Michael Rufer · Iver Hand · Heike Alsleben · Anne Braatz · Jürgen Ortmann · Birgit Katenkamp · Susanne Fricke · Helmut Peter

Long-term course and outcome of obsessive-compulsive patients after cognitive-behavioral therapy in combination with either fluvoxamine or placebo

A 7-year follow-up of a randomized double-blind trial

■ **Abstract** Longitudinal studies with very long follow-up periods of patients with obsessive-compulsive disorder (OCD) who have received adequate treatment are rare. In the current study, 30 of 37 inpatients (81 %) with severe OCD were followed up 6–8 years after treatment with cognitive-behavioral therapy (CBT) in combination with either fluvoxamine or placebo in a randomized design. The significant improvements (with large effect-sizes) in obsessive-compulsive symptoms from pre- to post-treatment (41 % reduction on the Y-BOCS) remained stable at follow-up (45 %). Responder rates, defined as ≥35 % reduction on the Y-BOCS, were 67 % and 60 %, respectively. Depressive symptoms decreased significantly not only from pre- to post-treatment but also during follow-up. Re-hospitalization, which occurred in 11 patients (37 %), was associated with more severe depressive symptoms at pre-treatment and living without a partner. Full symptom remission at follow-up, defined as both Y-BOCS total score ≤7 and no longer meeting diagnostic criteria for OCD, was achieved by 8 patients (27 %). Patients without full remission at follow-up had a significantly longer history of OCD, assessed at pre-treatment, compared to remitted patients. The short-term treatment outcome had no predictive value for the long-term course. Throughout the naturalistic follow-up, nearly all patients (29 patients) received additional psychotherapy and/or medication. This might indicate that such chronic OCD patients usually need additional therapeutic support after effective inpatient treatment to maintain their improvements over long periods.

■ **Key words** obsessive-compulsive disorder · cognitive-behavioral therapy · fluvoxamine · outcome · follow-up

M. Rufer, MD · I. Hand · H. Alsleben · A. Braatz · J. Ortmann · B. Katenkamp · S. Fricke · H. Peter
University Hospital of Hamburg
Centre of Psychosocial Medicine
Dept. of Psychiatry and Psychotherapy

M. Rufer, MD (✉)
University Hospital of Zürich
Psychiatric Department
Culmannstrasse 8
8091 Zürich, Schweiz
Tel.: +41-1/255-3455
Fax: +41-1/255-4408
E-Mail: michael.rufer@usz.ch

Introduction

Obsessive-compulsive disorder (OCD) is a severe and disabling illness which is frequently associated with considerable psychosocial handicaps and reduced quality of life comparable to those of psychotic disorders [4, 16, 17, 27]. The course of illness, if untreated, is mostly chronic with varying intensity of symptoms [34, 38]. Until 30 years ago, OCD was considered a treatment refractory illness. Since then, the development of cognitive-behavior therapy (CBT) and, during the last years, of non-selective and selective serotonin reuptake inhibitors (SRIs and SSRIs) has provided effective treatments. Patients treated with medication alone showed high relapse-rates following drug discontinuation [24, 33], whereas several prospective follow-up studies showed that improvement after CBT tends to persist (for a review, see [21, 25]). A meta-analysis of 6 studies with follow-up periods of 7–24 months showed that treatment gains were maintained up to 2 years after CBT [36]. However, longer follow-up periods are important in chronic diseases to evaluate what happens after treatment. Five- to 10-year follow-up studies are expected after treatment of heart disease or cancer and are equally valuable for serious mental health problems [32]. Such follow-up studies of patients with chronic OCD who have received effective treatments are rare. In a 6-year follow-up study after exposure and clomipramine therapy for 34 OCD inpatients, 25 pa-

tients (74 %) were classified as "improved" or "much improved" in a self-rating at follow-up (the Yale-Brown Obsessive-Compulsive Scale was not used) [32]. However, only 10 patients (29 %) remained drug-free throughout the follow-up and 5 patients received further exposure therapy. At the time of follow-up assessment, 20 of 33 patients (61 %) were taking medication.

Although both CBT and pharmacological treatment with (S)SRIs have proven to be effective in OCD, only a few studies compared the combination of pharmacotherapy and CBT with CBT alone, with inconsistent results (see the overview in [21]). Cottraux et al. [9] found a short-term advantage for the combination of the SSRI fluvoxamine with CBT compared to placebo plus CBT. However, in the 48th week and at the 18-month follow-up, no differences were detectable any more between the groups [8]. Hohagen et al. [22] evaluated 49 inpatients in a multicenter study, carried out in three centers in Germany (Department of Psychiatry and Psychotherapy, University of Freiburg; Department of Psychiatry and Psychotherapy, University of Hamburg; Central Institute of Mental Health at Mannheim). Patients were treated with CBT in combination with either fluvoxamine or placebo in a double-blind, randomized design. The following pre to post results were reported:

- Both treatment groups showed a highly significant symptom reduction.
- There were no significant differences between the groups concerning the total score of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the subscore for compulsions.
- A significantly higher reduction of obsessions was found in the combination treatment group than in the CBT plus placebo group.
- Severely depressed patients receiving the combination treatment presented a significantly better treatment outcome (Y-BOCS scores) than patients with the CBT plus placebo treatment.
- The responder rate (defined as ≥35 % reduction on the Y-BOCS) was significantly higher in the combination treatment group (n = 21; 88 %) than in the CBT plus placebo group (n = 15; 60 %).

These results suggest that a combination of CBT and fluvoxamine is superior to CBT alone, regarding the short-term treatment results, when obsessions dominate the clinical picture and/or when a severe secondary depression is present. However, so far, no follow-up study has been published investigating the long-term course after the end of the trial.

The present study reports the results of a 7-year follow-up of inpatients who were treated in a double-blind, randomized design in the University Hospital in Hamburg between 1993 and 1995. The two primary aims of our study were [1] to evaluate the long-term development of psychopathology, social functioning and the frequency of additional treatments and re-hospitalizations during the naturalistic follow-up period and [2] to examine the association of re-hospitalizations and full symptom remission/non-remission at follow-up with sociodemographic or clinical variables. A secondary aim was to compare the short- and long-term outcome of both treatment groups (CBT and fluvoxamine; CBT and placebo).

Method

Patient sample

During 1993–1995, 37 inpatients with chronic OCD were randomly allocated to two experimental groups: In addition to CBT, one group received fluvoxamine and the other group placebo. At study entry, all patients received placebo during a 1-week period. After this wash-out phase, they entered 9 weeks of treatment with CBT plus fluvoxamine (250–300 mg) or CBT plus placebo. All patients were treated by experienced therapists with multimodal CBT including exposure in-vivo and in-sensu as well as specific interventions for developmental deficits (like social deficits) and problems in daily life conduct (for details of this concept, see Hand [20]). Exclusion criteria were: primary affective disorder; current or previous psychotic disorder; current substance abuse or dependency; organic brain disorder; epilepsy; acute suicidal tendency; pregnancy. Twenty (54 %) of these patients participated in the multicenter study mentioned above, for further methodological details see [22].

Seven years (range: 6–8 years) after the end of the trail, all 37 patients were asked to participate in the follow-up. Those who refused to come for a face to face interview were offered an interview by telephone. Three patients (all from the group "CBT plus placebo") refused to participate. The main reasons were that they did not want to be reminded of their symptoms and their whole situation at the time of hospitalization. Four patients (3 from the group "CBT plus placebo", 1 from the group "CBT plus fluvoxamine") could not be located. All together, 30 out of 37 patients (81 %) were followed up, 21 by face to face interview and 9 by telephone. Written consent was gained from all participants and the trial was approved by the local ethical committee.

Assessments

Clinically experienced raters, who had not been involved in the patients' treatments, conducted the expert ratings. The psychiatric diagnosis was determined at the start of trial using the Structured Clinical Interview (SKID) for DSM-III-R [39] (German translation by Wittchen et al. [44]). The severity of obsessive-compulsive symptoms was rated at three assessment-points (pre-treatment, post-treatment, follow-up) using the Y-BOCS [14, 15] (German translation by Büttner-Westphal and Hand [6]). The clinician-administered Y-BOCS is regarded as the gold standard to assess the severity of obsessive-compulsive symptoms. It comprises 10 items, rated on a 5-point Likert scale ranging from 0 (no symptoms) to 4 (severe symptoms). The total score ranges from 0 to 40 and consists of two subscores for compulsions (range 0 to 20) and obsessions (range 0 to 20). The severity of depressive symptoms was assessed using the 21-item version of the Hamilton Depression Rating Scale (HDRS) [18] (German translation [7]), a clinician-administered instrument to quantify depressive symptoms with a score range of 0 to 65. Apart from its utilization in depression studies, the HDRS is often administered along with the Y-BOCS in OCD research, as comorbid depressive symptoms are frequent in OCD [30]. At follow-up, patients rated themselves by using the Clinical Global Improvement (CGI) scale, comparing their complaints at follow-up with pre-treatment. A score of 1 corresponds with very much improved and 2 with much improved, 3 denotes minimal improvement, and 4 represents no change. Scores of 5, 6, or 7 indicate deterioration (minimally worse, much worse, or very much worse, respectively).

In addition, all patients were submitted to a semistructured interview regarding the course during the follow-up period, interim treat-

ments and the status at follow-up. Psychiatric diagnoses at follow-up were determined using the Mini International Neuropsychiatric Interview (MINI), a structured diagnostic psychiatric interview for DSM-IV and ICD-10 [23, 37].

Statistical analysis

Chi-square tests or, when cell frequency was low, Fisher's exact tests were used for between-group comparisons for categorical variables, Student's t-test for continuous variables. Changes of continuous variables within a group were tested with the Wilcoxon paired t-test. The scores of the Y-BOCS and HDRS, assessed at 3 time points (pre-treatment; post-treatment; follow-up), were submitted to analyses of variance (ANOVAs) with repeated measures with time as within-subject factor. In addition, the influence of the factor "treatment group" (CBT and fluvoxamine versus CBT and placebo) was calculated. For 2 patients, the pre- and post-treatment results of the HDRS were not available; therefore, the analyses of the HDRS scores could only be calculated for 28 out of 30 patients.

In accordance with the multicenter study [22], a reduction of the Y-BOCS total score by at least 35% between pre- and post-treatment was defined as short-term response. Correspondingly, long-term response was defined as a reduction of the Y-BOCS score by at least 35% between pre-treatment and follow-up. The Statistical Package for Social Sciences (SPSS), version 11.5, was used for all calculations.

Results

Follow-up participants versus non-participants

The 7 patients who were not rated at follow-up did not differ from the 30 who were rated on any sociodemographic or psychometric measure at pre- or post-treatment. The following mean Y-BOCS total scores were found: 27.6 (SD = 4.3) in follow-up participants and 29.7 (SD = 4.1) in non-participants at pre-treatment ($t = -1.2$, df = 35, $P = 0.26$); and at post-treatment 16.4 (SD = 7.4) and 18.7 (SD = 6.1) respectively ($t = -0.77$, df = 35, $P = 0.45$).

Pre-treatment data

The mean age of the follow-up participants, 12 men and 18 women, was 32.4 years (SD = 9.2). Thirteen patients

(43%) were employed before treatment, more than a third (38%) of these were on sick leave before treatment. Disabled or retired were 9 patients (30%) and the other 8 patients (27%) were students or doing housework. Eighteen patients (60%) were married or cohabiting.

The mean age at onset of OCD was 24.0 years (SD = 9.3) with a mean duration of 8.3 years (SD = 7.3) until the start of treatment. The mean Y-BOCS and HDRS scores at pre-treatment are shown in Table 1. Most patients (80%) had severe or extreme obsessions and compulsions (Y-BOCS total score above 23, see Fig. 1), the mean Y-BOCS total score was 27.6 (SD = 4.3).

Symptom changes over the 10-weeks treatment period and the follow-up period

Obsessive-compulsive symptoms

The follow-up assessment was carried out after a mean period of 7.2 years (with a range of 6–8 years). At post-treatment, the Y-BOCS total score was reduced by 41%, from 27.6 (SD = 4.3) at pre-treatment to 16.4 (SD = 7.4). At follow-up, the mean Y-BOCS score was 14.9 (SD = 9.5), a reduction by 45% compared to pre-treatment. The repeated measures ANOVAs showed highly significant time effects and large effect-sizes for the changes of the Y-BOCS total scores and the two sub-scores for obsessions and compulsions (Table 1). The mean scores decreased highly significantly from pre- to post-treatment, without significant changes from post-treatment to follow-up.

Following several authors, e. g. Alonso et al. [1], the ranges of the Y-BOCS total scores were divided into levels of severity, in order to clarify the clinical significance of a patient's score. An individual scoring from 0 to 7 is considered "subclinical" in relation to OCD symptoms, 8 to 15 "mild", 16 to 23 "moderate", 24 to 31 "severe", and a score of 32 or higher is considered "extreme". The results are shown in Fig. 1.

From pre- to post-treatment, a significant shift towards milder levels of symptom severity could be ob-

Fig. 1 Number of patients with respect to Y-BOCS severity categories at pre-treatment, post-treatment and after 7 years (n = 30)
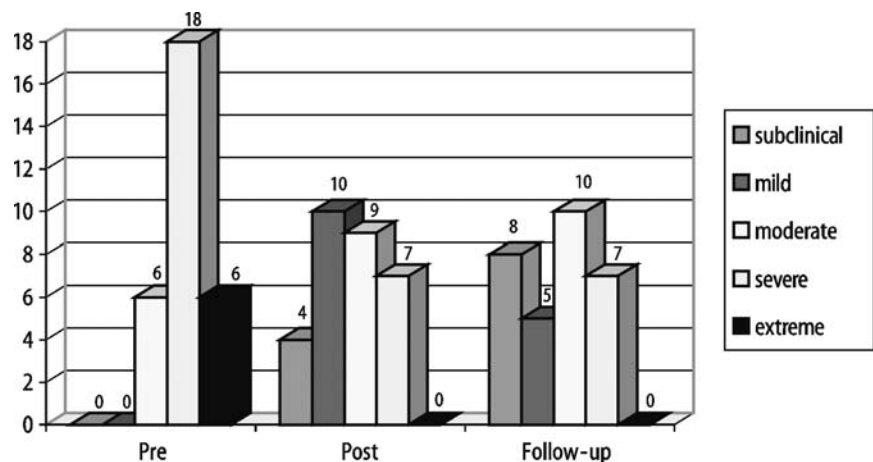
Table 1 ANOVAs with repeated measures (pre-treatment, post-treatment and follow-up) and paired t-tests for Y-BOCS and HDRS scores

	Pre-treatment	Post-treatment	Follow-up	ANOVA (df = 2)		
				F	P	Effect size partial Eta^2
Y-BOCS: mean (SD) n = 30						
Total	27.6 (4.3)	16.4 (7.4)	14.9 (9.5)	F (58) = 39.24	< 0.001[1]	0.58
Compulsions	13.7 (1.9)	7.8 (3.7)	8.0 (4.7)	F (58) = 35.11	< 0.001[2]	0.55
Obsessions	13.8 (2.9)	8.6 (4.3)	7.3 (4.9)	F (58) = 32.76	< 0.001[3]	0.53
HDRS: mean (SD) n = 28	18.2 (8.6)	12.4 (9.9)	8.0 (7.9)	F (54) = 16.05	< 0.001[4]	0.41

Y-BOCS Yale-Brown Obsessive Compulsive Scale; *HDRS* Hamilton Depression Rating Scale; *ANOVA* analysis of variance
[1] Pre and post comparison: t = 9.2, df = 29, P < 0.001; post and follow-up comparison: t = 0.9, df = 29, P = 0.38 (paired t-tests)
[2] Pre and post comparison: t = 8.2, df = 29, P < 0.001; post and follow-up comparison: t = −0.23, df = 29, P = 0.82 (paired t-tests)
[3] Pre and post comparison: t = 8.0, df = 29, P < 0.001; post and follow-up comparison: t = 1.5, df = 29, P = 0.16 (paired t-tests)
[4] Pre and post comparison: t = 3.0, df = 27, P < 0.01; post and follow-up comparison: t = 2.4, df = 27, P < 0.05 (paired t-tests)

served. During follow-up, the number of patients with mild symptoms declined from 10 to 5 patients, while the number of patients with subclinical OCD symptoms doubled from 4 to 8 patients. Almost unchanged remained the number of patients with medium and severe OCD symptoms (16 patients at post-treatment, 17 at follow-up). Concerning the individual courses, 24 patients (80 %) shifted to a lesser OCD severity level from pre- to post-treatment, 6 patients remained unchanged, whereas none of the patients shifted to a higher severity level. From post-treatment to follow-up, 12 patients remained unchanged (40 %), 9 patients (30 %) shifted to a lesser and also 9 patients to a higher OCD severity level.

None of the 8 patients with a subclinical degree of OCD symptom severity met diagnostic criteria for OCD according to the MINI at follow-up. From the other 22 patients with at least mild obsessive-compulsive symptoms at follow-up, 3 patients (13 %) showed an episodic course during the follow-up period, characterized by complete remission of OCD symptoms for a period of at least 6 months, and 19 patients (87 %) showed a continuous, chronic course.

Twenty patients (67 %) were classified as short-term responders (≥ 35 % reduction on the Y-BOCS from pre- to post-treatment) and 18 patients (60 %) as long-term responders (≥ 35 % reduction on the Y-BOCS from pre-treatment to follow-up). This difference was not significant (McNemar Test: *P* = 0.75).

Depressive symptoms

The repeated measures ANOVA for the HDRS scores showed a highly significant time effect (see Table 1). The means of HDRS scores decreased significantly not only from pre- to post-treatment but also from post-treatment to follow-up.

Comparison of symptom-scores between both treatment groups (CBT + fluvoxamine; CBT + placebo)

In addition to CBT, 19 patients received during the randomized trial fluvoxamine and 11 patients placebo. At pre-treatment, there were no significant differences in sex, age, education, employment, marital status, duration of OCD and severity of obsessive-compulsive and depressive symptoms between the two treatment-groups (data not shown). The repeated measures ANOVAs for the Y-BOCS scores over the treatment and follow-up time points did not show significant differences between the groups: No significant group effects (all Fs (1,28) < 1.0, all Ps > 0.28) and no significant interaction effects (all Fs (2,56) < 1.6, all Ps > 0.22) were found for Y-BOCS total scores and the two subscores (obsessions and compulsions). Similarly, ANOVA showed no significant group effects (*F* (1,26) = 1.24, *P* = 0.28) and interaction effects (*F* (2,52) = 0.95, *P* = 0.39) for the HDRS scores. There were also no significant differences between both treatment groups concerning the frequencies responders/non-responders (at post-treatment χ^2 = 0.07, df = 1, *P* = 0.79; at follow-up χ^2 = 1.53, df = 1, *P* = 0.22).

■ Re-hospitalization during the follow-up period: frequency and association with psychopathological and sociodemographic variables

During the follow-up period, 11 patients (37 %) were at least once re-hospitalized. Psychopathological and sociodemographic variables at the time of the randomized trial were compared between re-hospitalized patients and those without re-hospitalization (see Table 2). Significant differences were only found for HDRS scores at pre-treatment and the marital status. Patients who were re-hospitalized during follow-up had at pre-treatment a higher mean score of depression and were less often married or cohabiting. In addition, a statistical trend (*t* = −1.85, df = 28, *P* = 0.07) toward longer history of OCD in re-hospitalized patients was seen.
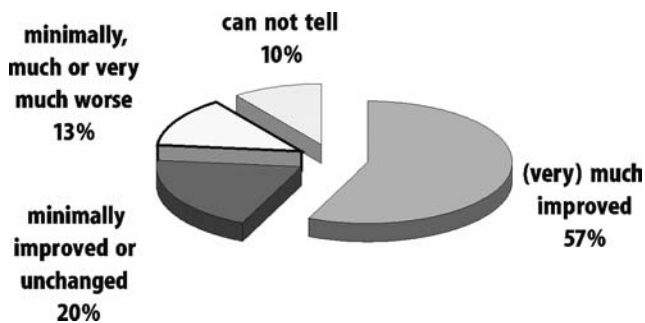
■ Patients' rating of improvement at follow-up compared to pre-treatment

In the self-rated CGI, 17 patients (57 %) rated themselves as "much improved" or "very much improved" at follow-up compared to pre-treatment (Fig. 2 shows the results

Table 2 Association of re-hospitalization with psychopathological and sociodemographic variables at the time of the randomized trial

	Re-hospitalized patients (n = 11)	Patients without re-hospitalization (n = 19)	p value
Male/female (n)	5/6	7/12	0.71[a]
Age (years): mean (SD)	30.7 (9.9)	33.3 (8.9)	0.47[b]
Years of school education: mean (SD)	11.7 (1.6)	10.9 (1.5)	0.17[b]
Married/not married or cohabiting (n)	4/7	14/5	df = 1, p = 0.04[a]
Employed/not employed patients (n)	4/7	9/10	0.71[a]
Duration of OCD (years): mean (SD)	11.5 (8.0)	6.5 (6.4)	0.07[b]
Fluvoxamine/placebo during randomized trial (n)	7/4	12/7	1.00[a]
Y-BOCS at the start of the randomized trial: mean (SD)	27.6 (5.1)	27.5 (3.9)	0.95[b]
Y-BOCS at the end of the randomized trial: mean (SD)	18.2 (8.1)	15.4 (7.0)	0.32[b]
HDRS at the start of the randomized trial: mean (SD)	23.8 (7.9)	15.6 (7.8)	t = −2.6, df = 28, p = 0.02[b]
HDRS at the end of the randomized trail: mean (SD)	15.4 (9.5)	11.0 (10.0)	0.27[b]
Responder[c]/Non-responder at the end of the randomized trial (n)	6/5	14/5	0.43[a]

[a] Fisher's exact test; [b] Student's t-Test; [c] Responder: Y-BOCS reduction (pre-treatment to post-treatment) ≥ 35%

Fig. 2 Patients' rating of improvement at follow-up compared to pre-treatment (n = 30)

in more detail). The mean CGI score in all patients was 2.5 (SD = 1.6), in long-term responders 3.8 (SD = 1.6) and in long-term non-responders 1.6 (SD = 0.6). This difference between responders and non-responders was highly significant (t = 5.1, df = 25, P < 0.001).

■ Changes in work status and marital status during the follow-up period

The number of patients who were married or cohabiting slightly increased from 18 (60%) at pre-treatment to 20 (67%) at follow-up. The number of employed patients also increased during this period, from 13 (43%) to 17 (57%). Two patients (7%) were out of work at follow-up, 6 (20%) were students or doing housework. Correspondingly, the number of patients who were on sick leave decreased from 5 (17%) to 2 patients (7%) and the number of retired or disabled patients from 9 (30%) to 7 (23%).

■ Medication and/or psychotherapy during the follow-up period

Overall, 29 of the 30 patients were treated with psychotherapy or medication for at least 3 months during the follow-up period. Twenty-three patients (77%) received additional psychotherapy, 15 of these were treated with CBT, 8 with other approaches of psychotherapy (psychodynamic, client-centered and other). Only 9 patients (30%) remained without medication during the entire follow-up period. At the follow-up assessment, 13 patients (43%) were taking medication: 10 were taking antidepressants (2 of these in combination with benzodiazepines) and 3 were taking benzodiazepines. The mean HDRS score in patients who were taking medication at follow-up was 13.8 (SD = 8.7), significantly higher compared to 5.0 (SD = 6.1) in patients without medication (t = −3.2, df = 28, P < 0.01). In contrast, the mean Y-BOCS scores in both groups did not differ significantly (t = −1.3, df = 28, P = 0.22).

■ Association of full symptom remission at follow-up with psychopathological and sociodemographic variables at the time of treatment

Remission at follow-up was defined as both no longer meeting diagnostic criteria for OCD according to the MINI and a Y-BOCS total score ≤ 7. The group of remitters at follow-up was compared to the group of patients with at least mild obsessive-compulsive symptoms at follow-up with respect to psychopathological and sociodemographic variables at the time of the randomized trial (Table 3). Patients without a full symptom remission at follow-up had a highly significant longer history of OCD, assessed at pre-treatment, compared to remitted patients.

Table 3 Association of long-term symptom remission with psychopathological and sociodemographic variables at the time of the randomized trial

	Remission at follow-up (n = 8)	At least mild OCD at follow-up (n = 22)	p value
Male/female (n)	2/6	10/12	0.42[a]
Age (years): mean (SD)	29.0 (6.2)	33.6 (9.9)	0.23[b]
Years of school education: mean (SD)	10.8 (1.4)	11.4 (1.6)	0.36[b]
Married/not married or cohabiting (n)	5/3	13/9	1.00[a]
Employed/not employed patients (n)	4/4	9/13	0.70[a]
Duration of OCD (years): mean (SD)	2.4 (1.4)	10.5 (7.4)	t = −3.0, df = 28, p = 0.005[b]
Fluvoxamine/placebo during randomized trial (n)	6/2	13/9	0.67[a]
Y-BOCS at the start of the randomized trial: mean (SD)	27.8 (4.2)	27.5 (4.4)	0.89[b]
Y-BOCS at the end of the randomized trial: mean (SD)	14.4 (7.0)	17.1 (7.5)	0.38[b]
HDRS at the start of the randomized trial: mean (SD)	17.5 (6.0)	18.5 (9.6)	0.79[b]
HDRS at the end of the randomized trail: mean (SD)	10.1 (9.6)	13.3 (10.2)	0.46[b]
Responder[c]/Non-responder at the end of the randomized trial (n)	6/2	14/8	0.68[a]

[a] Fisher's exact test; [b] Student's t-Test; [c] Responder: Y-BOCS reduction (pre-treatment to post-treatment) ≥35%

Discussion

Long-term course and outcome

In order to assess in detail the course of obsessive-compulsive symptoms over the 7-year follow-up, we calculated (1) changes in the mean Y-BOCS scores, (2) changes in the Y-BOCS severity categories and (3) short- and long-term rates of response and remission. The further slight (not significant) decrease of the mean Y-BOCS scores from post-treatment to follow-up and the higher rate of "remitters" (patients with subclinical obsessive-compulsive symptoms and no longer meeting diagnostic criteria for OCD according to the MINI) at follow-up compared to post-treatment indicate a further slight improvement during the follow-up period. In contrast, the rate of non-responders slightly increased (not significantly) during the follow-up period from 10 to 12 patients. However, the responder criterion of 35% or more reduction on the Y-BOCS is arbitrary and disputed. Nevertheless, it has often been the criterion of choice in previous treatment studies of OCD [e.g., 22, 29] and therefore, it is useful for comparing results of different OCD studies. The responder rates of 67% for short-term outcome and 60% for long-term outcome in our study are in line with numerous previous studies which demonstrated short- and long-term responder rates of 50–80% after CBT alone or in combination with (S)SRIs [2, 5]. The clinical relevance of our long-term responder rate is supported by the results of the patients' self-ratings: Similar to the responder-rate, 57% of patients rated themselves as "much improved" or "very much improved" at the 7-year follow-up compared to pre-treatment and the long-term responders rated themselves highly significantly better than the non-responders.

Similar to the results of the multicenter study by Hohagen et al. [22], we found no significant differences between both treatment groups (CBT plus fluvoxamine; CBT plus placebo) concerning obsessive-compulsive symptoms (as measured by the Y-BOCS total score) and compulsions. In contrast to the multicenter study, the combination treatment in our study also did not show a significantly better outcome for obsessions and depressive symptoms and no higher responder rates. However, the small sample size of our study clearly compromises the statistical power to detect differences between these two highly effective treatments for OCD and thus we can not draw definite conclusions from this negative finding.

In contrast to the stable obsessive-compulsive symptoms during follow-up, the severity of depressive symptoms significantly decreased not only from pre- to post-treatment but also during follow-up. It must be noted that primary depression was defined as an exclusion criterion in our study. Thus, this further improvement after the end of treatment might be a delayed reaction to the reduction of the distress caused by obsessive-compulsive symptoms and its negative consequences for work, social life and relationships. This assumption is supported by our findings of positive changes in daily functioning throughout the follow-up period. In addition, similar findings were reported in agoraphobics with further amelioration of secondary depression during long-term follow-up periods [19]. However, when interpreting our finding, one ought to keep in mind that additional treatments during the naturalistic follow-up period probably also have had a therapeutic effect on depression.

Nearly all patients had received additional treatments throughout the follow-up period. Regarding the mostly chronic course of OCD in our patients (the mean duration of OCD was 8 years at pre-treatment), the high rate of additional treatments during the follow-up period might indicate that such a group of patients with chronic OCD usually need additional therapeutic support after an effective treatment to maintain their improvements over a very long time. Probably, these additional treatments have assumed a major role in the

long-term course. Because of our small sample size and the lack of more detailed information on the extent and duration of additional treatments, further analyses of subgroups of our patients were limited. However, a comparison of the 13 patients who received drugs at the follow-up assessment with the drug free patients might help to explain the need of this medication treatment: While the intensity of obsessive-compulsive symptoms was not significantly different, the patients who received medication were significantly more depressed. Therefore, patients might have been drug-treated because of depression rather than obsessive-compulsive symptoms. More prospective long-term follow-up studies with larger sample-sizes are needed, specifically designed to evaluate which factors are related to the need of further drug treatments in patients with OCD after effective treatment.

■ Variables that were associated with re-hospitalization and long-term symptom remission/non-remission

In view of the low quality of life in many patients with OCD and the findings in various studies that 20 to 50 % of patients do not achieve sufficient improvement with CBT and/or (S)SRI [20, 21], predictors of outcome are urgently needed. So far, in previous OCD studies most of the examined variables have not been consistently associated with outcome [29, 35, 42, 43]. The results of the present study concerning the association of re-hospitalization with psychopathological and sociodemographic variables showed that patients with more severe depressive symptoms at pre-treatment were more often re-hospitalized during the follow-up period. These findings are in line with previous studies which reported a negative impact of comorbid depression on short- or long-term outcome of CBT alone or in combination with (S)SRI in obsessive-compulsives [11, 12, 26, 41]. However, in some other studies such an association was not found [3, 13, 28, 32, 40]. These controversial results may be partly due to the different treatment approaches used in the different studies and the use of various psychometric ratings, which clearly compromises the comparability. The additional result of our study, that patients who were married or cohabiting were less often re-hospitalized, might be interpreted as an indication that living together with a (marriage) partner can help some patients to get over periods of increased symptoms without the need of a re-hospitalization. However, we have not enough data to confirm this interpretation and more research is needed focusing on the possible impact of close relationships on the risk of re-hospitalization after inpatient CBT.

During the past decade many researchers emphasized that full remission should be the main treatment goal for depression and anxiety disorders [10, 31]. In our study, a highly significant association was found between the duration of illness before treatment and achievement of symptom remission/non-remission at follow-up: A longer history of OCD before treatment was associated with non-remission at follow-up and (but only as a statistical trend) with the need of re-hospitalization during the follow-up period. These findings are in accordance with the 2.5-year follow-up study by Alonso et al. [1] in which 60 outpatients with OCD were treated with CBT and (S)SRI: Long-term non-responders showed a statistical trend for a longer history of illness compared to responders. Conversely, in several other CBT or drug studies the duration of OCD was not associated with outcome of treatment [42, 43]. However, follow-up periods of the most studies were only 1 to 3 years and the outcome of obsessive-compulsive symptoms was often measured by "response" rates (partial remission) or by statistically significant improvement in symptom rating scale scores. In conclusion, our study points out that a very long duration of OCD before inpatient treatment means a poorer likelihood to achieve full remission of obsessive-compulsive symptoms several years after treatment.

Finally, the two most important limitations of our study need to be emphasized. First, the methodological difficulties inherent in such naturalistic long-term follow-up studies limit the possibilities to draw firm conclusions about specific treatment effects. Second, the sample-size is rather small and 6 out of 17 patients of the CBT plus placebo group did not take part in the follow-up compared to only 1 out of 20 patients of the combination treatment group. However, the comparisons of psychometric and sociodemographic variables between follow-up participants and dropouts showed no significant differences and the very high participation rate (81 %) strengthens our results.

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