ORIGINAL ARTICLE

A Randomized Placebo-Controlled Trial of Fluoxetine in Body Dysmorphic Disorder

Katharine A. Phillips, MD; Ralph S. Albertini, MD; Steven A. Rasmussen, MD

Background: Research on the pharmacotherapy of body dysmorphic disorder (BDD), a common and often disabling disorder, is limited. Available data suggest that this disorder may respond to serotonin reuptake inhibitors. However, no placebo-controlled treatment studies of BDD have been published.

Methods: Seventy-four patients with *DSM-IV* BDD or its delusional variant were enrolled and 67 were randomized into a placebo-controlled parallel-group study to evaluate the efficacy and safety of fluoxetine hydrochloride. After 1 week of single-blind placebo treatment, patients were randomized to receive 12 weeks of double-blind treatment with fluoxetine or placebo. Outcome measures included the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS) (the primary outcome measure), the Clinical Global Impressions Scale, the Brown Assessment of Beliefs Scale, and other measures.

Results: Results of the BDD-YBOCS indicated that fluoxetine was significantly more effective than placebo for BDD beginning at week 8 and continuing at weeks 10 and 12 ($F_{1,64}=16.5$; $P<.001$). The response rate was 18 (53%) of 34 to fluoxetine and 6 (18%) of 33 to the placebo ($\chi^2_1=8.8$; $P=.003$). The BDD symptoms of delusional patients were as likely as those of nondelusional patients to respond to fluoxetine, and no delusional patients responded to the placebo. In the sample as a whole, treatment response was independent of the duration and severity of BDD and the presence of major depression, obsessive-compulsive disorder, or a personality disorder. Fluoxetine was generally well tolerated.

Conclusion: Fluoxetine is safe and more effective than placebo in delusional and nondelusional patients with BDD.

Arch Gen Psychiatry. 2002;59:381-388

From Butler Hospital and the Department of Psychiatry and Human Behavior, Brown University School of Medicine, Providence, RI. Dr Phillips has received research support and occasional speaking honoraria from Eli Lilly & Co, Indianapolis, Ind.

BODY DYSMORPHIC disorder (BDD), also known as dysmorphophobia, consists of a distressing or impairing preoccupation with an imagined or slight defect in appearance. Although BDD was first described more than a century ago,[1] research on its pharmacologic treatment remains limited and no placebo-controlled pharmacotherapy studies have been done to our knowledge. Such research is needed since BDD causes severe distress and marked impairment in functioning.[1-6] A high percentage of patients require hospitalization, become housebound, and attempt suicide.[3,7] Completed suicide has been reported in both psychiatric[1] and dermatologic[8,9] settings, and quality of life is notably poor.[10]

Body dysmorphic disorder seems to be relatively common in community,[11-13] psychiatric,[14-16] cosmetic surgery,[17-19] and dermatologic[20] settings. As many as 50% of patients with BDD receive surgery or dermatologic treatment, often with poor outcomes.[2,3,7] In all of these settings, BDD has been reported to be extremely difficult to treat.[21-23]

Early case reports noted mixed but largely negative outcomes with a variety of psychotropic agents and electroconvulsive therapy.[1] However, subsequent data from case series and 2 open-label fluvoxamine maleate trials suggest that BDD may respond to serotonin reuptake inhibitors (SRIs).[3,7,24-30] The only published controlled pharmacotherapy trial on BDD to our knowledge was a double-blind crossover study, which found that the SRI clomipramine hydrochloride was more effective than the non-SRI antidepressant desipramine hydrochloride,[31] supporting earlier retrospective findings[3,7,25] that SRIs may be selectively effective for BDD and that the treatment response of BDD differs from that of depression.

Most patients with BDD have poor insight or are delusional regarding their appearance flaws,[7] which has the potential to complicate treatment. Available data suggest that patients with delusional BDD respond to SRIs as well as[3,7,28,32] or even better than[31]

PATIENTS AND METHODS

PATIENTS

The study was done in outpatients at a single academic site. Patients were entered into the study from August 1995 through February 2000. All patients met *DSM-IV* criteria for BDD[33]: (1) preoccupation with an imagined defect in appearance; if a slight physical anomaly is present, the person's concern is markedly excessive; (2) the preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning; and (3) the preoccupation is not better accounted for by another mental disorder (eg, dissatisfaction with body shape and size in anorexia nervosa). Because the Structured Clinical Interview for *DSM-III-R* (SCID-P)[34,35] did not include BDD, BDD was diagnosed with the Body Dysmorphic Disorder Diagnostic Module, a reliable semistructured SCID-like diagnostic instrument based on *DSM-IV* criteria.[36] Patients with delusional beliefs about their appearance (delusional disorder, somatic type) were included because the delusional and nondelusional forms of BDD seem to constitute the same disorder,[7] and patients with delusional BDD may be diagnosed with both BDD and delusional disorder according to the *DSM-IV*[33] (patients with other types of somatic delusions but no appearance-related delusions were excluded). Body dysmorphic disorder was diagnosed by the consensus of the first 2 authors. A family member or other informant was interviewed (for the 36 patients willing and able to do this); in all cases, the BDD diagnosis was confirmed. Comorbid disorders were diagnosed by the first author with the SCID-P and the Structured Clinical Interview for *DSM-III-R* Personality Disorders.[37,38] Data on the clinical characteristics of BDD were obtained with a semistructured instrument (K.A.P., unpublished data, 1992).

Inclusion criteria were (1) presence of *DSM-IV* BDD or its delusional variant currently and for at least 6 months; (2) age 18 to 65 years; (3) score of 24 or higher on the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS)[39]; (4) score of at least moderate on the Clinical Global Impression Scale for BDD (BDD-CGI)[40]; (5) ability to communicate and give written informed consent.

Exclusion criteria were (1) schizophrenia, schizoaffective disorder, or another current or lifetime psychotic disorder not attributable to delusional BDD; (2) current or lifetime bipolar disorder; (3) alcohol or substance dependence or abuse in the past 6 months; (4) body image concerns better accounted for by an eating disorder, including eating disorder not otherwise specified; (5) primary body image concern with weight and BDD criteria not met if weight concerns were excluded from consideration; (6) recent suicide attempt or clinically significant suicidal ideation; (7) use of psychoactive medication within 2 weeks of placebo lead-in (6 weeks for fluoxetine); (8) use of investigational medication within 3 months or a depot neuroleptic within 6 months of placebo lead-in; (9) past treatment with fluoxetine for 8 weeks or longer or with a dose of 40 mg/d or more; (10) initiation of psychotherapy (including cognitive-behavioral therapy) within 4 months of lead-in; (11) significant or unstable medical illness; (12) history of seizures; (13) pregnancy, lactation, or lack of contraception in women of childbearing potential; (14) clinically relevant abnormal laboratory tests; (15) requirement for psychotropic medication; (16) inability to cooperate with the protocol.

Potential participants (n=296) were screened by telephone, 158 of whom seemed to qualify and were evaluated in person by the first author. Seventy-four patients were enrolled in the study; 54% (n=40) were self-referred, 35% (n=26) were referred by a professional, and 11% (n=8) responded to an advertisement. The protocol and informed consent documents were approved by the institutional review board. After a thorough description of the study to patients, including its rationale, procedures, and potential risks and benefits, voluntary written informed consent was obtained.

STUDY DESIGN AND PROCEDURES

After completing the screening evaluations during 2 to 3 weeks, patients received single-blind pill placebos for 1 week. Patients whose BDD-YBOCS score decreased by 30% or more during this week were terminated from the study; those who still qualified were randomly assigned in a 1:1 ratio to 12 weeks of double-blind treatment with fluoxetine or placebo. Randomization was performed by a technician with no clinical contact who kept the code during the trial. A computer-generated urn randomization procedure[41] balanced the 2 study groups for current major depression, current OCD, and whether the appearance-related beliefs were currently delusional.

Patients received fluoxetine, 20 mg/d, or pill placebo–equivalent (identical-appearing capsules) for 2 weeks. The dose was increased by 20 mg/d every 10 days to a maximum of 80 mg/d, as tolerated, and could be decreased by 10 mg/d or 20 mg/d at any time as clinically indicated. Patients who could not tolerate at least 20 mg of fluoxetine or placebo per day were terminated from the study. No other psychotropic medications were taken except chloral hydrate, 0.5 to 2.0 g/d, no more than 3 times per week if needed for insomnia. Psychotherapy of any type was not initiated during the study.

One of us (K.A.P.), who was blind to adverse events, did all of the ratings. Adverse events were assessed by the second

nondelusional patients, although most studies did not assess delusionality (insight) with a reliable and valid scale. In addition, several studies found that delusionality improves with SRI treatment.[31,32] Although data are very limited, antipsychotics alone seem ineffective for delusional BDD.[3,7]

We report the first placebo-controlled treatment study of BDD and its delusional variant. We hypothesized that (1) fluoxetine hydrochloride would be more effective than placebo (the primary hypothesis); (2) delusional BDD would respond as well as nondelusional BDD to fluoxetine; and (3) illness severity and the presence of major depression, obsessive-compulsive disorder (OCD), or a personality disorder would not predict outcome.

RESULTS

PATIENT SAMPLE DESCRIPTION

Of the 74 enrolled patients, 6 were discontinued from the study during the screening period and 1 was discon-

author, who also adjusted the medication dose. Returned medication was counted to verify compliance. After completing the double-blind phase, placebo-treated patients were offered 12 weeks of open-label fluoxetine treatment.

ASSESSMENTS

The BDD-YBOCS was selected a priori as the primary outcome measure. This 12-item semistructured clinician-rated scale,[39] adapted from the Y-BOCS,[42,43] assesses BDD severity during the past week. Each item is scored on a 5-point scale from 0 (least symptomatic) to 4 (most symptomatic), with a total score of 0 to 48. Items assess preoccupation with the perceived defect (time occupied, interference with functioning due to the preoccupation, distress, resistance, and control), associated repetitive behaviors, such as mirror-checking (time spent, interference with functioning, distress if the behaviors are prevented, resistance, and control), insight, and avoidance. The scale is reliable, valid, and sensitive to change.[39] Response was defined as a 30% or greater decrease in total score, an empirically derived cut point that corresponds to clinically significant improvement in BDD symptoms.[39] Secondary measures of BDD outcome were the CGI improvement scale[40] and the National Institute of Mental Health Global Obsessive Compulsive Scale,[44] a 15-point global rating of BDD severity (BDD-NIMH). Clinical Global Impressions Scale ratings were done for BDD symptoms and for global outcome; patients and the clinician provided separate ratings. A CGI score of much or very much improved (score of 1 or 2) was defined as improvement. The CGI severity scale[40] assessed illness severity at baseline.

The delusionality (insight) of beliefs about appearance (patient's conviction that his or her appearance was abnormal) was assessed with the Brown Assessment of Beliefs Scale. This 7-item semistructured clinician-administered scale assesses delusionality during the past week both dimensionally and categorically.[45] Patients were categorized at baseline as delusional (n=27) or nondelusional (n=37) using an a priori empirically derived cut point.[45] The scale is reliable, valid, and sensitive to change.[45] Items are conviction, perception of others' views, explanation of differing views, fixity, attempts to disprove beliefs, insight (recognition that the belief has a psychiatric etiology), and ideas/delusions of reference. Scores range from 0 to 24. Three patients could not be assessed because they had clearly noticeable skin lesions due to skin picking.

The 17-item Hamilton Rating Scale for Depression (HAM-D)[46] assessed current severity of depressive symptoms, and the Brief Psychiatric Rating Scale (BPRS)[47] assessed severity of psychopathology. The Social and Occupational Functioning Scale (SOFAS)[33] evaluated psychosocial functioning, and the Global Assessment of Functioning (GAF)[48] rated symptom severity and functioning.

All patients received an electrocardiogram, physical examination, and standard laboratory tests, including a drug screen; another physical examination was done at study end point. The BDD-YBOCS, BDD-NIMH, Brown Assessment of Beliefs Scale, and HAM-D were administered at each visit, the CGI severity scale was rated at baseline, and the CGI improvement scale was rated at all visits subsequent to randomization. The BPRS, GAF, and SOFAS were completed at baseline and end point. At each visit, patients were asked whether they had any adverse physical symptoms since the last visit, which were rated for severity, action taken, outcome, and seriousness. At termination, patients and the first author judged which treatment had been received.

STATISTICAL ANALYSES

All data were double entered to ensure accuracy. Data were analyzed with the Statistical Package for the Social Sciences, version 6.1 for the Macintosh (SPSS Inc, Chicago, Ill). All tests of group differences on outcome variables used an intent-to-treat analysis plan that included all randomized patients, with last observation carried forward for dropouts. Except for CGI improvement ratings, the dependent variable was the change in outcome from baseline. All tests were 2-tailed. An α level of .05 was used to determine statistical significance.

Efficacy analyses for continuous variables were performed using analysis of covariance (ANCOVA), with baseline measures as the covariate. A repeated-measures ANCOVA further tested for a time effect, a treatment effect, and a time-by-treatment interaction on the dependent measure between groups. The ANCOVA, using the baseline score as a covariate, determined when significant drug-placebo differences occurred. When tests of sphericity were violated, the Huynh-Feldt statistic was used. Independent sample *t* tests were also used to analyze continuous variables (when tests of homogeneity of variance were violated, the nonparametric alternative, the Mann-Whitney *U* test, was used). The χ^2 analysis and Fisher exact test were used to analyze dichotomous variables. The effect size (f) and 95% confidence intervals were calculated to measure treatment strength. An effect size (f) of 0.25 is considered a medium effect and 0.40 is considered large.[49] The Pearson product moment correlation coefficient was used to examine correlations between variables, and stepwise multiple regression assessed predictors of treatment outcome. The incidence of adverse events was based on the number of patients who reported a given treatment-emergent event (ie, an event that first appeared or worsened during double-blind therapy).

tinued after the single-blind placebo lead-in week because her BDD-YBOCS score decreased to less than 24 (**Figure 1**). No patients responded to the single-blind placebo. Sixty-seven patients were randomized to receive double-blind treatment with fluoxetine (n=34) or placebo (n=33). Three patients (9%) randomized to receive fluoxetine and 5 (15%) randomized to receive placebo discontinued study participation (χ^2_1=0.64; *P*=.42).

There were no significant differences between the fluoxetine (n=34) and placebo (n=33) groups on baseline demographic and clinical characteristics (**Table 1**). For example, skin (eg, acne) and hair (eg, hair loss) were the most common appearance concerns (skin: 25 [74%] in the fluoxetine group and 26 [79%] in the placebo group; hair: 14 [41%] in the fluoxetine group and 19 [58%] in the placebo group). Twelve patients (37.5%) in the fluoxetine group and 15 patients (46.9%) in the placebo group were delusional at baseline. Ongoing psychotherapy (begun before study entry) was received during the study by 3 patients in the fluoxetine group and 3 patients in

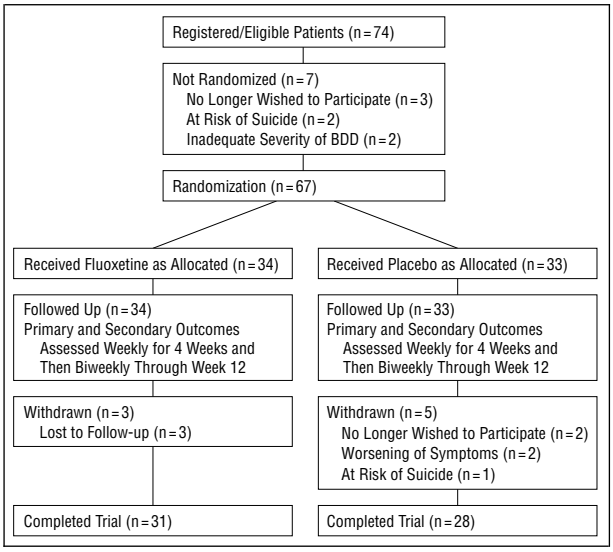

Figure 1. Progress of 74 patients through the trial. BDD indicates body dysmorphic disorder.

the placebo group; none of these patients were receiving cognitive-behavioral therapy.

TREATMENT OUTCOME OF BDD

Fluoxetine was superior to placebo for BDD symptoms as measured by the primary and secondary BDD outcome measures and both clinician and patient ratings (**Table 2**). Controlling for baseline group differences in BDD severity, on the BDD-YBOCS (the primary outcome measure), fluoxetine was more effective than placebo ($F_{1,64}=16.5$; $P<.001$) beginning at week 8 ($F_{1,64}=4.63$; $P=.04$) and continuing at weeks 10 and 12 (**Figure 2**). The mean change from baseline in the BDD-YBOCS total score was more than twice as large with fluoxetine as with placebo treatment (35% vs 14% decrease; $t_{65}=3.54$; $P=.001$), with a similar decrease for BDD preoccupations and repetitive behaviors. The response rate on the BDD-YBOCS to fluoxetine was 53% (18/34) vs 18% (6/33) to placebo ($\chi^2_1=8.8$; $P=.003$). The treatment effect size was medium to large (f=0.35; 95% confidence interval, 0.22-0.48; d equivalent=0.70).

On the clinician-rated BDD-CGI, 14 patients (41%) treated with fluoxetine were much improved and 5 (15%) were very much improved. Functional impairment as assessed by the GAF and SOFAS improved more with fluoxetine than placebo (Table 2).

The mean±SD time to fluoxetine response (as assessed by a 30% decrease in BDD-YBOCS score) was 7.7±3.5 (range, 2-12) weeks and to placebo was 5.3±3.2 (range, 1-8) weeks ($t_{29}=1.97$; $P=.6$). The mean±SD fluoxetine dose at end point was 77.7±8.0 (range, 40-80) mg/d; the fluoxetine equivalent in the placebo group was 76.0±13.1 (range, 20-80) mg/d.

Of the 21 patients treated with open-label fluoxetine after placebo treatment during the double-blind phase (mean±SD fluoxetine dose at end point, 61.1±21.4 mg/d), 5 (24%) responded to the BDD-YBOCS. Scores decreased from a mean±SD score of 29.3±7.4 to 22.3±7.2 ($t_{20}=5.14$; $P<.001$). On the clinician-rated BDD-CGI, 9 (43%) responded, with 7 (33%) much improved and 2 (10%) very much improved.

In 34 cases (69%), the clinician correctly judged whether the patient had received fluoxetine or placebo; this was the case for 25 (63%) patients. The clinician's judgment was incorrect in 6 (12%) cases and the patient's in 10 (25%). The clinician was unsure of group assignment in 9 (18%) of cases and the patient in 5 (13%).

Table 1. Demographic and Clinical Characteristics of Intent-to-Treat Sample at Baseline*

Characteristics	Fluoxetine (n = 34)	Placebo (n = 33)
Age, mean ± SD, y	31.7 ± 11.8	32.6 ± 9.1
Sex, female	24 (70.6)	22 (66.7)
Marital status		
Single	22 (64.7)	20 (60.6)
Married	9 (26.5)	8 (24.2)
Divorced	3 (8.8)	5 (15.2)
Ethnicity		
White	29 (85.3)	31 (93.9)
African American	3 (8.8)	1 (3.0)
Hispanic	2 (5.9)	1 (3.0)
Education		
High school or less	4 (11.8)	6 (18.2)
Some college	12 (35.3)	11 (33.3)
College graduate	13 (38.2)	12 (36.4)
Graduate school	5 (14.7)	4 (12.1)
Employment		
Employed	17 (50.0)	24 (72.7)
Unemployed	10 (29.4)	5 (15.2)
Student	7 (20.6)	4 (12.1)
Living situation		
With spouse/children/other	18 (52.9)	11 (33.3)
With parents	10 (29.4)	11 (33.3)
Alone	6 (17.6)	11 (33.3)
Clinical features of BDD		
Age at BDD onset, mean ± SD, y	17.2 ± 6.5	17.1 ± 8.7
Duration of illness, mean ± SD, y	14.7 ± 12.6	14.2 ± 9.5
Mean ± SD body areas of concern	4.1 ± 2.5	4.9 ± 5.8
Mean ± SD repetitive behaviors	6.4 ± 2.6	5.7 ± 2.2
Patients with delusional BDD	12 (37.5)	15 (46.9)
Current comorbidity†		
Major depression	21 (61.8)	22 (66.7)
Social phobia	10 (29.4)	14 (42.4)
Obsessive-compulsive disorder	6 (17.6)	10 (30.3)
Personality disorder	22 (64.7)	13 (39.4)
CGI severity		
Moderately ill	4 (11.8)	3 (9.1)
Markedly ill	27 (79.4)	26 (78.8)
Severely ill	3 (8.8)	3 (9.1)
Most severely ill	0 (0)	1 (3.0)
Prior SRI treatment	13 (38.2)	15 (45.5)

*There were no statistically significant differences between groups. Data are given as number (percentage) of patients unless otherwise indicated. BDD indicates body dysmorphic disorder; CGI, Clinical Global Impression Scale; and SRI, serotonin reuptake inhibitor.

†These disorders were the most common current comorbid disorders.

OUTCOME IN DELUSIONAL AND NONDELUSIONAL PATIENTS

We tested for a difference in the amount of improvement in BDD symptoms from baseline to end point for delusional (n=27) vs nondelusional (n=37) patients, covary-

Table 2. Baseline and End Point Efficacy Measures by Treatment Group*

Measure	Baseline		End Point		Test Statistic	*P* Value
	Fluoxetine (n = 34)	Placebo (n = 33)	Fluoxetine (n = 34)	Placebo (n = 33)		
BDD-YBOCS	31.5 ± 5.6	30.8 ± 5.8	21.0 ± 9.8	26.9 ± 9.5	F = 16.5	<.001
Preoccupation subscale	13.1 ± 2.7	12.6 ± 2.5	8.9 ± 4.1	11.4 ± 3.7	F = 3.8	.01
Behaviors subscale	13.4 ± 2.5	12.9 ± 3.0	8.9 ± 4.1	10.9 ± 4.1	F = 3.0	.01
CGI (clinician), No. (%) much or very much improved						
BDD	. . .	. . .	19 (55.9)	8 (25.8)	χ^2 = 6.0	.02
Global	. . .	. . .	19 (55.9)	6 (19.42)	χ^2 = 9.1	<.001
CGI (patient), No. (%) much or very much improved						
BDD	. . .	. . .	14 (41.2)	4 (12.1)	χ^2 = 6.5	.02
Global	. . .	. . .	14 (41.2)	6 (18.2)	χ^2 = 3.6	.06
BDD-NIMH	8.6 ± 1.5	8.8 ± 1.6	6.6 ± 3.0	7.9 ± 2.2	F = 4.9	.04
Brown Assessment of Beliefs Scale	17.5 ± 4.2	18.5 ± 4.7	13.8 ± 7.2	15.4 ± 7.1	F = 0.2	.68
HAM-D	19.8 ± 8.3	21.5 ± 8.1	12.5 ± 10.1	19.5 ± 10.5	F = 7.5	.01
BPRS	28.8 ± 5.4	30.2 ± 4.9	26.2 ± 5.3	29.5 ± 6.0	F = 4.8	.03
GAF	54.4 ± 8.1	53.9 ± 7.6	68.9 ± 15.7	57.0 ± 12.3	F = 12.8	<.001
SOFAS	55.8 ± 9.1	56.3 ± 9.1	71.1 ± 17.8	59.9 ± 14.6	F = 9.1	<.001

*Data are given as mean ± SD unless otherwise indicated. BDD-YBOCS indicates Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder; CGI, Clinical Global Impressions Scale; BDD-NIMH, National Institute of Mental Health Global Obsessive Compulsive Scale modified for BDD; HAM-D, Hamilton Rating Scale for Depression (17-item); BPRS, Brief Psychiatric Rating Scale; GAF, Global Assessment of Functioning Scale; SOFAS, Social and Occupational Functioning Scale; and ellipses, not applicable.

ing for baseline BDD severity. We found no interaction between delusionality and improvement in BDD symptoms over time using a repeated-measures analysis ($F_{2.7,162}$=1.06; *P*=.36). The BDD symptoms of patients categorized as delusional at baseline were as likely as those of patients who were nondelusional at baseline to respond to fluoxetine (50% [6/12] vs 55% [11/20]; χ^2_1=0.08; *P*=.78). However, BDD symptoms of delusional patients were significantly less likely than those of nondelusional patients to respond to placebo (0% [0/15] vs 35% [6/17]; χ^2_1=6.51;*P*=.01). Although delusional patients had more severe BDD symptoms at baseline (delusional patients' mean±SD BDD-YBOCS scores, 33.0±5.1; nondelusional patients, 29.4±5.6; t_{62}=2.65; *P*=.01), an ANCOVA that controlled for BDD severity at baseline indicated that this did not account for their lower placebo response rates ($F_{1,61}$=1.91; *P*=.17). In delusional patients, the response rate of BDD symptoms to fluoxetine was significantly higher than to placebo (50% vs 0%; χ^2=9.6$_1$; *P*=.002). This was not the case for nondelusional patients (55% vs 35%; χ^2_1=1.44; *P*=.23), although power was limited (1–β=.27).

We also examined a second question: with treatment, did patients' conviction that their appearance was abnormal (delusionality) change with fluoxetine compared with placebo treatment? While Brown Assessment of Beliefs Scale scores decreased between baseline and end point for both the fluoxetine and placebo groups, the difference between them was not significant (Table 2). However, scores decreased significantly more in treatment responders than in treatment nonresponders (for both treatment groups combined ($F_{3.8,233.6}$=9.5; *P*<.001).

OUTCOME OF DEPRESSION

Hamilton Rating Scale for Depression scores improved significantly more with fluoxetine than with placebo (Table 2). Change in BDD-YBOCS and HAM-D scores was correlated *r*=0.65 (*P*<.001) for the fluoxetine group and *r*=0.58 (*P*<.001) for the placebo group. Two patients (6%) treated with fluoxetine and 10 (30%) treated with placebo had an increase (ie, worsening) on the HAM-D suicidal ideation item between baseline and end point (*P*=.001).

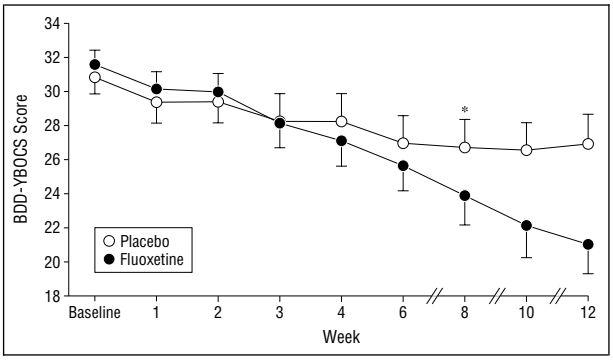

Figure 2. Scores over time on the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS) by treatment group for the intent-to-treat sample (n=67). Last observation carried forward ANCOVA (controlling for baseline BDD-YBOCS): $F_{1,64}$=16.5; *P*<.001. Response to placebo=6/33 (18.2%) vs fluoxetine=18/34 (52.9%) χ^2=8.8; *P*=.003. The asterisk indicates the 2 groups significantly differed beginning at this time point (*P*=.04). Bars represent 1 SE.

PREDICTORS OF TREATMENT OUTCOME

In the entire sample, BDD duration, BDD severity, and the presence of a personality disorder, current OCD, or current major depression did not predict response of BDD in a stepwise regression analysis. Furthermore, with regard to depression, there was no main effect of the diagnosis of major depression at baseline on BDD outcome ($F_{1,63}$=1.0; *P*=.32) and no interaction between major

Table 3. Incidence of Treatment-Emergent Adverse Events Occurring in 5% or More of Patients or With Significantly Greater Frequency in One Treatment Group in the Intent-to-Treat Sample*

Event	Fluoxetine (n = 34)	Placebo (n = 33)	*P* Value
Insomnia	13 (38.2)	9 (27.3)	.44
Drowsiness	12 (35.3)	2 (6.1)	.01
Stomach/abdominal discomfort	11 (32.4)	0 (0)	<.001
Headache	5 (14.7)	7 (21.2)	.54
Weakness/fatigue	5 (14.7)	2 (6.1)	.43
Nausea/vomiting	4 (11.8)	3 (9.1)	>.99
Tremor	4 (11.8)	0 (0)	.12
Dizziness	3 (8.8)	1 (3.0)	.62
Decreased libido	2 (5.9)	3 (9.1)	.67
Memory impairment	2 (5.9)	2 (6.1)	>.99
Rapid heartbeat	2 (5.9)	2 (6.1)	>.99
Diarrhea	1 (2.9)	3 (9.1)	.36

*Adverse events are listed irrespective of relationship to study drug and were counted once per subject. Data are expressed as number (percentage) of patients unless otherwise indicated. Group differences were determined using the Fisher exact test.

depression at baseline and treatment group on BDD outcome ($F_{1,63}$=0.70; *P*=.41). There was a significant effect of fluoxetine on BDD symptoms even after covarying for main and interactive effects of baseline depressive symptoms (HAM-D score; $F_{1,64}$=5.4; *P*=.02). As previously noted, delusional patients were less likely than nondelusional patients to respond to placebo. Treatment outcome did not differ by sex or minority status, although power to assess the latter was limited.

SAFETY AND TOLERABILITY

Treatment-emergent adverse events (irrespective of relationship to study drug) were reported by 82% of patients (n=28) treated with fluoxetine and 64% (n=21) treated with placebo (χ^2_1=3.0; *P*=.08). The only adverse events that were significantly more frequent with fluoxetine treatment were drowsiness and stomach/abdominal discomfort (**Table 3**). Five patients (7%) took chloral hydrate for insomnia. Adverse events were often transient, and nearly all were of mild to moderate severity and well tolerated. No patients discontinued the study because of adverse events. No serious adverse events (eg, suicide attempts or hospitalizations) occurred.

COMMENT

This study, the first placebo-controlled trial on BDD, indicates that fluoxetine is safe and more effective than placebo for BDD, including delusional patients. Fluoxetine was more effective for BDD on the primary and secondary BDD outcome measures and as assessed by both clinician and patient ratings, with a medium to large effect size. Depressive symptoms, global symptomatology, and functioning also improved significantly more with fluoxetine than with placebo.

Consistent with previous studies, fluoxetine was as effective for BDD symptoms in delusional as in nondelusional patients.[3,7,28,31,32] Unlike one previous study[31] in which an SRI was even more effective for delusional than nondelusional patients, we found a similar fluoxetine response rate in both groups, although in our study, the incremental effect of fluoxetine over placebo for BDD symptoms was greater for delusional than nondelusional patients. While patients with delusional symptoms are generally treated with antipsychotics, this finding suggests that SRIs may be effective for patients with certain types of delusional symptoms.[32] Whether antipsychotics alone are effective for delusional BDD has received virtually no investigation and needs to be studied. It is striking that no delusional patients responded to placebo. Given that delusional and nondelusional patients had significantly different placebo response rates, delusionality should be carefully assessed in future BDD treatment studies.

Our finding that delusionality (patient's conviction that his or her appearance was abnormal) did not improve significantly more with fluoxetine than with placebo contrasts with a previous study in which delusionality (insight) improved more with clomipramine than with desipramine (although we did find that delusionality improved more in treatment responders than in nonresponders).[31] The reason for these somewhat discrepant findings is unclear, although the 2 studies used different measures of delusionality. Further investigation of change in insight with SRI treatment is needed.

Although the dose was increased relatively rapidly, mean±SD time to fluoxetine response (7.7±3.5 weeks) was lengthy, consistent with previous studies indicating time to response of 6 to 9 weeks.[25,28,29] The mean±SD fluoxetine dose at study end point was relatively high (77.7±8.0 mg/d), although we attempted to reach 80 mg/d to avoid undertreatment. The efficacy of lower fluoxetine doses is unknown, and dose-finding studies are needed to ascertain the optimal dose of fluoxetine and other SRIs. Despite the relatively rapid titration and the high mean dose attained, the medication was generally well tolerated.

The only predictor of treatment outcome was delusionality, with delusional patients less likely than nondelusional patients to respond to placebo. Consistent with previous studies,[28,29] BDD symptoms improved regardless of whether patients had major depression or OCD at baseline. Although BDD severity did not predict treatment outcome, all subjects were required to have at least moderately severe BDD symptoms. Including patients with milder BDD might have yielded an association between BDD severity and treatment response and produced a higher placebo response rate, as has been found in other disorders.[50-52] This issue, however, requires investigation.

While the response rate on the BDD-YBOCS to open-label fluoxetine (subsequent to the double-blind phase) was relatively low, several patients were not classified as responders but their BDD-YBOCS scores decreased by nearly 30%. The mean magnitude of change on the BDD-YBOCS with open-label fluoxetine treatment was nearly as great as with double-blind treatment. In addition, given that 86% of patients treated with open-label fluoxetine had been placebo nonresponders, a somewhat lower re-

sponse rate to subsequent open-label fluoxetine (compared with double-blind fluoxetine) might be expected.

This study has several limitations characteristic of efficacy trials. It was conducted in a university-affiliated private psychiatric hospital, and the sample was selected to meet strict inclusion and exclusion criteria. Patients with milder BDD symptoms were excluded as were patients who were highly suicidal or who needed inpatient treatment. Future studies are required to determine how generalizable the results are to other populations of patients with BDD. Another limitation is that a longer treatment trial might have yielded a slightly higher fluoxetine response rate since an open-label fluvoxamine trial found that 5.3% of responders required more than 12 weeks to respond.[29]

These results, while promising, require replication. Placebo-controlled studies of other SRIs and parallel-group studies comparing SRIs with other medications (eg, antipsychotics) are needed, as are longer-term treatment studies (eg, continuation and maintenance studies), especially because BDD seems to be a chronic illness.[7] While it is our clinical impression that the response of BDD to SRIs is usually maintained or further increases over time with continued treatment, this impression requires empirical validation. It is worth underscoring that only slightly more than half of patients responded to fluoxetine, and even though their response was clinically significant, it was usually partial. It is therefore critically important to determine whether adding other pharmacologic agents or psychotherapy (eg, cognitive-behavioral therapy) to fluoxetine or other SRIs might enhance treatment outcome. In the meantime, this study suggests that fluoxetine is a safe and effective treatment for BDD—a distressing, relatively common, and severe mental disorder.

Submitted for publication February 28, 2001; final revision received August 3, 2001; accepted August 13, 2001.

This study was supported by a 1995-2000 FIRST Award (R-29; MH54841) from the National Institutes of Mental Health, Bethesda, Md (Dr Phillips). The study medication and matching placebo were supplied by Eli Lilly & Co, Indianapolis, Ind.

We thank Jason Siniscalchi, MS, for assistance with data analysis and graphics.

Corresponding author and reprints: Katharine A. Phillips, MD, Butler Hospital, 345 Blackstone Blvd, Providence, RI 02906 (e-mail: katharine_phillips@brown.edu).

REFERENCES

1. Phillips KA. Body dysmorphic disorder: the distress of imagined ugliness. *Am J Psychiatry*. 1991;148:1138-1149.
2. Hollander E, Cohen LJ, Simeon D. Body dysmorphic disorder. *Psychiatr Ann*. 1993;23:359-364.
3. Phillips KA, McElroy SL, Keck PE Jr, Pope HG Jr, Hudson JI. Body dysmorphic disorder: 30 cases of imagined ugliness. *Am J Psychiatry*. 1993;150:302-308.
4. Perugi G, Giannotti D, Frare F, Di Vaio S, Valori E, Maggi L, Cassano GB, Akiskal HS. Prevalence, phenomenology, and comorbidity of body dysmorphic disorder (dysmorphophobia) in a clinical population. *Int J Psychiatry Clin Pract*. 1997;1:77-82.
5. DeMarco LM, Li LC, Phillips KA, McElroy SL. Perceived stress in body dysmorphic disorder. *J Nerv Ment Dis*. 1998;186:724-726.
6. Phillips KA. *The Broken Mirror: Understanding and Treating Body Dysmorphic Disorder*. New York, NY: Oxford University Press; 1996.
7. Phillips KA, McElroy SL, Keck PE Jr, Pope HG Jr, Hudson JI. A comparison of delusional and nondelusional body dysmorphic disorder in 100 cases. *Psychopharmacol Bull*. 1994;30:179-186.
8. Cotterill JA. Dermatological non-disease: a common and potentially fatal disturbance of cutaneous body image. *Br J Dermatol*. 1981;104:611-619.
9. Cotterill JA, Cunliffe WJ. Suicide in dermatological patients. *Br J Dermatol*. 1997;137:246-250.
10. Phillips KA. Quality of life for patients with body dysmorphic disorder. *J Nerv Ment Dis*. 2000;188:170-175.
11. Faravelli C, Salvatori S, Galassi F, Aiazzi L, Drei C, Cabras P. Epidemiology of somatoform disorders: a community survey in Florence. *Soc Psychiatry Psychiatr Epidemiol*. 1997;32:24-29.
12. Bienvenu OJ, Samuels JF, Riddle MA, Hoehn-Saric R, Liang KY, Cullen BAM, Grados MA, Nestadt G. The relationship of obsessive-compulsive disorder to possible spectrum disorders: results from a family study. *Biol Psychiatry*. 2000;48:287-293.
13. Mayville S, Katz RC, Gipson MT, Cabral K. Assessing the prevalence of body dysmorphic disorder in an ethnically diverse group of adolescents. *J Child Fam Stud*. 1999;8:357-362.
14. Simeon D, Hollander E, Stein DJ, Cohen L, Aronowitz B. Body dysmorphic disorder in the *DSM-IV* Field Trial for obsessive compulsive disorder. *Am J Psychiatry*. 1995;152:1207-1209.
15. Phillips KA, Nierenberg AA, Brendel G, Fava M. Prevalence and clinical features of body dysmorphic disorder in atypical major depression. *J Nerv Ment Dis*. 1996;184:125-129.
16. Perugi G, Akiskal HS, Lattanzi L, Cecconi D, Mastrocinque A, Patronelli A, Vignoli S, Berni E. The high prevalence of "soft" bipolar (II) features in atypical depression. *Compr Psychiatry*. 1998;39:63-71.
17. Sarwer DB, Whitaker LA, Pertschuk MJ, Wadden TA. Body image concerns of reconstructive surgery patients: an underrecognized problem. *Ann Plast Surg*. 1998;40:403-407.
18. Sarwer DB, Wadden TA, Pertschuk MJ, Whitaker LA. Body image dissatisfaction and body dysmorphic disorder in 100 cosmetic surgery patients. *Plast Reconstr Surg*. 1998;101:1644-1649.
19. Ishigooka J, Iwao M, Suzuki M, Fukuyama Y, Murasaki M, Miura S. Demographic features of patients seeking cosmetic surgery. *Psychiatry Clin Neurosci*. 1998;52:283-287.
20. Phillips KA, Dufresne RG Jr, Wilkel C, Vittorio C. Rate of body dysmorphic disorder in dermatology patients. *J Am Acad Dermatol*. 2000;42:436-441.
21. Cotterill JA. Body dysmorphic disorder. *Dermatol Clin*. 1996;14:457-463.
22. Munro A, Chmara J. Monosymptomatic hypochondriacal psychosis: a diagnostic checklist based on 50 cases of the disorder. *Can J Psychiatry*. 1982;27:374-376.
23. Fukuda O. Statistical analysis of dysmorphophobia in out-patient clinic. *Jpn J Plast Reconstruct Surg*. 1977;20:569-577.
24. Hollander E, Liebowitz MR, Winchel R, Klumker A, Klein DF. Treatment of body-dysmorphic disorder with serotonin reuptake blockers. *Am J Psychiatry*. 1989;146:768-770.
25. Hollander E, Cohen L, Simeon D, Rosen J, DeCaria C, Stein DJ. Fluvoxamine treatment of body dysmorphic disorder [letter]. *J Clin Psychopharmacol*. 1994;14:75-77.
26. Sondheimer A. Clomipramine treatment of delusional disorder, somatic type. *J Am Acad Child Adolesc Psychiatry*. 1988;27:188-192.
27. Phillips KA, Atala KD, Albertini RS. Body dysmorphic disorder in adolescents. *J Am Acad Child Adolesc Psychiatry*. 1995;34:1216-1220.
28. Albertini RS, Phillips KA. 33 cases of body dysmorphic disorder in children and adolescents. *J Am Acad Child Adolesc Psychiatry*. 1999;38:453-459.
29. Phillips KA, Dwight MM, McElroy SL. Efficacy and safety of fluvoxamine in body dysmorphic disorder. *J Clin Psychiatry*. 1998;59:165-171.
30. Perugi G, Giannotti D, Di Vaio S, Frare F, Saettoni M, Cassano GB. Fluvoxamine in the treatment of body dysmorphic disorder (dysmorphophobia). *Int Clin Psychopharmacol*. 1996;11:247-254.
31. Hollander E, Allen A, Kwon J, Aronowitz B, Schmeidler J, Wong C, Simeon D. Clomipramine vs desipramine crossover trial in body dysmorphic disorder: selective efficacy of a serotonin reuptake inhibitor in imagined ugliness. *Arch Gen Psychiatry*. 1999;56:1033-1039.
32. Phillips KA, McElroy SL, Dwight MM, Eisen JL, Rasmussen SA. Delusionality and response to open-label fluvoxamine in body dysmorphic disorder. *J Clin Psychiatry*. 2001;62:87-91.
33. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*. Washington, DC: American Psychiatric Association; 1994.

34. Spitzer RL, Williams JBW, Gibbon M, First MB. The Structured Clinical Interview for *DSM-III-R* (SCID), I: history, rationale, and description. *Arch Gen Psychiatry*. 1992;49:624-629.
35. Williams JBW, Gibbon M, First MB, Spitzer RL, Davies M, Borus J, Howes MJ, Kane J, Pope HG, Rounsaville B, Wittchen H. The Structured Clinical Interview for *DSM-III-R* (SCID), II: multisite test-retest reliability. *Arch Gen Psychiatry*. 1992; 49:630-636.
36. Phillips KA, Atala KD, Pope HG. Diagnostic instruments for body dysmorphic disorder. In: *New Research Program and Abstracts of the 148th Annual Meeting of the American Psychiatric Association; May 24, 1995; Miami, Fla*. Abstract NR375: 157.
37. First MB, Spitzer RL, Gibbon M, Williams JBW. The Structured Clinical Interview for *DSM-III-R* Personality Disorders (SCID-II), part I: description. *J Personal Disord*. 1995;9:83-91.
38. First MB, Spitzer RL, Gibbon M, Williams JBW, Davies M, Borus J, Howes MJ, Kane J, Pope HG, Rounsaville B. The Structured Clinical Interview for *DSM-III-R* Personality Disorders (SCID-II): multi-site test-retest reliability study. *J Personal Disord*. 1995;9:92-104.
39. Phillips KA, Hollander E, Rasmussen SA, Aronowitz BR, DeCaria C, Goodman WK. A severity rating scale for body dysmorphic disorder: development, reliability, and validity of a modified version of the Yale-Brown Obsessive Compulsive Scale. *Psychopharmacol Bull*. 1997;33:17-22.
40. National Institute of Mental Health. Special feature: rating scales and assessment instruments for use in pediatric psychopharmacology research. *Psychopharmacol Bull*. 1985;21:714-1124.
41. Stout RL, Wirtz PW, Carbonari JP, Del Boca FK. Ensuring balanced distribution of prognostic factors in treatment outcome research. *J Stud Alcohol*. 1994;12: 70-75.
42. Goodman WK, Price LH, Rasmussen SA, Mazure C, Fleischman RL, Hill CL, Heninger GR, Charney DS. The Yale Brown Obsessive Compulsive Scale (Y-BOCS), part I: development, use, and reliability. *Arch Gen Psychiatry*. 1989; 46:1006-1016.
43. Goodman WK, Price LH, Rasmussen SA, Mazure C, Delgado P, Heninger GR, Charney DS. The Yale Brown Obsessive Compulsive Scale (Y-BOCS), part II: validity. *Arch Gen Psychiatry*. 1989;46:1012-1016.
44. Insel TR, Murphy DL, Cohen RM, Alterman I, Kilts C, Linnoila M. Obsessive-compulsive disorder: a double-blind trial of clomipramine and clorgyline. *Arch Gen Psychiatry*. 1983;40:605-612.
45. Eisen JL, Phillips KA, Baer L, Beer DA, Atala KD, Rasmussen SA. The Brown Assessment of Beliefs Scale: reliability and validity. *Am J Psychiatry*. 1998;155: 102-108.
46. Miller IW, Bishop S, Norman WH, Maddever H. The modified Hamilton Rating Scale for Depression: reliability and validity. *Psychiatry Res*. 1985;14:131-142.
47. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale (BPRS): recent developments in ascertainment and scaling. *Psychopharmacol Bull*. 1988;24:97-99.
48. Endicott J, Spitzer RL, Fleiss JL, Cohen J. The Global Assessment Scale: a procedure for measuring overall severity of psychiatric disturbance. *Arch Gen Psychiatry*. 1976;33:766-771.
49. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. New ork, NY: Lawrence Erlbaum Associates Inc; 1988.
50. Coryell W, Noyes R. Placebo response in panic disorder. *Am J Psychiatry*. 1988; 145:1138-1140.
51. Greist JH, Jefferson JW, Kobak KA, Katzelnick DJ, Serlin RC. Efficacy and tolerability of serotonin transport inhibitors in obsessive-compulsive disorder: a meta analysis. *Arch Gen Psychiatry*. 1995;52:53-60.
52. Wilcox CS, Cohn JB, Linden RD, Heiser JF, Lucas PB, Morgan DL, DeFrancisco D. Predictors of placebo response. *Psychopharmacol Bull*. 1992;28:157-162.