8)	16 (8.1)	2.7	223	.008	0.7 to 4.7
Chronicity, n (%)[c]	171 (63)	61 (59)	0.70[a]	1	.40	NA
Family history of OCD, n (%)[d]			11.7[a]	3	.008	NA
0[e]	161 (60)	72 (69)				
1	74 (27)	20 (19)				
2	28 (10)	20 (19)				
≥ 3[e]	7 (3)	9 (9)				
Family history of tics, n (%)[d]			27.9[a]	3	< .001	NA
0	238 (88)	72 (69)				
1	27 (10)	20 (19)				
2	5 (2)	9 (9)				
≥ 3	0 (0)	4 (4)				
Y-BOCS severity score, mean (SD)	21.3 (6.7)	21.1 (7.9)	0.13	167	.9	−1.6 to 1.8
BDI score, mean (SD)	15.6 (9.3)	17.5 (11.7)	−1.4	143	.17	−4.5 to 0.8
BAI score, mean (SD)	18.4 (11.9)	18.1 (12.5)	.21	355	.84	−2.5 to 3.1
Total ADHD symptom score, mean (SD)	4.9 (3.7)	6.7 (3.9)	−4.2	372	< .001	−2.7 to −1.0
Attention deficit subscore	2.8 (2.3)	3.9 (2.4)	−3.9	375	.002	−1.6 to −0.5
Hyperactivity subscore	2.05 (2.1)	2.8 (2.4)	−2.6	171	.009	−1.2 to −0.2
Autism-Spectrum Quotient score, mean (SD)	113.6 (15.5)	119.0 (17.4)	−2.8	356	.005	−9.1 to −1.6
Probable autism spectrum disorder, n (%)[f]	12 (5)	13 (13)	8.0[a]	1	.005	NA
Y-BOCS, mean (SD)						
Check/aggression (range, 0–20)	4.5 (3.2)	5.1 (4.0)	−1.5	155	.15	−1.5 to 0.2
Symmetry/ordering (range, 0–10)	2.4 (2.6)	3.4 (3.0)	−3.1	164	.002	−1.7 to −0.4
Contamination/cleaning (range, 0–9)	2.2 (2.4)	2.5 (2.5)	−1.1	367	.29	−0.8 to 0.3
Hoarding (range, 0–2)	0.3 (0.6)	0.4 (0.7)	−1.5	170	.15	−0.3 to 0.04
Current medication use, n (%)						
Any antidepressant	162 (60)	69 (65)	0.65[a]	1	.42	NA
SSRI	112 (42)	47 (44)	0.19[a]	1	.67	NA
TCA	37 (14)	13 (12)	0.16[a]	1	.69	NA
Antipsychotic	45 (17)	20 (19)	0.22[a]	1	.63	NA
Psychostimulant	0 (0)	5 (5)	12.8[a]	1	.000	NA

[a] χ^2.
[b] Because of missing data, n=242 for OCD without tics and n=101 for OCD with tics.
[c] Because of missing data, n = 104 for OCD with tics.
[d] Number of first-degree relatives with obsessive-compulsive symptoms or tics.
[e] Because of missing data, n=105 for OCD with tics.
[f] Because of missing data, n = 260 for OCD without tics and n = 99 for OCD with tics.
Abbreviations: ADHD = attention-deficit/hyperactivity disorder, BAI = Beck Anxiety Inventory, BDI = Beck Depression Inventory, NA = not applicable, OCD = obsessive-compulsive disorder, SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

was dichotomized as present (1) or absent (0) according to Baron-Cohen et al,[37] with a cutoff at 32 or higher indicative for the presence of an autism spectrum disorder. Subscales on the ADHD Rating Scale and the Autism Quotient are shown in eTable 1. The presence and severity of depressive and anxiety symptoms were measured with the self-rated Beck Depression Inventory[38] and Beck Anxiety Inventory.[39]

Follow-Up Assessments

At 2-year follow-up, comprehensive assessments including interviews and questionnaires were repeated. The Y-BOCS severity scores were used as the main outcome measure of disease severity for this study. During the follow-up period, participants received treatment as usual tailored to their individual needs. Medication use was recorded at follow-up (eTable 2). Complete 2-year follow-up data were present in 203 (75%) of the tic-free OCD group and 70 (65%) of the tic-related group (Supplementary Results describes characteristics of the participants without follow-up).

Statistical Analyses

Statistical analyses were conducted with SPSS version 20 (IBM Corp; Armonk, New York). Demographic and clinical variables at baseline were compared between the tic-related and tic-free groups with 2-tailed independent sample *t* tests for continuous variables and χ^2 tests for categorical variables, with significance set at $P < .05$. To examine the 2-year course of symptom severity between groups, linear mixed models

Table 3. Lifetime Comorbidity Rates With *DSM-IV* Diagnoses

	OCD Without Tics (n = 270)		OCD With Tics (n = 107)			
Lifetime Comorbidity	n	%	n	%	$\chi^2(df=1)$	*P* Value
Comorbid (SCID-I/P) diagnosis						
Major depressive disorder	156	58	58	54	0.4	.53
Dysthymic disorder	14	5	7	7	0.3	.61
Bipolar disorder	6	2	7	7	4.3	.04
Social anxiety disorder	62	23	29	27	0.7	.40
Panic disorder with/without agoraphobia	58	22	25	23	0.2	.69
Generalized anxiety disorder	24	9	11	10	0.2	.68
Posttraumatic stress disorder	10	4	8	8	2.4	.12
Specific phobia	29	11	10	9	0.2	.69
Psychotic disorders	14	5	4	4	0.4	.55
Substance dependence	26	10	15	14	1.5	.22
Somatoform disorders[a]	11	4	11	10	5.4	.02
Eating disorders[b]	35	13	6	6	4.3	.04
No. of lifetime comorbid diagnoses					1.3 ($df=3$)	.73
0	61	23	22	21		
1	75	28	26	24		
2	69	26	33	31		
≥ 3	65	24	26	24		
No. of current comorbid diagnoses					0.2 ($df=3$)	.98
0	122	45	46	43		
1	85	32	34	32		
2	39	14	17	16		
≥ 3	24	9	10	9		

[a]Hypochondriasis in 12 patients, pain disorder in 4 patients, body dysmorphic disorder in 8 patients, somatization disorder in 2 patients, and undifferentiated somatoform disorder in 1 patient. The total number is higher than 22 because some patients had more than 1 comorbid somatoform disorder.
[b]Anorexia nervosa in 13 patients, bulimia nervosa in 8 patients, eating disorder not otherwise specified in 20 patients. There were no significant group differences for the separate eating disorders.
Abbreviations: OCD = obsessive-compulsive disorder, SCID-I/P = Structured Clinical Interview for *DSM-IV-TR* Axis I Disorders-Research Version, Patient Edition.

were used. Linear mixed models account for missing data due to dropout without the need for data imputation.[40] The first model included a regressor for the change in Y-BOCS between baseline and follow-up, a regressor for group (to account for baseline differences in Y-BOCS between groups), and a regressor to test the interaction between change in Y-BOCS and group. All variables were entered as fixed effects, with subject as the only random factor. The analysis was repeated excluding those patients who reported tics in the past, but no current tics. Additionally, each variable that differed between groups at baseline was tested for interaction with Y-BOCS change over time. Each significant interaction was added as a regressor to the model to test if this changed the effect of tics on the 2-year course.

RESULTS

Between-Group Differences on Baseline Characteristics

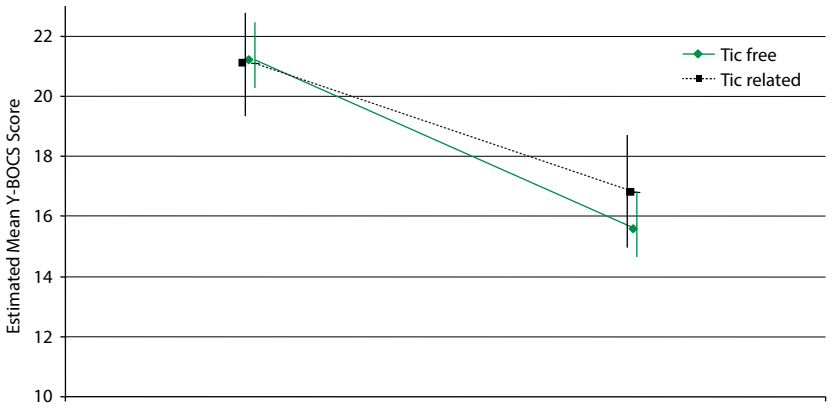
Of 377 OCD patients, 107 (28%) were tic related and 270 (72%) were tic free. The majority of the tic-related group (n = 75, 70%) currently reported tics, and the mean ± SD Y-GTSS for this group was 9.7 ± 9 (range, 0–39). Table 2 shows characteristics of both groups. Gender distribution showed a (trend level) larger proportion of men in the tic-related group (51% vs 40% in tic-free OCD). Obsessive-compulsive symptom severity at baseline was similar across groups. The tic-related OCD group reported more symmetry/ordering symptoms and more often an early onset of OCD. In both groups, a similar proportion had chronic OCD symptoms during the 2 years previous to the baseline interview. Patients with tic-related OCD reported a higher proportion of relatives with tic disorders and high familial load (2 relatives or more) for OCD. Patients with tic-related OCD reported increased ADHD and autistic traits but similar severity of depressive and anxiety symptoms.

The overall number of current or lifetime comorbid diagnoses did not differ between groups, nor did comorbidity with depression or anxiety disorders. Lifetime comorbid bipolar and somatoform disorders occurred more frequently in tic-related OCD, and eating disorders occurred more frequently in tic-free OCD (Table 3). Current comorbidity patterns did not differ much from lifetime comorbidity (eTable 3).

Natural Course of Tic-Related and Tic-Free OCD

Linear mixed models analysis showed a significant main effect of time on the Y-BOCS, with a mean decrease on the Y-BOCS of 5.3 points in 2 years ($F_{1,328} = 114$, $P < .001$, 95% CI = 4.3 to 6.3), but no effect of group ($F_{1,570} = 0.01$, $P = .91$)

Figure 1. Y-BOCS Score at Baseline and at 2-Year Folllow-Up For Patients With Tic-Related and Tic-Free OCD



	Estimated Mean	95% CI	Estimated Mean	95% CI
Tic free	21.2	20.3–22.2	15.6	14.5–16.6
Tic related	21.1	19.6–22.6	16.8	15.0–18.6

Abbreviations: OCD = obsessive-compulsive disorder, Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

and no interaction between group and time ($F_{1,333} = 1.4$, $P = .24$), indicating that both groups had a similar course of symptom severity over 2 years. Figure 1 shows estimated mean Y-BOCS values and 95% CIs for both groups and the change over 2 years. Comparing only the subgroup with current tics (n = 75) with the tic-free group revealed similar results (interaction between group and Y-BOCS change: $F_{1,308} = 0.8$, $P = .39$).

The Y-BOCS symmetry/ordering subscore, Autism-Spectrum Quotient score, ADHD score, disease onset, family history of OCD and tics, education, and gender distribution differed between groups at baseline (Table 2). Each variable was tested for interaction with change in Y-BOCS by performing separate linear mixed models. Only ADHD symptoms interacted with the change in Y-BOCS at trend level ($F_{1,338} = 3.8$, $P = .052$), with higher ADHD scores being associated with a greater decrease in Y-BOCS rating across the groups. Subsequently, ADHD scores and the interaction between ADHD and Y-BOCS change were added as covariates to the linear mixed model with tic status. The interaction between tic status and Y-BOCS change remained nonsignificant ($F_{1,333} = 2.5$, $P = .12$), indicating no mediating effect of ADHD symptoms on outcome for tic-related OCD. The number of current or lifetime comorbid diagnoses did not differ between groups, but to test the influence of comorbidity, a linear mixed model was performed within a subgroup of OCD patients with no current comorbid diagnosis (n = 122) and the tic-related OCD group with no other current comorbid diagnosis than tics (n = 46). No interaction between tics and change in Y-BOCS was detected ($F_{1,150} = 1.8$, $P = .19$). An analysis limited to the group with current tics (n = 75) showed no interaction between change in Y-BOCS and tic severity ($F_{1,59} = 0.3$, $P = .58$).

DISCUSSION

This study examined differences in clinical profile and natural course between tic-related and tic-free OCD in adult patients, using a large dataset and a prospective design. In line with the literature, 28% classified as having tic-related OCD, and according to expectations, this group contained fewer women, more often had early-onset OCD, and reported more symmetry/ordering symptoms. The lifetime comorbidity pattern was similar with regards to comorbid depression and anxiety disorders. The tic-related group showed a small increase in rates of somatoform and bipolar disorders and decreased rates of eating disorders. Additionally, the tic-related group reported increased traits of ADHD and autism spectrum disorders. Both groups showed a similar 2-year course with respect to obsessive-compulsive symptom severity.

Differences Between Tic-Related and Tic-Free OCD

The proportion of OCD patients with comorbid tics in the current study (28%) is remarkably similar to that in a cross-sectional study with 813 adult OCD patients (29%).[6] The association between early age at onset, symmetry symptoms, and tics is consistent with the literature.[14,15,41–43] To confirm the relation between symmetry/precision symptoms and tic-related OCD, a post hoc analysis was performed using the precision subscale of the Padua Inventory-Revised.[44] Precision behavior was increased in tic-related OCD (tic free, mean ± SD = 6.5 ± 5.8 vs tic related, 8.3 ± 6.6; $t_{159} = -2.4$, $P = .02$). Symmetry behavior appears to be consistently associated with tic-related OCD, but other symptom dimensions may not discriminate the tic-related subtype from tic-free OCD. The present study found no between-group differences for other symptom dimensions, in contrast

with previous studies that reported increased proportions of hoarding and aggressive obsessions in tic-related OCD[6,15,41] and with studies that found either decreased[9,10] or increased[41,45] frequencies of contamination symptoms in tic-related OCD. Correlating specific symptom dimensions to tic-related OCD apparently yields inconsistent findings, which may partly be explained by sample selection (adult vs pediatric, OCD patients vs Tourette syndrome patients), sample size, and the use of different approaches to define symptom dimensions.

Rates of anxiety disorders were similar in both groups, which is consistent with some[41] but not all studies.[6,11] The observed differences in rates of bipolar disorder, somatoform disorder, and ADHD concur with previous findings[11] in patients diagnosed with OCD and Tourette syndrome compared to patients with tic-free OCD. However, since the number of patients with comorbid bipolar or somatoform disorders is small, differences in comorbidity rates should be interpreted cautiously. Increased rates of eating disorders in tic-free OCD may be explained by a larger proportion of females in this group, since gender is the best predictor for eating disorders in OCD.[46] Nestadt et al[7] conducted a latent-class analysis to assess comorbidity patterns in 706 OCD patients. Tic disorders loaded both on a "tic-related class" (also high loading of social anxiety and grooming disorders) and on an "affective class" (also high loading of anxiety, mood, somatoform, and grooming disorders).[7] Tics seem to be associated with multiple comorbidity patterns, which may explain differences in observed comorbidity between studies.

ADHD traits were increased in the tic-related sample. An association between (early-onset) OCD, tics, and ADHD has been suggested by several authors,[11,15,18,29,47] and the combination of these disorders may have increased heritability.[48] The latter concurs with increased familiality in tic-related OCD in the present study. Reports on the interrelation between OCD, tics, and autism spectrum disorders in adults are scarce.[49] In a subsample of the current cohort, increased rates of autistic traits were present in OCD patients with ADHD[17] when compared to a control group. After reporting autistic traits in up to 20% of the OCD patients,[50] Bejerot et al[51] proposed an autistic subtype for OCD, characterized by increased symmetry, counting, and grooming behaviors. As an alternative to defining various different OCD subtypes (such as an early-onset, tic-related, or autism-related subtype), the combination of high familiality, tics, (early-onset) OCD, ADHD, and autistic traits could instead characterize a neurodevelopmental subtype of OCD. These disorders typically have a childhood onset, share (repetitive) symptoms, and are all, to a certain extent, characterized by executive dysfunction.[49] Aberrant development of (partially distinct and partially overlapping) frontostriatal brain circuits may be a shared neurobiological substrate for these disorders.[52,53] Future studies are needed to validate such a putative neurodevelopmental subtype by using multivariate techniques and by taking a cross-disorder, symptom-based approach.

Natural Course of Tic-Related OCD

The current study was carried out in a large, representative sample, sufficiently powered to detect a small effect of tics on the course of OCD. A similar course of tic-related and tic-free OCD is in line with most of the treatment studies[12,23,24] in adults reporting no influence of tics on treatment response. In the largest treatment study,[22] with 196 OCD patients randomized to CBT or medication, a negative effect of a family history of tics was found, but no effect of the presence of tics on outcome was reported. Family history (of tics or OCD) did not interact with outcome in the current study. Secondary analyses on remission rates also showed a comparable course for tic-related and tic-free OCD (see Supplementary Results). Reassuringly, confining the tic-related group to patients with current tics did not change the results, nor did tic severity relate to outcome. None of the clinical variables that differed between groups at baseline significantly influenced outcome. This is in contrast with Eisen et al,[25] who reported an effect of male gender and early onset on the 2-year course of OCD. However, this finding was not replicated at 5-year follow-up.[2] Our results are also in contrast with a pediatric OCD cohort in which tics appeared to be a predictor for remission during the 9 years that patients were followed.[54] Our sample may represent a relatively refractory type of tic-related OCD (not in remission after childhood), and these results cannot be generalized to pediatric populations.

It is surprising that neither autistic nor ADHD traits negatively impacted symptom severity at follow-up since ADHD was previously associated with a less favorable treatment outcome in children with OCD or Tourette syndrome[55–57] and autism with poor outcome in a small subgroup in a clinical trial.[58] But in line with our results, comorbid autism spectrum disorders did not influence the outcome in OCD patients during a 48-week clinical trial.[16] In the present study, elevated ADHD traits at baseline showed a trend-level significant interaction with better 2-year outcome across the groups. Since only 5 (tic-related) participants used psychostimulants, it is unlikely that this effect was caused by medication. Apparently, the influence of comorbid ADHD traits is somewhat different in adults than in children, but further studies are needed to investigate the role of comorbid ADHD in adult OCD.

Limitations

Since only 61% of the eligible outpatients who were approached agreed to participate in the original cohort of the NOCDA study,[26] results may not be generalizable to all OCD patients. However, clinical and demographic characteristics of the NOCDA cohort are similar to other large OCD studies,[4,6] suggesting that a possible selection bias is unlikely to be specific to the NOCDA study. Two-year dropout rates were 28%. Nonrandom loss to follow-up may have affected our results, even though participants without follow-up data did not differ on most clinical variables. Using mixed models is currently the best available way to deal with this issue and to estimate effects when data are missing.[40]

Another limitation is that no diagnostic interviews including reports of childhood behavior were used to establish ADHD and autism.

Additional waves that are currently collected will provide information on the course of tic-related OCD beyond 2 years.

CONCLUSION

Although both tic-related and tic-free OCD in adults run a similar 2-year natural course, the differences in clinical profile do support tic-related OCD as a subtype in *DSM-5*. Clinicians should pay attention to possible comorbidity with ADHD and autism spectrum disorders when treating patients with tic-related OCD. Tic-related OCD may be a neurodevelopmental subtype, but further investigations are necessary to validate this possibility.

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Supplementary material: See accompanying pages.

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Supplementary material follows this article.

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Supplementary Material

Article Title: Tic-related Versus Tic-Free Obsessive-Compulsive Disorder: Clinical Picture and 2-Year Natural Course

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List of Supplementary Material for the article

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Supplementary methods and results

Supplementary methods:

NOCDA study

The purpose and set up of the Netherlands OCD Association (NOCDA) study is described in Schuurmans et al [1]. We cite some sections from the original paper:

The Medical Ethical Committee VUmc gave their approval for the current study in October 2005 (NL41717.029.12) and all of the participating centres have acquired permission to cooperate in this study from their own local Medical Ethical Committees. All participants to the study received written and verbal information with regard to the study with specific attention drawn to their right to refuse or stop participating at any time during the study, as well as specific information on the investment required from the participant.

Data collection was performed by research assistants that were either research nurses or psychologists with considerable clinical experience with OCD. They received a two-day training course and regular follow-up training sessions to address questions raised during data collection. The first two interviews were audiotaped and monitored by the fieldwork coordinator to address any misunderstandings or errors in performing the measurements. All subsequent interviews were audiotaped and about 10% of the interviews was randomly monitored to assure consistent quality of the data collection.

Comprehensive baseline assessments consisted of interviews (11 interviews) and self reports (18 self report measures) a medical examination and blood sampling for DNA analysis. See table 1 in Schuurmans et al. [1] for all measures that were taken. The baseline assessment took approximately five hours (composed of three hours interview and two hours self-report). In some cases the assessment was done in two visits. If necessary the interviewers assisted participants with filling out self-reports. Notably not all measures taken at baseline were used for the current report.

The follow-up visit after two-years consisted of a comparable extensive assessment, including interviews and self-report measures and was performed by the same research assistants. From

these follow-up measurements only the Y-BOCS severity interview and information on the treatment over the past two years were used for the current paper.

Y-BOCS symptom checklist

The Y-BOCS symptom checklist (Y-BOCS-SC) was developed by the Obsessive Compulsive Foundation International Genetics Consortium and is a self-report version based on the original interview version of Goodman et al.[2]. Although some items from different dimensions were left out, factor analysis of the present version led to the same symptom dimensions as the original list [3]. Four symptom dimensions were assessed [4], including 'aggressive, sexual, religious, somatic obsessions, checking compulsions' (20 items), 'symmetry obsession, repeating, counting, ordering compulsions' (10 items), 'contamination obsessions and cleaning compulsions' (9 items) and hoarding obsessions and compulsions (2 items).

Tic screener.

"A tic is a sudden, non-purposeful, twitch or movement. Do you currently or did you ever experience any of the following (common) tics?"

1. Eyeblinking?
2. Other facial tics?
3. Head shaking?
4. Shrugging?
5. Cussing, using foul language?
6. Making sounds?
7. Growling?
8. Throat clearing/coughing/sniffing?

Tic disorder diagnoses

Tics were categorized in chronic motor tics (one or more motor tics), chronic vocal tics (one or more vocal tics), Tourette's Syndrome (two or more motor tics as well as one or more vocal tics) and tics not otherwise specified (one motor tic and one or more vocal tics) according to reported tics on the Yale Global Tic Severity Scale.

ADHD subcategories

Current scores of ADHD symptoms were used to calculate a probable diagnosis of ADHD of the inattentive subtype (6 or more symptoms present), hyperactive subtype (6 or more symptoms present) or combined (10 or more symptoms present). As reports on current symptoms were regarded more reliable than reports on past symptoms, only scores for current symptoms were used.

Autism subscales

The Autism Quotient was used to construct five subscales; contact and communication skills, social skills, attention switching, attention to detail and (lack of) fantasy [5].

Remission rates

A secondary analysis was conducted to determine remission rates in both groups, for which only cases with follow-up data were used. Remission was defined as (i) a decrease in the Y-BOCS of 7 points or more and (ii) a Y-BOCS score<13. The improvement criterion of the Y-BOCS of > 7 is derived from calculations of 'the reliable change index'. The formula to calculate this index takes into account the unreliability of a certain measurement instrument. Thus, by using the reliable change index, the clinician can be sure that the change measured with the Y-BOCS is not merely a chance finding, accounted for by the unreliability of the measurement instrument, but is in fact a 'really' observed change. In addition, we used a data driven cut-off point indicating remission on the Y-BOCS of 12, determined with the reliable change index set at > 1.96 [6-9].

Supplementary results

Tic disorder diagnoses

Within the tic-related group 36% of the patients had chronic motor tics, 12% chronic vocal tics, 52% Tourette's Syndrome and 7% tics not otherwise specified.

Participants with no follow-up data

Complete two-year follow-up data were present in 203 (75%) of the tic-free OCD group and 70 (65%) of the tic-related group. The subjects who were lost to follow-up had significantly lower levels of education (11.3 ± 3.2 vs. 13.0 ± 3.1 years of education in the follow-up sample $t_{(374)}$=-4.7, p<0.001). The participants with no two-year follow-up also had non-significantly higher Y-BOCS scores at baseline ($t_{(373)}$=1.7, p=0.09) and were non-significantly more often from the tic-related than tic-free group (χ^2=3.7, p=0.06). Within the tic-related OCD group, the participants with or without follow-up data available did not differ on tic severity ($t_{(73)}$=0.81, p=0.9).

Remission rates

No significant differences were found in remission rates between the two groups with complete follow-up data (non-tic related group: 32% remission; tic-related group: 24% remission; χ^2=1.3, p=0.25).

Supplementary eTable 1: Subscales for autism and probable diagnosis of ADHD.

	OCD without tics (n=270)		OCD with tics (n=107)				
	n	%	n	%	X^2	df	p
Probable current ADHD diagnosis (number)	52	19%	36	34%	8.9	1	0.003
ADHD combined type	10	4%	8	8%	6.1	3	0.11
ADHD hyperactive type	20	7%	17	16%	9.6	3	0.023
ADHD inattentive type	42	16%	27	25%	8.5	3	0.037
	mean	SD	mean	SD	t	df	p
Autism Quotient total score	113.6	15.5	119.0	17.4	-2.8	356	0.005
Social skills subscale	21.8	5.5	22.6	5.3	-1.2	356	0.23
Attention switching subscale	26.6	5.1	27.2	5.7	-0.9	356	0.39
Attention to detail subscale	23.1	5.2	24.6	5.4	-2.4	354	0.02
Communication subscale	20.3	4.2	21.8	4.7	-2.9	354	0.004
Imagination subscale	21.8	4.8	22.7	4.5	-1.6	353	0.12

Supplementary eTable 2: medication use at follow-up

medication use at follow-up	OCD without tics (n=184)		OCD with tics (n=59)			
	number	%	number	%	X^2(df=1)	p-value
any antidepressant	107	58%	35	59%	3.2	0.20
SSRI	76	41%	18	31%	5.1	0.079
TCA	19	10%	11	19%	6.1	0.047
antipsychotic	22	12%	12	20%	5.9	0.053
psychostimulant	0	0%	4	7%	15.9	0.00

SSRI; selective serotonine reuptake inhibitor, TCA; tricyclic antidepressant, df; degrees of freedom

Supplementary eTable 3: Current co-morbid axis I diagnoses

Current co-morbidity	OCD without tics (n= 270)		OCD with tics (n=107)			
	Number	%	Number	%	χ^2(df=1)	p
Major depressive disorder	53	20%	17	16%	0.7	0.40
Dysthymic disorder	14	5%	7	7%	0.3	0.61
Bipolar disorder	4	2%	0	0%	1.6	0.21
Social anxiety disorder	48	18%	24	22%	1.1	0.30
Panic disorder with or without agoraphobia	29	11%	6	6%	2.4	0.12
Generalized anxiety disorder	24	9%	11	10%	0.2	0.68
Post traumatic stress disorder	5	2%	7	7%	5.5	0.02
Specific phobia	23	9%	8	8%	0.1	0.74
Psychotic disorders	7	3%	3	3%	0.01	0.91
Substance dependence	10	4%	6	6%	0.7	0.41
Somatoform	11	4%	11	10%	5.4	0.02
Eating disorders	16	6%	3	3%	1.6	0.21

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