

ORIGINAL PAPER

Raşit Tükel · Handan Meteris · Ahmet Koyuncu · Alper Tecer · Olcay Yazıcı

The clinical impact of mood disorder comorbidity on obsessive-compulsive disorder

Received: 20 April 2005 / Accepted: 4 October 2005 / Published online: 12 May 2006

Abstract The present study examines the effect of concomitant major depressive or bipolar disorder on clinical symptoms of patients with obsessive-compulsive disorder (OCD). Forty-nine patients classified as OCD without a mood disorder, 26 classified as OCD with bipolar disorder (OCD-BD) and 42 classified as OCD with major depressive disorder (OCD-MDD) according to DSM-IV diagnostic criteria were included in the study. The groups were compared with respect to demographic variables and scores obtained on various scales. The OCD-BD group had more symmetry/exactness obsessions and ordering/arranging compulsions, and a more episodic course of illness and had better insight compared to the other two groups. Levels of anxiety, depression, disability and obsessive-compulsive symptom severity were significantly higher in the OCD-MDD group. The rate of social phobia was higher in OCD-BD patients, whereas the rates of generalized anxiety disorder and simple phobias were higher in OCD-MDD group. These findings suggest that comorbidity of major depressive disorder may increase the severity of OCD symptoms. On the other hand, bipolar disorder comorbidity may constitute a subgroup which is characterized by a higher rate of episodic course and better insight.

Key words obsessive-compulsive disorder · mood disorders · comorbidity · episodic course

Introduction

The comorbidity of obsessive-compulsive disorder (OCD) with depression has been investigated extensively. Studies on clinical samples have shown that 29.6%–43% of OCD patients have comorbid major depressive disorder (Rasmussen and Tsuang 1986; Rasmussen and Eisen 1988; Kolada et al. 1994; Okasha et al. 1994; Lensi et al. 1996; Perugi et al. 1997; Tükel et al. 2002). Coexistence of major depression with OCD was found to be related to chronicity and severity of obsessive-compulsive symptoms, poor response to treatment and bad prognosis (Angst and Dobler-Mikola 1985; Stavrakaki and Vargo 1986; Wittchen and Essau 1989; Hecht et al. 1989). In addition, OCD patients with non-bipolar major depression comorbidity had a higher number of suicide attempts and hospitalizations, had greater comorbidity with generalized anxiety disorder and caffeine abuse, compared to non-major depressive OCD patients (Perugi et al. 1997).

Angst et al. (2005) reported that OCD was significantly comorbid with bipolar I/II and minor bipolar disorders and anxiety states (generalized anxiety disorder, repeated panic attacks). Relatively few studies were conducted on bipolar disorder and OCD comorbidity. Various studies found bipolar disorder rates ranging from 2.7% to 17.7% in OCD patients (Kolada et al. 1994; Lensi et al. 1996; Perugi et al. 1997). Perugi et al. (1997) found that OCD with bipolar disorder (OCD-BD) patients had a significantly higher rate of sexual and religious obsessions, and a significantly lower rate of checking rituals. The authors also suggested that bipolarity should take precedence in diagnosis, course and treatment considerations when bipolar and obsessive-compulsive disorders coexist.

Strong evidence concerning the high prevalence of OCD among unipolar and bipolar disorder patients was obtained from the comorbidity studies (Chen and Dilsaver 1995; Kruger et al. 1995). Chen and Dilsaver (1995) found that the lifetime rates of suicidality and panic dis-

Prof. R. Tükel, M.D. (✉) · H. Meteris, M.D. · A. Koyuncu, M.D. · A. Tecer, M.D. · Prof. O. Yazıcı, M.D.
Istanbul University
Istanbul Faculty of Medicine
Department of Psychiatry
Capa Istanbul, Turkey
Tel.: +90-212/414-2000/31335
Fax: +90-212/274-4352
E-Mail: rtukel@superonline.com

order were significantly increased in the presence of concurrent OCD in the bipolar disorder group.

The aim of this study was to assess the impact of comorbid major depressive or bipolar disorder on the clinical features of obsessive-compulsive disorder in a clinical sample. It was also aimed to test the hypothesis that OCD patients with major depression or bipolar disorder comorbidity would show significant differences with respect to symptomatology and course of the disorder and that these would constitute clinically distinct subtypes. The patients with OCD were grouped as OCD with major depressive disorder (OCD-MDD), OCD with bipolar disorder (OCD-BD) and OCD without a mood disorder (OCD-non-mood disorder) (OCD-NOMD). The three groups were compared with respect to sociodemographical features, symptom severity, course of illness, insight, history of OCD in first-degree relatives and other comorbid axis I disorders.

Methods

A total of 115 consecutive OCD patients from the Anxiety Disorders Outpatient Clinic of the Psychiatry Department of Istanbul Faculty of Medicine were interviewed with the Structured Clinical Interview for DSM-IV/Clinical Version (SCID-I/CV) (First 1997) between March 2001 and March 2003. From these OCD patients, 5 were diagnosed with bipolar I, 2 were diagnosed with bipolar II, and 3 patients who developed a hypomanic episode while taking antidepressants were diagnosed as bipolar disorder not otherwise specified. Among the 42 patients who had current major depressive disorder, 29 patients were diagnosed with major depressive disorder, single episode, and 13 patients were diagnosed with major depressive disorder, recurrent. Fourteen patients without a current episode had a past history of major depressive disorder. Current or past history of mood disorder was not present in 49 of the 115 OCD patients.

Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) Symptom Checklist was applied to 208 consecutive bipolar disorder patients who were followed up by the Mood Disorders Outpatient Clinic of the Psychiatry Department of Istanbul Faculty of Medicine between March 2001 and July 2002, to determine OCD comorbidity. Current or past obsessive-compulsive symptoms were present in 41 patients. Forty patients were interviewed with SCID-I/CV; one patient who did not want to participate was excluded from the study. It was found that 16 out of 40 bipolar disorder patients had comorbid OCD diagnosis. According to SCID-I/CV results, 10 patients were diagnosed with bipolar I disorder, and 1 patient was diagnosed with bipolar II disorder. The diagnosis of bipolar disorder not otherwise specified was given to 3 patients who developed a manic episode and 2 patients who developed a hypomanic episode while on antidepressant medication.

Patients were diagnosed with bipolar disorder not otherwise specified when hypomanic or manic episodes appeared while taking antidepressant medication, but there was insufficient evidence to determine whether the mood symptoms were due to a medication or were primary.

Forty-nine patients grouped as OCD-NOMD, 26 grouped as OCD-BD and 42 grouped as OCD-MDD were included in the study. The groups were compared with respect to sociodemographical and clinical features. All patients in the OCD-BD group were assessed in the interepisodic interval of BD. OCD patients who had a past history of major depressive disorder, but not a current episode, were not included in the study. Patients with schizophrenia or related psychotic disorders or organic mental syndromes were also excluded from the study, whereas patients with a lifetime history of comorbid mood disorder with psychotic features were included. Written informed consent was obtained from all subjects.

All OCD patients were assessed with Y-BOCS (Goodman et al. 1989a, 1989b), the State Trait Anxiety Inventory (STAI) (Spielberger et al. 1970), the Hamilton Anxiety Rating Scale (HARS) (Hamilton 1959), the Hamilton Depression Rating Scale (HDRS) (Hamilton 1967), the Beck Depression Inventory (BDI) (Beck et al. 1961), the Overvalued Ideas Scale (OVIS) (Neziroglu et al. 1999), and the Sheehan Disability Scale (SDS) (Sheehan 1983). Diagnoses were made at the first interview and the assessments mentioned above were done at the second interview. All bipolar disorder patients were assessed and diagnosed during interepisodic intervals. A semistructured interview form developed by the investigators was used in order to determine the demographic and clinical characteristics of the cases.

OCD patients who did not recognize that their obsessions or compulsions were excessive or unreasonable for most of the time during the current episode were specified as "with poor insight" according to the DSM-IV (1994). The use of different criteria for "episodic" in various studies was noticeable (Ravizza et al. 1997; Perugi et al. 1998). In our study, episodic course is defined as a full remission of obsessive-compulsive symptoms for at least 6 months, independent from the systematic antiobsessive treatment (drug therapy with serotonin reuptake inhibitors or cognitive-behavioral therapy) with retrospective evaluation.

Statistical analysis was made using SPSS 9.0 for Windows (SPSS Inc, Chicago, IL). One-way ANOVA was applied for continuous variables, chi-square test for categorical variables. *Post hoc* comparisons were made with Scheffe procedure.

Results

There were no statistically significant differences between the OCD-NOMD, OCD-BD and OCD-MDD groups, with respect to age, sex, marital status, and age of onset of OCD in our study (Table 1). The rate of unemployment due to the current illness was significantly different between the groups ($p = 0.002$) (Table 1). Dual comparisons of the groups revealed that the rate of un-

Table 1 Demographic characteristics

| | Non-mood disorder (n = 49) n (%) | Bipolar (n = 26) n (%) | Major depressive (n = 42) n (%) | χ^2 | p |
|---------------------------------|--|------------------------------|---------------------------------------|----------|-------|
| Sex (female) | 28 (57.1) | 16 (61.5) | 26 (61.9) | 0.25 | NS |
| Marital status (married) | 19 (38.8) | 7 (26.9) | 16 (38.1) | 1.18 | NS |
| Not working due to the disorder | 2 ^a (4.1) | 9 ^b (34.6) | 11 ^b (26.2) | 12.72 | 0.002 |
| | mean (SD) | mean (SD) | mean (SD) | F | p |
| Age at assessment | 28.4 (10.9) | 32.3 (14.3) | 29.0 (10.7) | 1.00 | NS |
| Age at onset | 20.2 (9.4) | 19.4 (7.3) | 19.0 (8.7) | 0.22 | NS |

employment due to the current illness was significantly higher in the major depressive and OCD-BD groups when compared to the OCD-NOMD group.

There were significant differences between the groups on the mean scores of the HARS, HDRS, BDI, STAI-state, STAI-trait, Y-BOCS-obsession, Y-BOCS-compulsion, Y-BOCS-total, SDS-work, SDS-social life and SDS-family life ($p=0.0001$ for each) (Table 2). In post-hoc evaluation, mean HARS, HDRS, BDI, STAI, Y-BOCS and SDS scores were found to be significantly higher in the OCD-MDD group compared to the OCD-BD and OCD-NOMD groups (Table 2).

As a result of the assessment carried out with the Y-

BOCS Symptom Checklist to determine the distribution of obsessions and compulsions, the rate of symmetry/exactness obsessions was found to be higher in the OCD-BD group compared to the other two groups ($p=0.03$) (Table 3). Ordering/arranging compulsions were significantly more frequent in the OCD-BD group, compared to the other two groups ($p=0.004$) (Table 3). There were no significant differences between the groups regarding obsessions and compulsions other than symmetry/exactness and ordering/arranging (Table 3).

When the course of the illness was assessed, the number of patients who had an episodic course was signifi-

Table 2 Mean scores on measures of anxiety, depression, obsessive-compulsive symptomatology and disability

| | Non-mood disorder (n = 49) mean (SD) | Bipolar (n = 26) mean (SD) | Major depressive (n = 42) mean (SD) | F | p |
|---------------------|--|----------------------------------|---|-------|--------|
| HRSD | 7.1 ^a (5.3) | 7.8 ^a (6.8) | 19.9 ^b (7.0) | 52.53 | 0.0001 |
| BDI | 14.9 ^a (9.2) | 10.1 ^a (8.5) | 28.8 ^b (9.9) | 38.26 | 0.0001 |
| HRSA | 13.1 ^a (9.6) | 11.8 ^a (8.7) | 27.5 ^b (9.7) | 33.58 | 0.0001 |
| STAI-state | 47.7 ^a (10.1) | 44.3 ^a (11.2) | 57.7 ^b (10.2) | 16.02 | 0.0001 |
| STAI-trait | 52.4 ^a (13.0) | 47.6 ^a (12.6) | 62.4 ^b (9.7) | 13.70 | 0.0001 |
| Y-BOCS – obsession | 11.6 ^a (3.6) | 10.2 ^a (3.7) | 14.8 ^b (3.0) | 17.47 | 0.0001 |
| Y-BOCS – compulsion | 10.9 ^a (4.4) | 9.2 ^a (4.5) | 13.7 ^b (4.6) | 8.91 | 0.0001 |
| Y-BOCS – total | 22.5 ^a (6.9) | 19.3 ^a (7.4) | 28.5 ^b (6.5) | 16.19 | 0.0001 |
| SDS-work | 5.3 ^a (2.9) | 4.2 ^a (2.5) | 7.6 ^b (2.3) | 14.88 | 0.0001 |
| SDS-social life | 5.4 ^a (2.9) | 4.3 ^a (2.6) | 8.1 ^b (1.7) | 21.29 | 0.0001 |
| SDS-family life | 5.6 ^a (3.0) | 4.6 ^a (2.6) | 7.6 ^b (2.8) | 9.63 | 0.0001 |

Note. Means in a row with different superscripts are significantly different at the 0.05 level using a Scheffe procedure. *HRSD* Hamilton Rating Scale for Depression; *BDI* Beck Depression Inventory; *HRSA* Hamilton Rating Scale for Anxiety; *STAI* State-Trait Anxiety Inventory; *YBOCS* Yale-Brown Obsessive Compulsive Scale; *SDS* Sheehan Disability Scale

Table 3 Obsessive-compulsive symptoms assessed by using the Y-BOCS symptom checklist

| | Non-mood disorder (n = 49) n (%) | Bipolar (n = 26) n (%) | Major depressive (n = 42) n (%) | χ^2 | p |
|---------------------|--|------------------------------|---------------------------------------|----------|-------|
| Obsessions | | | | | |
| Aggressive | 19 (38.8) | 14 (53.8) | 22 (52.4) | 2.31 | NS |
| Contamination | 37 (75.5) | 16 (61.5) | 31 (73.8) | 1.77 | NS |
| Sexual | 9 (18.4) | 5 (19.2) | 15 (35.7) | 4.20 | NS |
| Hoarding/saving | 5 (10.2) | 3 (11.5) | 4 (9.5) | 0.07 | NS |
| Religious | 13 (26.5) | 7 (26.9) | 16 (38.1) | 1.65 | NS |
| Symmetry/exactness | 20 ^a (40.8) | 19 ^b (73.1) | 20 ^a (47.6) | 7.28 | 0.03 |
| Somatic | 7 ^{a,b} (14.3) | 2 ^a (7.7) | 12 ^b (28.6) | 5.52 | 0.06 |
| Miscellaneous | 27 (55.1) | 10 (38.5) | 18 (42.9) | 2.34 | NS |
| Compulsions | | | | | |
| Cleaning/washing | 35 (71.4) | 16 (61.5) | 26 (61.9) | 1.18 | NS |
| Checking | 27 (55.1) | 18 (69.2) | 25 (59.5) | 1.41 | NS |
| Repeating | 21 (42.9) | 12 (46.2) | 18 (42.9) | 0.09 | NS |
| Counting | 14 (28.6) | 8 (30.8) | 13 (31.0) | 0.07 | NS |
| Ordering/arranging | 18 ^a (36.7) | 16 ^b (61.5) | 9 ^a (21.4) | 11.11 | 0.004 |
| Hoarding/collecting | 5 (10.2) | 4 (15.4) | 4 (9.5) | 0.63 | NS |
| Miscellaneous | 21 (42.9) | 14 (53.8) | 23 (54.8) | 1.53 | NS |

Note. Means in a row with different superscripts are significantly different at the 0.05 level by using chi-square test

cantly higher in the OCD-BD group compared to the other two groups ($p = 0.001$) (Table 4). The number of OCD patients with poor insight was found to be significantly different between the groups. It was lowest in the OCD-BD group, and highest in the OCD-MDD group ($p = 0.001$) (Table 4). The lifetime rate of suicidal ideation was found to be significantly lower in the OCD-NOMD group compared to the other two groups ($p = 0.0001$).

When the rates of the comorbidity of Axis I disorders other than mood disorders were examined by using SCID-I/CV, the rates of specific phobia and generalized anxiety disorder were found to be higher in the OCD-MDD group compared to the other two groups ($p = 0.01$ and $p = 0.005$, respectively) (Table 4). The rate of social phobia was found to be higher in the OCD-BD group compared to the other two groups ($p = 0.01$).

Discussion

Although the relation between depression and OCD has been known and studied for a long time, the relation between bipolar disorder and OCD has started to gain attention in recent years. There are few studies investigating the effects of bipolar disorder on the clinical features and the course of OCD.

In our study, the number of patients who could not work due to a psychiatric illness was found to be higher in OCD-MDD and OCD-BD groups compared to the OCD-NOMD group. It is not surprising to find the rate of unemployment to be higher in OCD patients with a comorbid mood disorder.

Perugi et al. (1997) reported religious and sexual obsessions to be significantly more frequent, and checking compulsions to be significantly less frequent in the bipolar OCD group compared to non-bipolar OCD group. They found aggressive obsessions significantly more

frequent in the major depressive group compared to the non-major depressive group. The authors finally compared the bipolar OCD group with the major depressive OCD group and reported that the rate of sexual and symmetry/order obsessions was significantly higher in the bipolar OCD group. In our study, the rates of symmetry/exactness obsessions and ordering/arranging compulsions in the OCD-BD group were found to be significantly higher compared to the other two groups.

Anxiety, depression, obsessive-compulsive symptom severity, and disabilities in work, social life and family life were found to be significantly higher in the OCD-MDD group, compared to the OCD-BD and OCD-NOMD groups, in our study. The differences between the groups should be interpreted cautiously because of the fact that OCD-BD patients were currently in between episodes, whereas OCD-MDD patients were currently depressed. The results should be better interpreted as comorbidity of major depression and OCD increases obsessive-compulsive symptom severity and the disability in OCD patients, as well as the levels of anxiety and depression, as was expected.

Chen and Dilsaver (1995) reported that comorbidity for OCD was associated with increased rates of suicidality in bipolar and unipolar patients. Angst et al. (2005) showed that the rate of suicide attempts was significantly higher in OCD patients who had comorbid anxiety disorders or bipolar disorder compared to the patients with pure OCD. In our study, the rate of lifetime suicidal ideation was found to be significantly higher in the OCD-MDD and OCD-BD groups, compared to the OCD-NOMD group, as was expected. This finding is worth emphasizing as it shows that suicidality is an important parameter that has to be considered in OCD patients, especially when a comorbid mood disorder is present.

Türksoy et al. (2002) investigated the relation between insight and obsessive-compulsive symptom

Table 4 Clinical features and comorbidity with axis I disorders

| | Non-mood disorder (n = 49) n (%) | Bipolar (n = 26) n (%) | Major depressive (n = 42) n (%) | χ^2 | p |
|------------------------|--|------------------------------|---------------------------------------|----------|--------|
| Clinical features | | | | | |
| Episodic course | 5 ^a (10.9) | 11 ^b (42.3) | 4 ^a (10.5) | 13.32 | 0.001 |
| Poor insight | 12 ^a (24.5) | 1 ^b (3.8) | 18 ^c (43.9) | 13.25 | 0.001 |
| Suicidal ideation | 10 ^a (20.4) | 13 ^b (50.0) | 28 ^b (66.7) | 20.24 | 0.0001 |
| Suicide attempts | 3 (6.1) | 6 (23.1) | 18 (19.0) | 5.01 | NS |
| First-degree relatives | | | | | |
| OCD | 17 (38.6) | 12 (48.0) | 8 (22.2) | 4.68 | NS |
| Comorbidity | | | | | |
| Specific phobia | 3 ^a (6.1) | 1 ^a (3.8) | 10 ^b (23.8) | 8.81 | 0.01 |
| Social phobia | 4 ^a (8.2) | 9 ^b (34.6) | 6 ^a (14.3) | 8.92 | 0.01 |
| GAD | 3 ^a (6.1) | 2 ^a (7.7) | 12 ^b (28.6) | 10.44 | 0.005 |
| Panic disorder | 2 (4.1) | 2 (7.7) | 3 (7.1) | 0.55 | NS |

Note. Means in a row with different superscripts are significantly different at the 0.05 level by using chi-square test. Axis I disorders, in which minimum expected count is less than 1, were excluded from the table
OCD Obsessive-Compulsive Disorder; GAD Generalized Anxiety Disorder

severity in OCD, and found that symptom severity was higher in the group with poor insight. Supporting these results, the OCD-BD group was found to be the group with the lowest level of obsessive-compulsive symptom severity and the highest level of insight; and the OCD-MDD group was found to be the group with the highest level of obsessive-compulsive symptom severity, and the lowest level of insight, in our study.

Reports by Perugi et al. (1998) and Shwartz and Shen (1998) have suggested that there might have been a relation between bipolar disorder and episodic OCD. Perugi et al. (1997) found the rate of episodic course to be 42.6% in OCD with bipolar disorder, and reported that the rate of episodic course was significantly higher in bipolar OCD, compared to non-bipolar OCD. Likewise, we found that episodic course was 42.3% in the OCD with bipolar disorder group, and that this rate was significantly higher compared to the other two groups. We think that this finding supports the view that there might be a relation between bipolar disorder and episodic OCD.

In our study, the rate of generalized anxiety disorder was found to be significantly higher in the OCD-MDD group compared to the OCD-BD and OCD-NOMD groups, supporting the study of Perugi et al. (1997). Wittchen et al. (1994) reported a strong association of generalized anxiety disorder not only with dysthymia and major depression but also with bipolar disorder. Roy et al. (1995) found a high genetic correlation between generalized anxiety disorder and unipolar depression, but not with bipolar disorder. A continuum of generalized anxiety disorder, OCD and depression, as supposed by Perugi et al. (1997), might be considered at least in some cases. The rate of specific phobia was found to be significantly higher in the group with major depression, compared to the other two groups. Another finding obtained from the comorbidity rates in our study was that the rate of social phobia in the OCD-BD group was significantly higher compared to the other two groups.

In various family studies (Lenane et al. 1990; Bellodi et al. 1992; Pauls et al. 1995; Nestadt et al. 2000), OCD symptoms were detected in the biological relatives of the patients, at a rate which was too high to be coincidental. This was suggested to be evidence of the familial transmission of OCD. Perugi et al. (1997) found no significant difference for the family history of OCD among the bipolar and non-bipolar OCD, and major depressive and non-major depressive OCD groups. In our study, although the groups did not differ in the rates of OCD in the first-degree relatives of the patients, the rate of OCD in the first-degree relatives of OCD-NOMD, OCD-BD and OCD-MDD groups was relatively high (38.6%, 48% and 22.2%, respectively), which supports the familial nature of OCD. On the other hand, these data were not obtained from interviews with the families, but from the patients, which limits the reliability of the results.

The following limitations must be considered when evaluating the results of our study. Firstly, as a limitation

of the design, the OCD-BD group included patients from two different sources (Anxiety Disorders Outpatient Clinic and Mood Disorders Outpatient Clinic), while the OCD-MDD group fully consisted of patients from one source (Anxiety Disorders Outpatient Clinic). Secondly, in the bipolar disorder group, we classified the patients who had a hypomanic/manic episode while on antidepressant medication as bipolar disorder not otherwise specified, which is a diagnosis still under debate. As Akiskal (2002) has mentioned, DSM-IV has denied bipolar legitimacy to these patients, despite the contrary evidence in a more extensive literature. However, progressive studies showed that nearly all of the patients with antidepressant-associated hypomanic episodes developed bipolar episodes with spontaneous hypomania or mania in the following months or years (Strober and Carlson 1982; Akiskal et al. 1983). Thirdly, the number of patients in each group, especially the bipolar group, was relatively small. Another possible limitation in our study was that the data to assess episodic OCD were derived from the retrospective information from the patients. Finally, it must be noted that all BD patients in the OCD-BD group were interepisodic.

Conclusion

The features that distinguish OCD-BD group from the other two groups were the higher rates of symmetry/exactness obsessions and ordering/arranging compulsions, the higher rate of patients with good insight, and the higher rate of episodic course. In the OCD-MDD group, however, the levels of anxiety, depression, obsessive-compulsive symptom severity, and disability were significantly higher compared to the other two groups. OCD with comorbid bipolar disorder was associated with a higher rate of social phobia, whereas OCD with comorbid major depression was associated with higher rates of generalized anxiety disorder and specific phobia.

The most important effect of comorbid major depression on OCD might be a more severe course of OCD, compatible with the results of earlier studies (Angst and Dobler-Mikola 1985; Stavrakaki and Vargo 1986; Wittchen and Essau 1989; Hecht et al. 1989; Perugi et al. 1997). Based on the opinions of Chen and Dilsaver (1995) who wrote that the clinical features defining bipolar disorder and OCD in subjects with bipolar disorder were the manifestation of a single underlying diathesis, the following conclusions can be made: OCD with bipolar disorder might be considered as a different subtype depending on features like the relatively high rate of episodic course, and an intact insight for the obsessive-compulsive symptoms. Treatment strategies that will be developed for OCD with bipolar disorder are an important area of research. Studies on larger samples are needed on this subject.

References

1. Akiskal HS, Walker P, Puzantian VR, King D, Rosenthal TL, Dranon M (1983) Bipolar outcome in the course of depressive illness: Phenomenologic, familial, and pharmacologic predictors. *J Affect Disord* 5:115–112
2. Akiskal HS (2002) Classification, diagnosis and boundaries of bipolar disorders: A review. In: Maj M, Akiskal HS, Lopez-Ibor JJ, Sartorius N (eds) *Bipolar disorder*. John Wiley and Sons, West Sussex
3. American Psychiatric Association (1994) *Diagnostic and statistical manual of mental disorders*, 4th edn (DSM-IV). American Psychiatric Press, Washington, DC
4. Angst J, Dobler-Mikola A: The Zurich study, VI (1985) A continuum from depression to anxiety disorders? *Eur Arch Psychiatry and Neurosci* 235:179–186
5. Angst J, Gamma A, Endrass J, Hantouche E, Goodwin R, Ajdacic V, Eich D, Rossler W (2005) Obsessive-compulsive syndromes and disorders: significance of comorbidity with bipolar and anxiety syndromes. *Eur Arch Psychiatry Clin Neurosci* 255:65–71
6. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J (1961) An inventory for measuring depression. *Arch Gen Psychiatry* 4: 561–571
7. Bellodi L, Sciuto G, Diaferia G, Ronchi P, Smeraldi E (1992) Psychiatric disorders in the families of patients with obsessive-compulsive disorder. *Psychiatry Res* 42:111–120
8. Chen YW, Dilsaver SC (1995) Comorbidity for obsessive compulsive disorder in bipolar and unipolar disorders. *Psychiatry Res* 59:57–64
9. First MB, Spitzer RL, Gibbon M, Williams JBW (1997) *Structured clinical interview for DSM-IV clinical version (SCID-I/CV)*. American Psychiatric Press, Washington DC
10. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischman RL, Hill CL, Heninger GR, Charney DS (1989) The Yale-Brown obsessive compulsive scale (Y-BOCS): Development, use and reliability. *Arch Gen Psychiatry* 46:1006–1011
11. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS (1989) The Yale-Brown obsessive compulsive scale (Y-BOCS): Validity. *Arch Gen Psychiatry* 46: 1012–1016
12. Hamilton M (1959) The assessment of anxiety states by rating. *Br J Med Psychology* 32:50–55
13. Hamilton M (1967) Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychology* 6:278–296
14. Hecht H, Von Zerssen D, Krieg C, Posselt J, Wittchen HU (1989) Anxiety and depression: Comorbidity, psychopathology and social functioning. *Compr Psychiatry* 30:420–433
15. Kolada JL, Bland RC, Newman SC (1994) Obsessive compulsive disorder. *Acta Psychiatr Scand* 376:24–35
16. Kruger S, Cooke RG, Hasey GM, Jorna T, Persad E (1995) Comorbidity of obsessive compulsive disorder in bipolar disorder. *J Affect Disord* 34:117–120
17. Lenane MC, Swedo SE, Leonard H, Pauls DL, Sceery W, Rapoport JL (1990) Psychiatric disorders in first degree relatives of children and adolescents with obsessive compulsive disorder. *J Am Acad Child Adolesc Psychiatry* 29:407–412
18. Lensi P, Cassano GB, Correddu G, Ravagli S, Kunovac JL, Akiskal HS (1996) Obsessive-compulsive disorder: familial-developmental history, symptomatology, comorbidity and course with special reference to gender-related differences. *Br J Psychiatry* 169:101–107
19. Nestadt G, Samuels J, Riddle M, Bienvenu III OJ, Liang K-Y, LaBuda M, Walkup J, Grados M, Hoehn-Saric R (2000) A family study of obsessive-compulsive disorder. *Arch Gen Psychiatry* 57: 358–363
20. Neziroglu F, McKay D, Yaryura-Tobias JA, Stevens KP, Todaro J (1999) The overvalued idea scale: Development, reliability and validity in obsessive-compulsive disorder. *Behav Res Ther* 37: 881–902
21. Okasha A, Saad A, Khalil AH, el Dawla AS, Yehia N (1994) Phenomenology of obsessive compulsive disorder: A transcultural study. *Compr Psychiatry* 35:191–197
22. Pauls DL, Alsobrook II JP, Goodman W, Rasmussen S, Leckman JF (1995) A family study of obsessive-compulsive disorder. *Am J Psychiatry* 152:76–84
23. Perugi G, Akiskal HS, Pfanner C, Presta S, Gemignani A, Milanfranchi A, Lensi P, Ravagli S, Cassano GB (1997) The clinical impact of bipolar and unipolar affective comorbidity on obsessive compulsive disorder. *J Affect Disord* 46:15–23
24. Perugi G, Akiskal HS, Gemignani A, Pfanner C, Presta S, Milanfranchi A, Lensi P, Ravagli S, Maremmanni I, Cassano GB (1998) Episodic course in obsessive-compulsive disorder. *Eur Arch Psychiatry Clin Neurosci* 248:240–244
25. Rasmussen SA, Tsuang MT (1986) Clinical characteristics and family history in DSM-III obsessive-compulsive disorder. *Am J Psychiatry* 143:317–322
26. Rasmussen SA, Eisen JL (1988) Clinical and epidemiologic findings of significance to neuropharmacologic trials in OCD. *Psychopharmacol Bull* 24:466–470
27. Ravizza L, Maina G, Bogetto F (1997) Episodic and chronic obsessive-compulsive disorder. *Depress Anxiety* 6:154–158
28. Roy MA, Neale MC, Pedersen NL, Mathe AA, Kendler KS (1995) A twin study of generalized anxiety disorder and major depression. *Psychol Med* 25:1037–1049
29. Sheehan DV (1983) *The Anxiety Disease*. Scribner, New York
30. Schwartz CM, Shen WW (1998) Is episodic obsessive compulsive disorder bipolar? A report of four cases. *J Affect Disord* 56:61–66
31. Spielberger CD, Gorsuch RL, Lushene RE (1970) *Manual for state-trait anxiety inventory*. Consulting Psychologists Press, California
32. Stavrakaki C, Vargo B (1986) The relationships of anxiety and depression: A review of literature. *Br J Psychiatry* 149:7–16
33. Strober M, Carlson G (1982) Bipolar illness in adolescents with major depression: Clinical, genetic, and psychopharmacologic predictors in a three-to four year prospective follow-up investigation. *Arch Gen Psychiatry* 39:549–555
34. Tükel R, Polat A, Özdemir Ö, Aksüt D, Türksoy N (2002) Comorbid conditions in obsessive-compulsive disorder. *Compr Psychiatry* 43:204–209
35. Türksoy N, Tükel R, Özdemir Ö, Karalı A (2002) Comparison of clinical characteristics in good and poor insight obsessive-compulsive disorder. *J Anxiety Disord* 16:413–423
36. Wittchen HU, Essau L (1989) Natural course and spontaneous remissions of untreated anxiety disorders. In: Hand I, Wittchen HU (eds) *Panic and phobias*. Springer Verlag, Berlin
37. Wittchen HU, Zhao S, Kessler RC, Eaton WW (1994) DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* 51:355–364