Impact of Age at Onset and Duration of Illness on the Expression of Comorbidities in Obsessive-Compulsive Disorder

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Background: Obsessive-compulsive disorder (OCD) patients usually experience comorbidities including tics, trichotillomania, body dysmorphic disorder, and mood and anxiety disorders. The present report verifies how age at onset of obsessive-compulsive symptoms and duration of illness are associated with comorbid diagnoses in OCD patients.

Method: Psychiatric comorbidity was assessed using a structured clinical interview in 161 consecutive outpatients referred for treatment between 1996 and 2001 who met DSM-IV criteria for OCD. Age at onset and duration of illness were retrospectively assessed by direct interviews.

Results: An earlier age at onset of obsessive-compulsive symptoms was associated with tic disorders, while longer illness duration was associated with depressive disorder (major depressive disorder or dysthymia) and social phobia.

Conclusion: Age at onset and duration of OCD illness are meaningful variables affecting the expression of comorbidities in OCD. Tic disorders and OCD may share common etiologic pathways. Depressive disorders, in contrast, may be secondary complications of OCD.

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Obsessive-compulsive disorder (OCD) patients frequently experience additional psychopathology. More specifically, tic disorders, trichotillomania, body dysmorphic disorder (BDD), eating disorders (anorexia and bulimia nervosa), mood disorders (both depressive and bipolar disorders), and anxiety disorders (mainly social phobia, simple phobia, panic disorder with or without agoraphobia, and generalized anxiety disorder) are frequently reported in patients with OCD.[1–6]

It has been proposed that age at onset of obsessive-compulsive (OC) symptoms is an important feature in distinguishing OCD subgroups.[7–10] It has also been reported that early-onset OCD patients have specific clinical correlates,[8] have higher comorbidity with tic disorders,[4,9] are more frequently male,[11] and have an increased familial loading for OCD.[12–14] However, there have been reports that the duration of illness might affect the OCD presentation as well.[15,16] Thus, differences in the frequencies of comorbidities in early- versus late-onset adult OCD patients could be artifacts of illness duration.

Trying to disentangle the effects of age at onset and duration of illness in OCD patients might have important clinical implications. For instance, if a specific comorbid disorder is secondary to the duration of illness, then early recognition and treatment of OCD will be extremely important and can reduce the risk of patients developing additional symptoms, as well as the potential for added disability.[17] Disorders associated with age at onset of OC symptoms may share common etiologic factors, adding support to the notion of specific OCD subtypes. However, these issues have not been answered in previous OCD literature.

Therefore, the current study was designed to verify how the age at onset of OC symptoms would affect the presence of comorbid diagnoses in OCD patients, taking into account the effects of duration of OCD illness. On the basis of previous findings,[1,8,9] we hypothesized that an earlier age at onset of OC symptoms would be associated with higher frequencies of tic disorders, BDD, trichotillomania, and eating disorders but not with mood disorders, which would be associated with duration of OCD illness.

Table 1. Frequency of Comorbid Psychiatric Diagnoses in 161 Obsessive-Compulsive Disorder Patients

Lifetime Comorbid Psychiatric Diagnosis	N (%)
At least 1 comorbid diagnosis	144 (89)
Tic disorders	64 (39)
Chronic motor/vocal tic disorder	34 (21)
Tourette's syndrome	30 (19)
Mood disorders	115 (71)
Depressive	100 (62)
Bipolar	15 (9)
Anxiety disorders	97 (60)
Agoraphobia with/without panic	27 (17)
Social phobia	63 (39)
Simple phobia	40 (25)
Generalized anxiety disorder	15 (9)
Posttraumatic stress disorder	6 (4)
Somatoform disorders	31 (19)
Body dysmorphic disorder	30 (19)
Hypochondriasis	1 (1)
Somatization	1 (1)
Eating disorders	17 (11)
Bulimia nervosa	5 (3)
Anorexia nervosa	6 (4)
Binge eating	6 (4)
Impulse-control disorders	30 (19)
Compulsive gambling	0 (0)
Compulsive buying	12 (7)
Pyromania	2 (1)
Trichotillomania	17 (10)
Kleptomania	6 (4)
Substance-related disorders	24 (15)
Psychotic disorders	5 (3)

METHOD

Our sample consisted of 168 consecutive outpatients referred to an OCD research program from 1996 to 2001. Referrals came from a university hospital (N = 96) and 2 private facilities (N = 72). Exclusion criteria were a history of cranial trauma (N = 1), refusal to complete interviews (N = 3), and comorbid diagnosis of schizophrenia (N = 3). After written informed consent was obtained, all subjects meeting DSM-IV criteria for OCD (N = 161) were interviewed.

Demographic characteristics were obtained by direct interview. Socioeconomic status was assessed according to a structured interview for Brazilian standards, which divides the population into 5 different statuses, A through E (A = upper class, B = upper-middle class, C = middle-middle class, D = low-middle class, E = poor class). Marital status was classified as married, never married, divorced, or widowed. Educational level was assessed by the number of years of education.

Interviewers were trained psychologists and psychiatrists from the OC Spectrum Disorder Project in the Department of Psychiatry of the University of São Paulo Medical School (São Paulo, Brazil). Each interview was reviewed by the first author, and diagnoses were assigned blindly by 2 psychiatrists (E.C.M. and R.G.S.) experienced in the evaluation of OCD patients, following a best-estimate procedure.[12]

Clinical Assessments

The presence and severity of OC symptoms and tics were determined by using the checklists and rating scales of the Yale-Brown Obsessive Compulsive Scale (YBOCS)[18,19] and the Yale Global Tic Severity Scale (YGTSS),[20] respectively.

Psychiatric Axis I comorbidity was assessed using the Structured Clinical Interview for DSM-IV[21] supplemented with additional modules based on DSM-IV criteria for Tourette's syndrome, chronic tic disorder, trichotillomania, kleptomania, compulsive gambling, and pyromania (available from the authors on request). Patients younger than 16 years were assessed with the Schedule for Affective Disorders and Schizophrenia, Epidemiologic Version,[22] administered to a parent. Subthreshold diagnoses were not considered. Lifetime diagnoses were used in the analysis.

Age at onset of OCD was defined as the earliest age that the patient remembered having OC symptoms and was assessed by direct interview with the patient as described elsewhere.[9] Duration of illness was defined as the difference between age at interview and age at onset of OC symptoms.

Statistical Analyses

Statistical analyses were performed using SPSS, version 10.0 (SPSS Inc., Chicago, Ill.). Categorical variables were compared on the bases of age at onset of OC symptoms and duration of OCD illness using the Student t test. A p value of $< .05$, 2-tailed, was considered significant.

To control for confounding covariates, psychiatric disorders present in more than 10% of our sample (Table 1) were selected for multivariate analysis. Only variables above a minimal prevalence in our sample were included in the multivariate analyses because logistic regression is not indicated for rare occurrences.[23] Stepwise logistic regression by likelihood ratio was used. Each psychiatric diagnosis was the dependent variable of a logistic model, and demographic characteristics (gender, years of education, socioeconomic status), age at onset of OC symptoms, duration of OCD illness, OCD severity, and comorbid tic disorder were the independent variables in all logistic models. For all stepwise variable selection procedures, the probability of F to enter the regression equations was set at 0.05, and to remove, at 0.10. Statistical power was maximized by collapsing disorders into broader categories including depressive disorders (major depressive disorder or dysthymia), bipolar mood disorders (bipolar type 1, 2, or unspecified), tic disorders (Tourette's syndrome or chronic motor/vocal tic disorders), eating disorders (bulimia, anorexia, or binge eating) and substance-related disorders (drug/alcohol abuse or dependence). Other disorders were analyzed individually.

Table 2. Comparison of Age at Onset of Obsessive-Compulsive Symptoms (OCS) and Illness Duration Between Patients With and Without Comorbid Psychiatric Diagnoses

	Patients With the Comorbid Diagnosis		Patients Without the Comorbid Diagnosis		
Comorbid Diagnosis	Mean	SD	Mean	SD	p Value[a]
Tic disorders					
Age at OCS onset, y	10.4	5.9	14.9	9.7	< .001
Illness duration, y	16.5	10.0	16.1	9.3	.748
Depressive disorder					
Age at OCS onset, y	12.6	8.2	13.9	9.6	.378
Illness duration, y	17.8	9.6	13.9	9.0	.013
Bipolar mood disorder					
Age at OCS onset, y	9.5	3.9	13.5	9.0	.003
Illness duration, y	15.6	8.3	16.4	9.7	.778
Social phobia					
Age at OCS onset, y	11.3	8.0	14.4	8.9	.029
Illness duration, y	19.1	10.6	14.4	8.4	.003
Eating disorder					
Age at OCS onset, y	10.2	4.4	13.5	9.0	.017
Illness duration, y	17.5	9.3	16.1	9.6	.572
Kleptomania					
Age at OCS onset, y	8.0	2.2	13.4	8.8	< .001
Illness duration, y	22.3	9.4	16.0	9.5	.085
Trichotillomania					
Age at OCS onset, y	10.3	4.8	13.4	8.9	.033
Illness duration, y	17.3	9.4	16.2	9.6	.620

[a]Derived from t tests.

RESULTS

Demographic and Clinical Characteristics

Fifty-nine percent (N = 95) of the patients were male and 41% (N = 66) were female. Their ages ranged from 12 to 59 years (mean [SD] age = 30 [10] years). Most of them (67%) had never been married, 46 (29%) were married, and 6 (4%) were divorced. They were distributed among all socioeconomic levels (A = 23%, B = 32%, C = 30%, D = 9%, and E = 3%). The mean (SD) number of years of education was 13 (5) years, ranging from 0 to 23 years. Patients had a mean age at onset of OC symptoms of 13.2 (8.7) years, ranging from 4 to 46 years. The mean illness duration in our sample was 16.3 (9.6) years, ranging from 1 to 46 years.

The mean YBOCS scores were 13.1 ± 3.6 for the obsession subscale and 13.5 ± 3.8 for the compulsion subscale.

As presented in Table 1, 144 patients (89%) had at least 1 comorbid diagnosis. The mean (SD) number of comorbid diagnoses was 2.9 (2.0). The frequencies of specific DSM-IV Axis I disorders are presented in Table 1. Depressive disorders, tic disorders, social phobia, and simple phobia were the most frequent comorbid disorders.

Univariate Analyses

Table 2 shows the associations between the mean age at onset of OC symptoms and duration of OCD illness and some comorbid disorders.

Tic disorders were significantly associated with an earlier onset of OC symptoms, and depressive disorders were significantly associated with duration of OCD illness but not with age at onset. An earlier onset of symptoms was also associated with bipolar disorders, eating disorders, kleptomania, and trichotillomania. Social phobia was associated with both age at onset and illness duration. Other disorders studied (drug/alcohol abuse, psychotic disorders, simple phobia, panic/agoraphobia, BDD) were not significantly associated with either of these parameters and are not shown in Table 2.

Multivariate Analyses

Table 3 presents a comparison of the results from the multivariate analyses for tic disorders, depressive disorders, and social phobia. Other independent variables such as gender, years of education, and socioeconomic status were not statistically significant in the regression models and are not described in the table.

The regression model represented in Figure 1 shows the decrease in the odds ratio (OR) for tic disorders as age at OCD onset increases. The regression model that describes the association of depressive disorder with duration of illness is presented in Figure 2. It is important to note that the risk for depressive disorders increases with a longer duration of OCD illness.

As described below, the results from the multivariate analyses for other comorbid disorders showed that variables such as gender, comorbid tic disorders, and OC symptom severity appeared to be better predictors of having the disorders than age at onset of OC symptoms or duration of illness.

For instance, BDD was associated with the presence of tic disorders (p = .034, OR = 2.528, 95% CI = 1.073 to 5.957), and eating disorders were associated with female gender (p = .023, OR = 3.6, 95% CI = 1.190 to 11.010).

Different results were found between social and simple phobia. While social phobia was associated only with illness duration, simple phobia was more frequently reported by women (p < .001, OR = 4.793, 95% CI = 2.013 to 10.023) and by patients with tics (p = .026, OR = 2.472, 95% CI = 1.159 to 5.736). No other anxiety disorders were associated with any of the variables included in regression analysis.

Substance abuse and dependence disorders were associated with neither age at onset of OC symptoms nor illness duration. However, the presence of lifetime substance-related disorder was associated with symptom severity, measured by YBOCS scores (OR = 1.09, 95% CI = 1.01 to 1.18, p = .029).

DISCUSSION

The current study replicates previous findings of high comorbidity rates among OCD patients.[1,5,17,24] In addition,

Table 3. Results of Stepwise Logistic Regression for the Most Frequent Comorbidities Among 161 OCD Patients

	Comorbid Disorder								
	Tic Disorder			Depressive Disorder			Social Phobia		
Covariate	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Age at onset of obsessive-compulsive symptoms	0.931	0.880 to 0.940	.008	NS	NS	NS	NS	NS	NS
Duration of OCD illness	NS	NS	NS	1.057	1.011 to 1.095	.006	1.055	1.016 to 1.094	.004
OCD severity measured by YBOCS score	NS	NS	NS	1.117	1.009 to 1.230	.030	NS	NS	NS

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

Figure 1. Odds Ratio for Lifetime Tic Disorders by Age at Onset of Obsessive-Compulsive Symptoms (binary logistic regression)

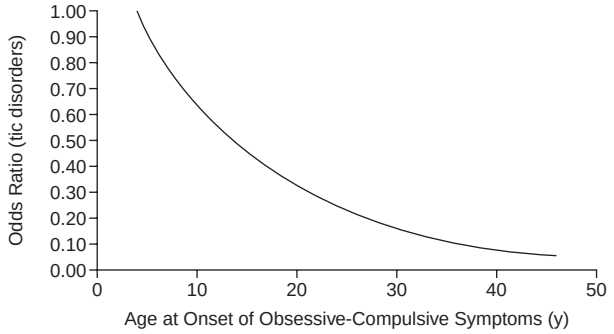
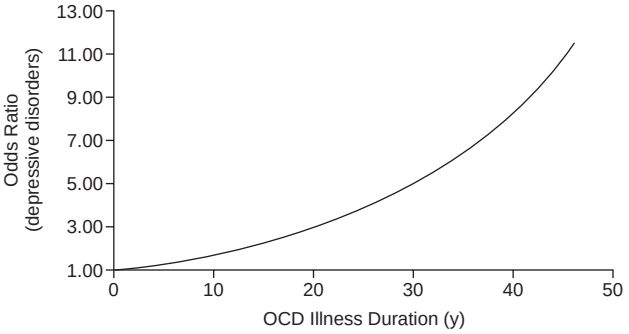


Figure 2. Odds Ratio for Lifetime Depressive Disorder by Duration of Obsessive-Compulsive Disorder (OCD) Illness (binary logistic regression)



it suggests different association patterns between comorbid diagnoses and early age at onset of OC symptoms and illness duration. More specifically, an early age at onset was associated with tic disorders, eating disorders, kleptomania, trichotillomania, and bipolar disorders. A longer duration of illness, on the other hand, was associated with depressive disorders. Social phobia was associated with both early onset and longer illness duration. When multiple confounding variables were controlled for, early age at onset of OC symptoms persisted as an important predictor of comorbid tic disorders, and longer illness duration persisted as an important predictor of depressive disorder and social phobia.

Previous clinical and genetic studies have suggested an association between tic disorders and early-onset OCD.[4,7,9,12,13,24,25] The results from the current study reinforce the idea that the tic-related OCD phenotype may represent a distinct OCD subgroup associated with early onset.

The association between depressive disorders and illness duration could be a consequence of the chronic course of OCD. Alternatively, major depressive disorder could be a risk factor for longer illness duration. In addition, the pathophysiology of OCD could make the brain more vulnerable to the development of additional psychopathology (manifested as depression or other comorbid disorders) as part of the natural history of OCD. Results from a recent OCD family study add support to the hypothesis that major depressive disorder is a consequence of OCD; the study showed higher rates of mood disorders in case relatives compared with control relatives only when the case relative also had OCD.[17]

Some epidemiologic and clinical studies have reported the onset of major depression both prior to[6] and later than[26] the onset of OCD. We could also speculate that depressive episodes that start early in the course of OCD could be part of bipolar disorder, since our results showed an association between bipolar disorder and early age at onset of OC symptoms in the univariate analyses. Other studies have also hypothesized that depressive disorders could be a complication of the chronic course of OCD while bipolar disorder and OCD might represent different manifestations of a single underlying diathesis.[27] However, the current study was not designed to answer these questions, and it was not possible to analyze the relationship between the ages at onset of depressive disorders and OCD in the current sample.

Social phobia was associated with both longer duration of OCD illness and early age at onset of OC symptoms in the univariate analysis, but only with illness duration in the multivariate analysis. Previous studies have reported that anxiety disorders, mainly social phobia, tend to occur early in the course of OCD.[28,29] In contrast with tic disorders, social phobia is not more prevalent among first-degree relatives of OCD probands when compared with controls.[17] It is important to mention that social phobia

may generate considerable subjective suffering and negative impact on work performance and social relationships[30] that could contribute to a worse OCD course.[31] In addition, patients with social phobia may delay seeking medical assistance due to difficulties inherent in the disorder (shyness) or because they do not expose themselves to social environments that could influence them to seek medical help. Therefore, we propose that social phobia is a risk factor for a longer OCD course. Further studies are necessary to confirm this hypothesis.

The results from the initial analyses also showed an association between an early onset of OC symptoms and kleptomania, trichotillomania, and eating disorders. Previous studies have already led to the hypothesis of a relationship between these disorders. For instance, trichotillomania has been associated with an OCD familial spectrum of disorders that includes BDD and grooming behaviors,[32] and it has been suggested that kleptomania could also be seen as part of the impulse-control disorders related to OCD.[1] Similarly, eating disorders, mainly anorexia, have been hypothesized to belong to the OC spectrum disorders,[33,34] an association also supported by recent family studies.[35,36] Taken together, these reports suggest that these disorders might share a common genetic and/or environmental vulnerability.

As mentioned earlier, BDD, along with tic disorders, is among the disorders with the most evidence of an association with OCD.[32] In the current study, BDD was associated with tic disorders by multivariate analyses, emphasizing previous findings suggesting a higher frequency of BDD in OCD patients with comorbid tics compared with patients with tics or OCD alone.[37] Future studies are necessary to clarify the reasons for this association.

Some limitations of this study should be noted. (1) Since the sample consisted of patients referred to a tertiary service, our patients could be more severely ill, with a higher number of comorbid diagnoses, and therefore it might not be possible to generalize to community samples. (2) Since most of our patients were adults, the sample does not include patients with early onset whose symptoms remitted during childhood or adolescence. (3) We relied on retrospective assessment of OC symptom onset, which may hamper the accuracy of our data. (4) As psychotic disorders and bipolar disorder tend to be given priority in treatment over OCD, patients with these diagnoses were rarely part of our sample, limiting the analysis of these disorders.

Despite these limitations, our findings suggest that age at onset of OC symptoms and duration of OCD illness are meaningful variables affecting the expression of comorbid disorders in OCD patients. Tic disorders and possibly trichotillomania may arise as a result of common etiologic pathways. Depressive disorders, in contrast, may be a secondary complication of OCD. Anxiety disorders such as social phobia may both reflect abnormalities in common neurobiological substrates and contribute as a risk factor for further psychopathology and more chronic course. This differential comorbidity pattern might have profound impact on the treatment of OCD patients.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

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