No effect of adding brief dynamic therapy to pharmacotherapy in the treatment of obsessive-compulsive disorder with concurrent major depression

NO EFFECT OF ADDING BRIEF DYNAMIC THERAPY TO PHARMACOTHERAPY IN THE TREATMENT OF OBSESSIVE-COMPULSIVE DISORDER WITH CONCURRENT MAJOR DEPRESSION

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ABSTRACT

Background: Until now no studies have investigated the benefits of adding brief dynamic therapy (BDT) to medication in obsessive-compulsive disorder (OCD), while a number of recent investigations have demonstrated the efficacy of supplemental BDT among patients with major depressive disorders (MDD). The objective of the present study was to explore the efficacy of BDT combined with pharmacotherapy in comparison with pharmacotherapy alone in the treatment of OCD with concurrent MDD.

Methods: A 12-month randomized clinical trial compared a standard selective serotonin reuptake inhibitor treatment with (n = 27) or without (n = 30) supplemental BDT in patients with OCD and concurrent MDD. Supplemental BDT was added during the first 16-week trial; all patients continued to be treated with only pharmacotherapy in the following continuation phase. The primary efficacy assessments were the Yale-Brown Obsessive Compulsive Scale and the 17-item Hamilton Rating Scale for Depression; the secondary efficacy measures included the Clinical Global Impression scale and the Global Assessment of Functioning. The data analysis was conducted on the 'intent-to-treat (ITT) efficacy patient sample'.

Results: Fifty patients completed the study. No difference between the 2 treatment groups was found at any point by any assessment method in the ITT study sample.

Conclusions: Supplemental BDT in the treatment of patients with OCD with concurrent MDD who are receiving effective medication has no significant clinical effect on both obsessive and depressive symptoms.

Key Words

- Obsessive-compulsive disorder
- Brief dynamic therapy
- Major depressive disorder
- Combined treatment
- Selective serotonin reuptake inhibitors

INTRODUCTION

Obsessive-compulsive disorder (OCD) is a psychiatric condition affecting an estimated 1–3% of the population worldwide [1] which shows considerable comorbidity with other disorders including depression. In population-based epidemiological studies, about 30–40% of lifetime occurrences of major depressive disorder (MDD) have been found in patients with OCD [2,3,4,5,6]. Moreover, regardless of the prevalence rate variability across studies (percentages ranging from 25 to 80%), MDD has consistently been found the most prevalent lifetime comorbid axis I disorder in OCD [1,7,8,9,10]. This raises the question of which type of treatment would have superior efficacy in the context of patients with concurrent OCD and MDD. Because most treatment studies of OCD have typically excluded patients with high levels of depressive symptoms or MDD, little is known about whether concurrent MDD influences the treatment response.

A number of smaller investigations have reported that depressive symptoms are generally associated with a diminished efficacy of both cognitive-behavioral techniques [11,12] and serotonin reuptake inhibitors [13]. Thus, patients with OCD and concurrent MDD need to be targeted as a special population for treatment studies, and new treatment options need to be explored.

Although OCD has received little attention in the recent history of psychoanalysis, psychoanalytic theory has provided important insights into the nature of this disorder and, recently, some authors have stated that a renewed interest is needed in research on psychodynamic theory and therapy for OCD [14,15]. Nevertheless, until now no studies have investigated the benefits of adding brief dynamic therapy (BDT) to medication for the treatment of this disorder, while a number of recent investigations have examined the treatment efficacy of BDT among patients with depressive disorders both in monotherapy [16] and in combination with pharmacotherapy: in the acute treatment of MDD, the provision of supplemental BDT with antidepressants has shown to be significantly more acceptable to patients [17], and significantly more cost-effective [18]. In addition, the combination of BDT with pharmacotherapy in the acute treatment of major depression has a significant long-term advantage in terms of both symptom recurrences and global functioning [19,20]. The efficacy of BDT in MDD has not been extensively shown, and evidence emerging from the literature is less solid than that from cognitive-behavioral therapy (CBT) [11].

The objective of the present study was to explore the efficacy of BDT combined with pharmacotherapy in comparison with pharmacotherapy alone in the treatment of OCD with concurrent MDD. We hypothesized that combined treatment adding BDT to pharmacotherapy would be an effective and acceptable treatment strategy in this special OCD population by reducing both obsessive and depressive symptoms and/or by improving global functioning.

PATIENTS AND METHODS

SAMPLE

Patients were recruited from referrals to the Mood and Anxiety Disorders Unit, Department of Neuroscience, University of Turin, Italy. This is a tertiary referral center mainly for patients from the Piedmont and Aosta Valley regions of Italy, located in the University General Hospital. Patients

are referred by general practitioners, psychiatrists or psychologists due to an anxiety or mood disorder diagnosis (or hypothesized diagnosis), although a few are self-referred (e.g. via information received from other patients). The majority of the referred patients had previously received ineffective or partly effective psychological and/or pharmacological treatments.

The participants were male or female outpatients, 18 years of age or older, who met the DSM-IV [21] criteria for a primary diagnosis of OCD with concurrent MDD. All patients' diagnoses were assessed by means of the criteria of the Structured Clinical Interview for DSM-IV Axis I Disorders [22]. Other inclusion criteria were as follows: (1) obsessive-compulsive symptoms had to have been present for at least 1 year prior to the study entry; (2) a Yale-Brown Obsessive Compulsive Scale (Y-BOCS) [23,24] total score of ≧16 had to be reached, and (3) a 17-item Hamilton Rating Scale for Depression (HAM-D-17) [25] score of ≧15 at the baseline evaluation was required. Moreover, all patients had to fulfill the following criteria for the BDT: (a) acceptance of a psychotherapeutic approach, and (b) the presence of a focal problem and/or of a recent precipitating life event, as suggested by Malan [26] and Horowitz et al. [27].

The exclusion criteria were: (1) a lifetime diagnosis of bipolar disorder, schizophrenia, other psychotic disorders, mental retardation or drug abuse; (2) an organic brain syndrome or medical illness that would contraindicate the use of fluvoxamine or sertraline; (3) a severe axis II psychopathology (cluster A personality disorder, antisocial personality disorder and borderline personality disorder according to the DSM-IV) that would contraindicate the treatment with BDT; (4) pregnant or nursing women and women of childbearing potential not using adequate contraceptive measures, and (5) an ongoing psychological treatment.

The sample selection via application of the inclusion/exclusion criteria is shown in figure 1. Written informed consent was requested for all patients who fulfilled the inclusion/exclusion criteria prior to their study enrolment, after the procedure had been fully explained.

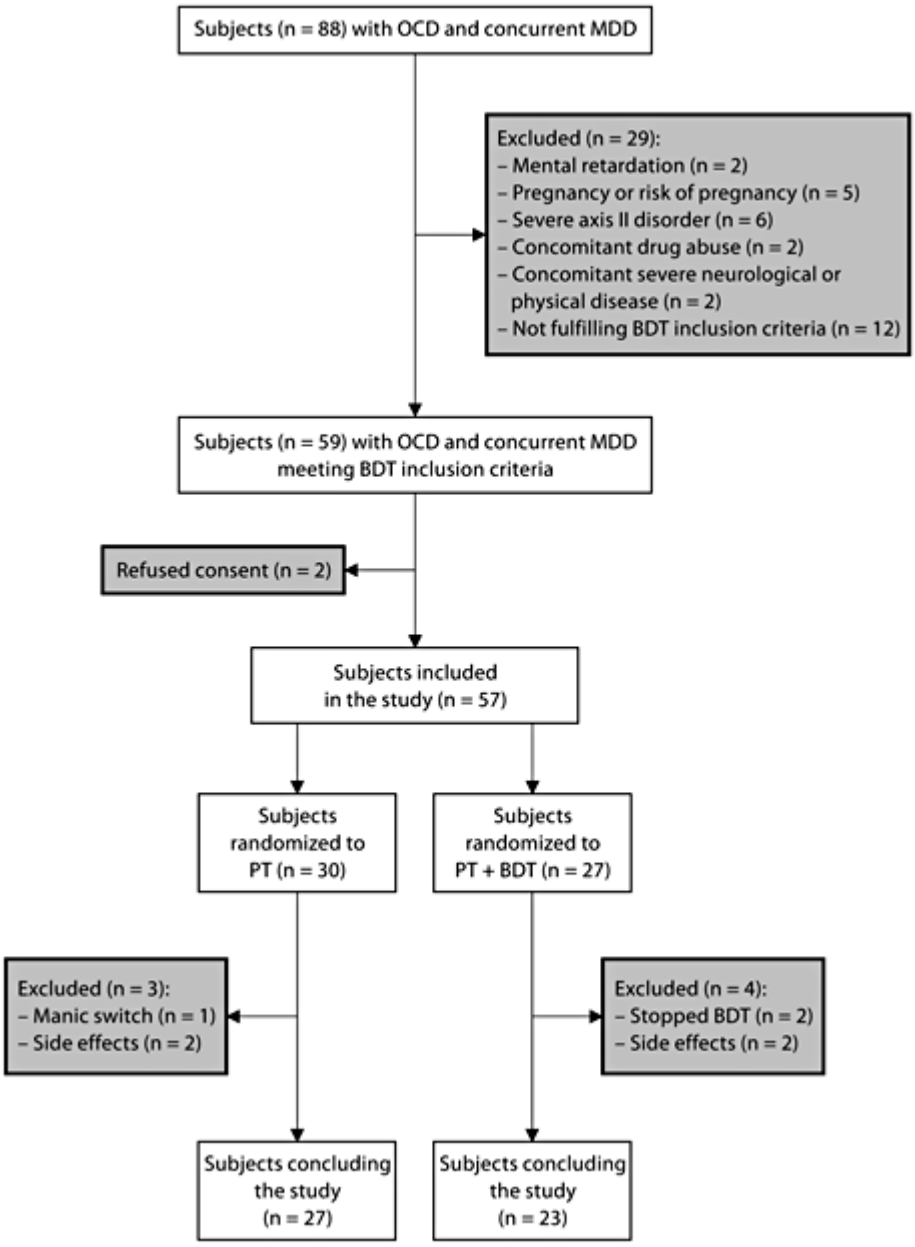

Fig. 1. Flow diagram of sample selection. PT = Pharmacotherapy.

PROCEDURE

The question of the relative efficacy of the addition of BDT to pharmacotherapy was addressed in a 12-month randomized parallel-group design. The patients were allocated randomly to pharmacotherapy plus BDT or pharmacotherapy alone by the study recruiter, who drew 1 of 2 colored balls from a bag, the assignment of each therapy to a different colored ball having been defined at the start of the study and maintained until the end of the recruitment period. The psychiatrist who conducted the randomization was not involved in the assessment/treatment of the patients. The intended medication period was 12 months with or without supplemental BDT in the first phase of the study (16 weeks).

The trial was preceded by a 2-week period in which the diagnosis was assessed by means of the Structured Clinical Interviews for DSM-IV Axis I [22] and II Disorders [28], the inclusion and exclusion criteria were checked and the baseline assessments made. If necessary, this period was used as a drug washout period (without placebo). The BDT started within 1 week after the initiation of pharmacotherapy; at the end of the randomized controlled trial (pharmacotherapy with or without combined BDT), the patients entered a continuation treatment period with pharmacotherapy (same drug at the same dose). The patients were treated by a psychiatrist (or an advanced supervised resident in psychiatry) who provided medication, and by a psychotherapist (who was not the psychiatrist providing the medication).

PHARMACOTHERAPY

All patients were treated with 1 of the 2 following selective serotonin reuptake inhibitors: fluvoxamine or sertraline. Fluvoxamine was given initially at a dose of 100 mg/day with increases in dosage every 3 days (100 mg) to a daily dose of 300 mg; sertraline was given initially at a dose of 50 mg/day, with increases every 3 days of 50 mg to a daily dose of 200 mg/day. The intended medication period was 12 months. The psychiatrist made 12 appointments of 20 min each with his patient, the first 4 appointments weekly, the following 5 monthly, and the last 3 every 2 months. Furthermore, the patients were informed to contact their psychiatrist every time they experienced a worsening of symptoms or side effects/adverse events. The task of the psychiatrist was to provide pharmacotherapy and clinical management. The latter consisted of providing psychoeducation, discussing the effects and side effects of the medication, and motivating the patient to comply with the medication regimen.

BRIEF DYNAMIC THERAPY

The primary objective of BDT is to enhance the patient's insight into repetitive conflicts (intrapsychic and interpersonal) and traumata that underlie and sustain the patient's problems. The principal instruments of BDT are interpretation and clarification: the therapist makes use of the actual relationship and attends to linkages with past significant relationships. The time limitation and the focal exploration of the patient's life and emotions distinguish the treatment from many current psychoanalytic psychotherapies. The psychotherapeutic technique we apply in our department as BDT derives from Malan's [29] focused short-term psychoanalytic psychotherapy. In the initial phase of BDT, the clinical picture is assessed and, identified as part of a treatable disorder, a primary problem area is defined as a focus.

According to the contributions by French [30,31], the focal problem refers to a situation where a wish or impulse, in contrast with a person's enduring values and expectations, leads to a defensive compromise. Since confrontation with all 3 features – wish, threat and defensive compromise – might help a patient to arrive at more adaptive positions, this model has been referred to as one of several 'triangles of insight'. The formulation of the focal problem in therapy serves to guide the interpretative work around an organizing theme. Symptoms, conflicts or crises may represent primary problem areas.

In the middle phase, the identified focus is addressed. In the terminal phase, the end of the treatment is explicitly discussed, progress is reviewed and gains are consolidated. The patients are told from the outset that their treatment will be limited in time, and the final session is previously established.

Two graduate therapists provided the BDT; they were both psychiatrists who had completed a personal training in psychodynamic psychotherapy. The sessions were weekly, lasting 45 min, individually administered and consisting of a face-to-face interview. The number of sessions ranged from 10 to 16. Any missed sessions were included as part of the psychotherapeutic protocol. An experienced BDT therapist, who reviewed the case notes and supervised treatment adherence according to the manuals, weekly monitored each BDT therapist.

CLINICAL ASSESSMENT

The primary efficacy assessments were the Y-BOCS and the HAM-D-17; the secondary efficacy measures included the Clinical Global Impression-Severity (CGI-S) scale [32], the Clinical Global Impression-Improvement (CGI-I) scale and the Global Assessment of Functioning (GAF) [33].

The patients were assessed while they were in the waiting list condition (pretest condition: T0), at the start of the treatment time (baseline: T1), at the end of the first phase of the study (medication with or without supplemental BDT; week 16: T2), and at the end of the 12-month study (T3). At each evaluation timepoint, all the primary and secondary outcome measures were employed; the CGI-I was rated from T1. In addition, all patients were informed to contact their psychiatrist every time they experienced a worsening of symptoms; in this case, another evaluation was conducted by the same rating scales.

Two raters assessed all patients; they were 2 psychiatrists who did not participate in the study as therapists and were kept blind with respect to the treatment assignment. The patients were advised not to talk to the evaluators about the type of psychotherapy they were on. In the early phase of the study, the interrater agreement on the diagnosis and on the primary efficacy measures was ascertained. The interrater reliability of the DSM-IV diagnosis was good ($\kappa = 0.79$; 95% CI = 0.71–0.87). Pearson's correlation coefficient between rater pairs and intraclass correlation coefficients demonstrated excellent agreement for the Y-BOCS total and individual items of 10 OCD patients assessed before the beginning of the study ($p < 0.0001$). In 10 depressed subjects, the correlation of the scores obtained by our raters from the HAM-D-17 was above 0.90.

STATISTICAL ANALYSIS

All statistical analyses were performed by SPSS software version 15.0. The results of the statistical comparisons of the treatment groups were presented as two-sided p values rounded off to 3 decimal places. The criterion for statistical significance in all comparisons was a p value <0.050.

Analysis of variance was performed to test the comparability of continuous variables in the 2 groups (index age and educational level). Analyses of covariance, including the initial measures as

covariants, were used to test intergroup and intragroup differences in rating scale scores (Y-BOCS, HAM-D-17, CGI and GAF).

Pearson's χ^2 calculations were used to compare sex ratio, marital status and occupational status among the groups. Pearson's χ^2 calculations (two-sided; $p < 0.05$) were used to compare the 4 different outcome measures of the qualitative evaluation: (a) Y-BOCS response (Y-BOCS reduction of at least 35% from baseline); (b) HAM-D-17 response (HAM-D-17 reduction of at least 50% from base rate); (c) HAM-D-17 remission (HAM-D-17 score of 7 points or less), and (d) CGI success (CGI-S score: 1–2).

The data analysis method used for outcome measures was performed on the 'intent-to-treat (ITT) efficacy' patient sample, which consisted of those patients randomized to the trial who took at least 1 capsule of study medication and had at least 1 valid postbaseline efficacy evaluation either on the study medication or within 3 days of drug discontinuation. Analyses were performed using both observed-cases and 'last-observation-carried-forward' data, i.e. in the case of a patient's missing data before the regular end, the last observation scores on the study drug were used.

To define the sample size of the 2 groups, we used the formula for minimum sample size related to the comparison of means (in particular, we considered the Y-BOCS means) [34], given a significance level of 0.05 and a statistical power of 90%; thus, the size of each subgroup had to be at least 15 patients.

RESULTS

A total of 57 participants were randomly assigned to combined BDT and medication (n = 27) or to medication alone (n = 30). The dropout rate was 14.8% (n = 4) in the medication plus BDT group, and 10% (n = 3) in the medication group (difference not statistically significant). All withdrawals from the study were between T1 and T2. In the group of patients treated with supplemental BDT, the dropouts were due to the fact that a patient stopped attending the psychotherapy sessions (n = 2) or to medication side effects (n = 2); in the group of patients only treated with pharmacotherapy, the dropouts were due to medication side effects (n = 2) or to a hypomanic switch (n = 1).

The ITT efficacy patient sample consisted of 54 patients (25 in combined treatment and 29 under medication alone) because 3 of the dropouts did not have any postbaseline assessment. The characteristics of the ITT sample are given in table 1. No statistically significant differences were found between the 2 treatment groups in demographic or baseline rates. In the subgroup treated with the combined treatment, the mean number of sessions was 14.0 ± 1.6 (mode = 16; median = 14).

No differences between the 2 treatment groups were found at any point by any assessment method in the ITT sample. Table 1 presents the efficacy results expressed in mean Y-BOCS scores (total score, and obsessions and compulsions subscale scores), HAM-D-17 score, CGI scores (severity and improvement) and GAF scores. The success rates (Y-BOCS response, HAM-D-17 response, HAM-D-17 remission and CGI-S success) are also shown in table 1.

Intragroup differences between baseline and discharge assessments (T3) were statistically significant in both treatment conditions: a significant reduction in symptomatology emerged from the Y-BOCS total and subscale scores as well as from the HAM-D-17 and CGI total scores. The results on the efficacy of both treatments from the GAF were not significant.

Concerning the additional information obtained by interviewing patients at the conclusion of the BDT sessions, the psychotherapy was 'extremely liked' by 15.5% of the BDT patients, and only 35% thought the therapy was 'extremely helpful'.

	PT + BDT (n = 25)	PT (n = 29)	Analysis		
			χ^2/F	d.f.	p
Sex			0.004	1	1.000
Males	11 (44)	13 (44.8)			
Females	14 (56)	16 (55.2)			
Age, years	30.32 ± 7.3	32.59 ± 7.6	1.236	1	0.271
Marital status			0.774	2	0.679
Married	8 (28)	10 (37.9)			
Divorced	3 (12)	4 (13.8)			
Never married	14 (60)	15 (48.3)			
Educational level, years	10.96 ± 3.9	11.68 ± 3.6	0.474	1	0.494
Working for pay			0.011	1	0.570
Yes	15 (60)	17 (58.6)			
No	10 (40)	12 (41.4)			
Y-BOCS total score					
Pretreatment (T0)	23.16 ± 3.7	23.39 ± 3.3	0.053	1	0.819
Baseline (T1)	23 ± 3.7	23.34 ± 3.2	1.808	1	0.185
Week 16 (T2)	18.48 ± 5.2	18.48 ± 5.2	0.016	1	0.900
Discharge (T3)	17.8 ± 6.1	17.79 ± 4.7	0.050	1	0.825
Y-BOCS obsessions subscale score					
Pretreatment (T0)	11.48 ± 2.2	11.62 ± 1.9	0.063	1	0.804
Baseline (T1)	11.44 ± 2.2	11.59 ± 1.9	0.008	1	0.928
Week 16 (T2)	8.92 ± 3.5	8.97 ± 2.6	0.022	1	0.882
Discharge (T3)	8.60 ± 3.4	8.59 ± 2.5	0.054	1	0.817
Y-BOCS compulsions subscale score					
Pretreatment (T0)	11.68 ± 2.4	11.79 ± 2.1	0.033	1	0.857
Baseline (T1)	11.56 ± 2.4	11.76 ± 2.1	1.406	1	0.241
Week 16 (T2)	9.44 ± 3.5	9.52 ± 2.9	0.003	1	0.954
Discharge (T3)	9.2 ± 3.2	9.21 ± 2.7	0.026	1	0.873
HAM-D-17 score					
Pretreatment (T0)	18.12 ± 4.6	20.48 ± 5.1	3.084	1	0.085
Baseline (T1)	17.56 ± 4.9	20.41 ± 5.1	4.551	1	0.058
Week 16 (T2)	13.52 ± 5.6	15.55 ± 5.6	0.117	1	0.734
Discharge (T3)	13.40 ± 5.3	15.10 ± 5.5	0.015	1	0.902
CGI-S score					
Pretreatment (T0)	4.16 ± 0.5	4.14 ± 0.5	0.023	1	0.880
Baseline (T1)	4.16 ± 0.5	4.14 ± 0.5	0.135	1	0.714
Week 16 (T2)	3.32 ± 1.4	3.45 ± 1.0	0.402	1	0.529
Discharge (T3)	3.32 ± 1.4	3.45 ± 1.0	0.402	1	0.529
CGI-I					
Baseline (T1)	3.78 ± 0.4	3.87 ± 0.3	0.759	1	0.136
Week 16 (T2)	2.92 ± 1.2	3.31 ± 0.8	1.573	1	0.215
Discharge (T3)	2.92 ± 1.2	3.31 ± 0.8	1.573	1	0.215
GAF score					
Pretreatment (T0)	72.2 ± 12.1	72.14 ± 9.8	0.000	1	0.984
Baseline (T1)	72.32 ± 12.3	72.45 ± 9.8	0.679	1	0.414
Week 16 (T2)	73.12 ± 11.6	72.97 ± 10.2	0.013	1	0.910
Discharge (T3)	73.36 ± 11.1	72.69 ± 10.3	0.420	1	0.520
Y-BOCS response					
Week 16 (T2)	6 (24)	11 (37.9)	1.208	1	0.380
Discharge (T3)	8 (32)	12 (41.4)	0.506	1	0.576
HAM-D-17 response					
Week 16 (T2)	6 (24)	8 (27.6)	0.090	1	1.00
Discharge (T3)	7 (28)	7 (24.1)	0.104	1	0.766
HAM-D-17 remission					
Week 16 (T2)	1 (4)	0 (0)	1.182	1	0.463
Discharge (T3)	1 (4)	0 (0)	1.182	1	0.463
CGI success					
Week 16 (T2)	7 (28)	6 (20.7)	0.393	1	0.751
Discharge (T3)	8 (32)	6 (20.7)	0.894	1	0.371

Values denote numbers or means ± SD. Figures in parentheses are percentages.

Table 1. Sociodemographic characteristics, mean scores of rating scales and response/remission rates of ITT study sample

DISCUSSION

This study addressed the pragmatic question of the clinical utility of the addition of BDT to pharmacotherapy in the treatment of OCD with concurrent MDD. This is the first randomized trial involving a clinical sample of patients with OCD and concurrent MDD in which two types of treatments – combined therapy (BDT added to medication) and medication alone – were compared in terms of obsessive-compulsive symptoms, depressive symptoms and global functioning. The duration of the study was 12 months; the patients were randomly assigned to receive a standard selective serotonin reuptake inhibitor treatment with or without supplemental BDT in the first part of the study, and they all continued the medication treatment in the following period. They were all assessed by blinded investigators. The randomization in our study appeared successful.

Considering the change scores of obsessive-compulsive measures, patients in both treatment groups showed a significant improvement over the study period in the mean Y-BOCS scores, with no differences between the treatment groups. The response rates at the end of the acute treatment phase (24 and 37.9% for pharmacotherapy with and without BDT, respectively) and after the following 6 months (32 and 41.4% for pharmacotherapy with and without BDT, respectively) were comparable between the two treatment groups. The fact that these response rates were lower and not consistent with those generally reported for OCD patients may be related to two aspects: a) the majority of the referred patients had previously received ineffective or partly effective psychological and/or pharmacological treatments; b) the concurrent major depression – studies on combined pharmacotherapy and CBT [11,12], and a large multicenter trial examining clomipramine treatment for OCD [13] already found that higher levels of initial depression were generally associated with a diminished efficacy.

Ratings of depressive symptoms suggested that the improvement in depression was correlated with the improvement in OCD: patients in both treatment groups showed a significant improvement over the study period in the mean HAM-D-17 scores with no differences between the treatment groups, and the response and remission rates were comparable between the two treatment groups. Substantially lower rates of response and, especially, of remission were evident if we consider the response/remission rates that are usually reported for the treatment of MDD. One explanation would be that MDD in the context of OCD is different than MDD without OCD. Alternatively, it seems possible that MDD is often secondary to functional impairment due to OCD: MDD is maintained by demoralization related to ongoing OCD symptoms and the associated negative impact of such symptoms on social and work functioning. The absence of a significant change in GAF scores in both groups supports this hypothesis.

However, there are three main limitations that need to be addressed regarding the present study: the first limitation concerns the absence of a control condition [35,36]. The second limitation regards the relatively small sample size. The third limitation is the fact that BDT (unlike CBT) is not considered to be a highly effective treatment for depression.

Nevertheless, two interesting findings emerged. First, supplemental BDT in the treatment of patients with OCD with concurrent MDD who are receiving effective medication has no significant advantages. Second, supplemental BDT that is effective in the long-term treatment of MDD is not active in MDD secondary to OCD.

Further studies of specific treatments for OCD without excluding concurrent major depression are warranted, and specific change measures of obsessive-compulsive symptoms, of depressive symptoms and of global functioning are indicated.

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