

Clomipramine vs Desipramine Crossover Trial in Body Dysmorphic Disorder

Selective Efficacy of a Serotonin Reuptake Inhibitor in Imagined Ugliness

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Background: Body dysmorphic disorder (preoccupation with an imagined or slight defect in appearance) is a common and disabling disorder associated with high rates of delusional symptoms and suicide attempts. Although preliminary studies suggest that serotonin reuptake inhibitors may be effective for body dysmorphic disorder, to date no controlled treatment studies have been published.

Methods: Forty patients were enrolled and 29 were randomized into a 16-week, double-blind, crossover-design study of clomipramine, a potent serotonin reuptake inhibitor, and active control desipramine, a selective norepinephrine reuptake inhibitor. Outcome measures included specific ratings of body dysmorphic disorder severity, delusionality, and functional impairment.

Results: Clomipramine was superior to desipramine in the acute treatment of body dysmorphic disorder symp-

toms as measured by assessment of patients' obsessive preoccupation with perceived body defects, repetitive behaviors in response to this preoccupation, and global ratings of symptom severity. Treatment efficacy was independent of the presence or severity of comorbid diagnoses of obsessive-compulsive disorder, depression, or social phobia. Likewise, clomipramine was equally effective regardless of whether the patients had insight or held their dysmorphic misperception with delusional intensity. Clomipramine was also superior to desipramine in improving functional disability.

Conclusions: Clomipramine is more effective than desipramine in the treatment of body dysmorphic disorder and is effective even among those patients who are delusional.

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BODY DYSMORPHIC disorder (BDD)—preoccupation with an imagined or slight defect in appearance—was formally recognized as a distinct disorder in 1987.¹ Subsequent research established that BDD results in severe distress, impairment in social and occupational functioning, and high rates of hospitalization, suicidal ideation, and suicide attempts.²⁻⁵ Body dysmorphic disorder is more common than initially believed; although there are no epidemiological studies of its prevalence, up to 1.9% of non-clinical samples⁶ and 12% of psychiatric outpatients⁷ may have BDD.

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Patients with BDD most commonly are concerned with perceived facial flaws, but may focus on any body part.^{3-5,8} Attempting to examine, mask, or change their appearance, patients perform compulsive/repetitive behaviors such as frequent mirror checking, excessive grooming, or skin picking.³⁻⁵ Up to 50% of patients with BDD turn to surgical procedures in futile attempts to correct perceived defects.^{4,5,8}

Body dysmorphic disorder has been considered an obsessive-compulsive spectrum disorder owing to the features it shares with obsessive-compulsive disorder (OCD), including intrusive obsessive thoughts and repetitive behaviors,⁹ age at onset, and course. If BDD is an obsessive-compulsive spectrum disorder, BDD and OCD would be expected to have similar pharmacological responses. Treatment studies of BDD are limited, but open data suggest a response to serotonin reuptake inhibitors (SRIs), such as clomipramine, fluoxetine, and fluvoxamine.¹⁰ Other pharmacological agents, such as neuroleptics, trazodone, lithium, benzodiazepines, tricyclics (excluding clomipramine), and anticonvulsants, have been much less beneficial or ineffective in BDD treatment.^{3,5} Preliminary data on SRI efficacy in BDD and similarities between BDD and OCD suggest that SRIs should be effective in BDD treatment.

This study is the first systematic, double-blind, controlled pharmacological treatment investigation of BDD. Using a crossover design, we investigated the efficacy of clomipramine, a potent SRI, in acute BDD treatment, compared with the active

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SUBJECTS AND METHODS

SUBJECTS

Patients were eligible if they were between 18 and 65 years of age, met *DSM-III-R* criteria for BDD, and suffered clinically significant distress or impairment in functioning due to BDD. Exclusion criteria included *DSM-III-R* psychotic disorders (other than delusional disorder, somatic type), bipolar I disorder, major depression with psychotic features, or current substance abuse; clinically significant suicidal ideation; known hypersensitivity to clomipramine or desipramine; or medical illness that would entail any risk while receiving clomipramine or desipramine. Patients were free of psychiatric medications for 2 weeks (6 for fluoxetine, monoamine oxidase inhibitors, or investigational drugs) prior to participation, and no concurrent psychotropic medications or cognitive or behavioral therapies were allowed during the study.

Forty subjects qualified for the study (see **Table 1** and **Table 2** for their profiles). On average, patients reported first experiencing BDD symptoms as teenagers, although onset was reported as early as age 5 years and as late as age 31 years; most had suffered with BDD for many years. They were concerned about a mean (SD) of 2.5 (1.3) different aspects of their appearance. The perceived defects primarily involved the head and face ($n = 33$), including hair ($n = 14$), complexion ($n = 9$), nose ($n = 8$), and eyes ($n = 5$). Patients also expressed dissatisfaction with their bodies ($n = 19$), including skin or veins ($n = 6$), legs ($n = 5$), and torso ($n = 5$).

None of the patients had received an adequate trial of clomipramine or desipramine in the past. Of those completing minimum treatment, 7 (30%) reported never having tried an antidepressant; 3 (13%) had inadequate trials of clomipramine, none had tried desipramine, and 6 (26%) had tried a tricyclic or monoamine oxidase inhibitor; 4 (17%) had received neuroleptics; and 12 (52%) had tried at least 1 SRI. None had a sustained therapeutic response to BDD treatment, although many had inadequate trials.

MEASURES

Primary Outcome Measures

Three clinician-rated primary outcome measures were used. (1) The BDD modification of the Yale-Brown Obsessive Compulsive Scale^{11,12} (BDD-YBOCS) was used to assess the severity of past-week BDD thoughts and behaviors. Piloted in the *DSM-IV* OCD Field Trial,² it has demonstrated reliability, validity, and sensitivity.¹³ The 10-item version was used for consistency with the YBOCS literature. (2)

A modification of the National Institute of Mental Health Global Obsessive-Compulsive Scale¹⁴ (BDD-NIMH) provided a global rating of BDD severity on a 15-point scale. (3) The Clinical Global Impression Scale, a standard scale with 7-point severity and improvement items, was applied specifically to BDD symptoms (BDD-CGI).¹⁵

Assessment of Comorbid Diagnoses

Lifetime and current Axis I disorders were diagnosed by the Structured Clinical Interview for *DSM-III-R* (SCID-I),¹⁶ a semistructured clinical interview. Depression severity was assessed by the 24-item Hamilton Depression Rating Scale (HAM-D).¹⁷ Obsessive-compulsive disorder severity was assessed by the YBOCS.^{11,12} Social anxiety severity was assessed by 2 self-administered, true-false questionnaires that do not explicitly measure social phobia, but are widely used to assess social anxiety with demonstrated reliability and validity: the 28-item Social Avoidance and Distress Scale,¹⁸ which measures social discomfort or avoidance and the 30-item Fear of Negative Evaluation Scale,¹⁸ which quantifies concerns about being judged negatively.

Assessment of Insight

Insight was assessed using the BDD modification of the Fixity of Beliefs Questionnaire,¹⁹ a direct adaptation of the Fixity of Beliefs Questionnaire for OCD. The first item was used because it explicitly addresses insight without including less relevant issues such as bizarreness. Although the BDD version has not been assessed, the OCD version of item 1 was judged to have acceptable reliability and validity in the *DSM-IV* OCD Field Trial.¹⁹ Twelve patients were categorized as delusional and 10 as not delusional; 1 could not be categorized.

Assessment of Functional Disability

The Schneier Disability Profile,²⁰ which is sensitive to the effects of social avoidance, was used to assess functional disability. It is a clinician-rated questionnaire that assesses ability to function in major life areas including work/school, family, marriage/dating, friendships, activities of daily living, and suicidal behavior.

PROCEDURE

After a telephone screen, potential participants had an in-person assessment. They were given a full explanation of the study, signed written informed consent, and were interviewed by a study psychiatrist to establish that they met all

control desipramine, a selective norepinephrine reuptake inhibitor. Using these 2 tricyclic antidepressants with similar adverse effect profiles enhances the treatment blind and isolates clomipramine's specific efficacy for BDD by controlling for nonspecific anxiolytic and antidepressant effects.

In BDD insight is often poor, and greater delusional severity is a key difference between BDD and OCD.^{2,5} In the *DSM-IV* OCD field trials, 30% of patients were completely or mostly lacking in insight regarding their OCD,² but 49% of those with comorbid BDD were completely or

mostly convinced their defect was real⁵; these patients were significantly less insightful regarding their BDD than their OCD.² Delusionality is of special interest because it may complicate pharmacological treatment.

In this study, we tested these hypotheses. (1) Clomipramine is more effective than desipramine in acute BDD treatment. (2) Comorbid diagnosis of major depression, social phobia, or OCD does not influence treatment outcome. (3) Delusional BDD is as likely to respond to clomipramine as nondelusional BDD. (4)

study criteria. An interviewer confirmed the BDD diagnosis and used the SCID-I¹⁶ to identify comorbid diagnoses. Eligible patients proceeded to a 2-week, single-blind placebo run-in, followed by 16 weeks of active medication (8 weeks receiving clomipramine, the active treatment, and 8 weeks receiving desipramine, the active control, with the order determined randomly). Both BDD and comorbid diagnoses were reconfirmed after the placebo run-in by a study psychiatrist and psychologist. All study personnel were blind to patients' medication conditions.

Of 40 eligible patients, 35 began the placebo run-in. Baseline severity of illness was assessed before and after this phase using the 3 BDD measures. Inclusion and exclusion criteria were reconfirmed after the placebo run-in. Eleven of the initial 40 did not enter active treatment: 5 did not return for subsequent appointment(s), 4 decided not to participate, 1 dropped out for medical reasons, and 1 dropped out due to perceived placebo adverse effects. No patients improved while receiving placebo (BDD-CGI improvement scores of 1 or 2). Therefore, 29 subjects entered active treatment. Of these, 18 completed the full 16 weeks, and another 5 completed at least 12 weeks (8 weeks of one phase and at least 4 weeks of the other). Six of the 29 dropped out without completing 12 weeks: 4 dropped out because of desipramine-related adverse effects (3 in the first phase and 1 in the second), 1 was dropped after missing multiple appointments while receiving desipramine (in phase 1), and 1 refused to continue after responding to clomipramine in phase 1.

A flexible titration schedule was used. For the first medication, patients were initially given 25 mg/d and slowly increased to a maximum of 250 mg/d or the highest tolerated dose. If adverse effects occurred, dosage increases were made slowly based on clinical judgment. During the first week of the second phase, the first medication was crossed over to an equivalent dose of the second. The mean (SD) dosages attained were 138 (87) mg/d for clomipramine and 147 (80) mg/d for desipramine.

The treating psychiatrist, who met with patients weekly for the first 4 weeks of each phase and biweekly for the last 4 weeks, adjusted medication, recorded adverse effects, monitored clinical state, conducted primary outcome measures, and offered general encouragement and support, but did not conduct insight-oriented, cognitive, or behavioral therapy. A study psychologist, kept blind to adverse effects and dosing schedule, conducted evaluations at 4-week intervals on both primary outcome and secondary rating scales.

STATISTICAL ANALYSIS

A minimum treatment rather than an intent-to-treat analysis was used owing to the difficulty of interpreting scores

carried forward from one arm of a crossover design to the other. The minimum treatment analysis was based on data from the 23 patients who completed at least 4 weeks of both phases of treatment; within each phase, the last available value on each measure was carried forward. Post-placebo ratings are used as baseline ratings throughout.

For the 3 primary outcome measures (BDD-YBOCS, BDD-NIMH, and BDD-CGI), the mean of the psychiatrist's and psychologist's ratings was used. For each measure, a preliminary repeated-measures analysis of covariance (ANCOVA) examined the drug \times covariate (baseline) interaction with drug and sequence as factors. If the covariate effects in the 2 drug conditions were not significantly different, the analysis was performed again without the covariate (ANOVA) for the within-subjects analysis (this is the same as using a common covariate effect for both drug conditions). Only significant covariate effects and interactions are discussed; the absence of significant covariate interactions implies that the association to baseline was similar in the 2 conditions. A secondary analysis used an ANCOVA to look at each of the 3 key variables for the first 8 weeks of the study alone. Paired *t* tests were used to assess pre-post change. One-sample *t* tests were used to test post-treatment improvement on the CGI vs 4 (no change). The McNemar test was used to test clomipramine vs desipramine response rates and adverse effects. Although directional hypotheses were stated, 2-tailed tests with $\alpha = .05$ were used throughout.

To assess the effect of comorbid diagnosis on treatment outcome, comorbid diagnoses were coded into 4 categories: none, depression, social phobia, or OCD based on SCID-I diagnosis. If more than 1 current comorbid diagnosis existed, the most clinically significant disorder was used. The basic ANCOVA/ANOVA was expanded to a drug \times sequence \times comorbid diagnosis design ($2 \times 2 \times 4$), with the BDD-CGI as the dependent measure. To assess the effect of the severity of comorbid symptoms, correlations were computed between baseline severity of comorbid symptoms (HAM-D, YBOCS, Social Avoidance and Distress Scale, and Fear of Negative Evaluation Scale) and treatment outcome (BDD-CGI improvement).

The effect of insight on treatment outcome was assessed by including delusionality at baseline as an additional factor in the basic ANCOVA/ANOVA for all 3 primary outcome measures. The effect of treatment on insight was examined by computing a paired *t* test on item 1 of the Fixity of Beliefs Scale after clomipramine treatment vs after desipramine treatment.

To measure the effect of treatment on functional disability, the basic ANCOVA/ANOVA procedure was performed on the Schneier Disability Profile with final score as the dependent variable covaried by baseline score.

Clomipramine is more effective than desipramine in reducing functional disability.

RESULTS

EFFICACY OF CLOMIPRAMINE VS DESIPRAMINE IN BDD

Clomipramine was superior to desipramine in the acute treatment of BDD symptoms as measured by all

primary outcome measures (BDD-YBOCS, BDD-NIMH, and BDD-CGI). Thus, the first hypothesis was fully supported.

The patients' obsessive preoccupation with perceived body defects and repetitive behaviors in response to this preoccupation, as measured by the mean (SD) BDD-YBOCS scores, were significantly lower following clomipramine treatment than following desipramine treatment (**Figure 1**): 16.2 (8.5) (low-moderate range) following clomipramine treatment, 20.7 (7.7) (mid-

Table 1. Profile of Sample: Demographics and BDD History*

	Total Sample (N = 40)
Age, y	34.5 (10.7)
Sex, No. (%)	
Male	23 (58)
Female	17 (42)
Marital status, No. (%)	
Single	28 (70)
Married	8 (20)
Divorced	4 (10)
Ethnicity, No. (%)	
White	31 (78)
African American	2 (5)
Hispanic	5 (12)
Asian	1 (2)
Biracial	1 (2)
Education, y	14.5 (2.4)
Employment, No. (%)	
Employed	22 (55)
Unemployed	13 (32)
Student	2 (5)
Retired	1 (2)
Age at BDD onset, y	16.2 (5.8)
Duration of illness, y	18.1 (12.5)
Severity of illness, CGI score at study entry	4.5 (0.7) (Moderately to markedly ill)

*Data are presented as mean (SD) unless otherwise indicated. BDD indicates body dysmorphic disorder; CGI, Clinical Global Impression Scale.

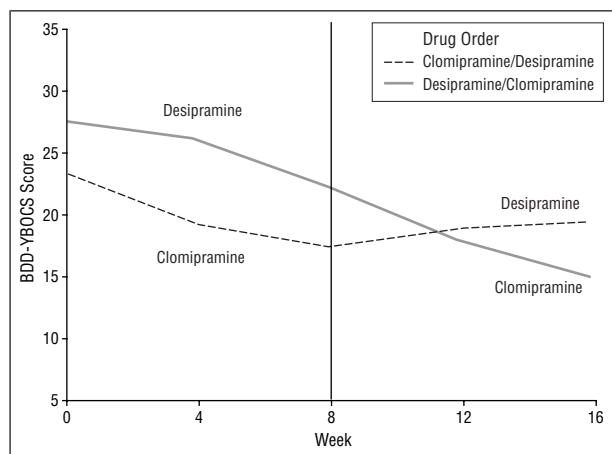


Figure 1. Change in Yale-Brown Obsessive Compulsive Scale (modified for body dysmorphic disorder) (BDD-YBOCS) score over time, based on the mean of psychiatrists' and psychologists' ratings (N = 23, $F_{1,21} = 11.02$, $P = .003$).

moderate range) following desipramine treatment, and 25.4 (7.2) (severe range) at baseline. There was a significant relationship between baseline and final BDD-YBOCS scores (covariate effect: $F_{1,19} = 18.65$, $P < .001$). Response rates were 65% for clomipramine and 35% for desipramine, based on 25% improvement on the BDD-YBOCS ($P = .09$).

Clomipramine was also significantly more effective than desipramine in reducing overall BDD severity as measured by the BDD-NIMH (**Figure 2**): mean (SD) scores were 5.6 (1.8) following clomipramine treatment, 8.02 (3.1) following desipramine treatment, and

Table 2. Current Comorbid Axis I and Axis II Diagnoses*

	Patients Treated (N = 29)
Axis I disorders	
Depression†	13
Dysthymia	10
Major depressive disorder	6
Social phobia	7
Obsessive-compulsive disorder	7
Generalized anxiety disorder	4
Agoraphobia without panic disorder	3
Eating disorder	2
Panic disorder	2
Somatoform disorders (other than BDD)	2
Trichotillomania	2
Developmental disorders	1
Simple phobia	1
Axis II disorders	
Personality disorders	
Avoidant	10
Obsessive-compulsive	7
Paranoid	5
Passive-aggressive	5
Borderline	4
Self-defeating	4
Dependent	2
Personality disorder NOS	2
Antisocial	1
Depressive	1
Histrionic	1
Schizotypal	1

*BDD indicates body dysmorphic disorder; NOS, not otherwise specified. †Of the depressed patients, 7 had only dysthymia, 3 had only major depressive disorder, and 3 had both depressive disorders.

8.85 (2.1) at baseline. There was a significant relationship between baseline and final BDD-NIMH scores (covariate effect: $F_{1,19} = 4.64$, $P < .04$). Clomipramine was more effective than desipramine regardless of the order in which the drugs were taken (main effect for order was not significant). However, those patients who were treated with clomipramine first showed a smaller difference in their response to the 2 treatment conditions than those who were treated with desipramine first (medication \times order interaction: $F_{1,21} = 5.71$, $P = .03$). This may be due to a carryover in the clomipramine treatment response resulting in a slow worsening in symptoms while receiving desipramine, compared with the rapid alleviation of symptoms in patients who had been taking desipramine and were switched to clomipramine. Alternatively, this interaction could be due to a difference in response to the drug taken first vs the drug taken second. Response rates were 70% for clomipramine and 30% for desipramine based on 25% improvement on the BDD-NIMH ($P = .02$).

Clomipramine was also significantly more effective than desipramine in decreasing the severity of patients' overall illness as measured by BDD-CGI improvement ratings (**Figure 3**): mean (SD) scores were 2.5 (0.8) following clomipramine treatment and 3.4 (1.1) following desipramine treatment. The main effects for sequence and the medication \times sequence interaction were not significant. Response rates were 44% for clomipra-

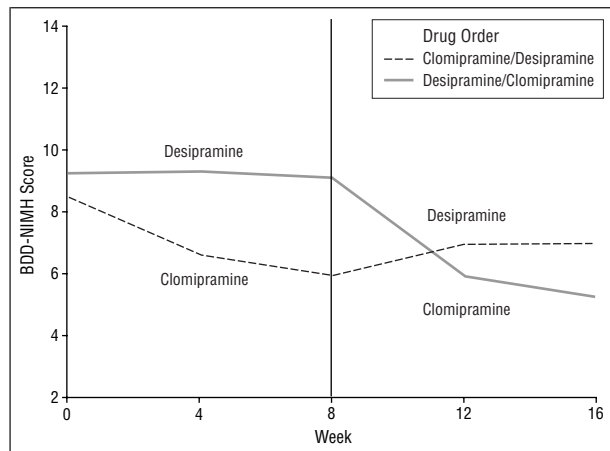


Figure 2. Change in National Institute of Mental Health Global Obsessive-Compulsive Scale (modified for body dysmorphic disorder) (BDD-NIMH) scores over time, based on the mean of psychiatrists' and psychologists' ratings ($N=23$, $F_{1,21}=19.22$, $P<.001$).

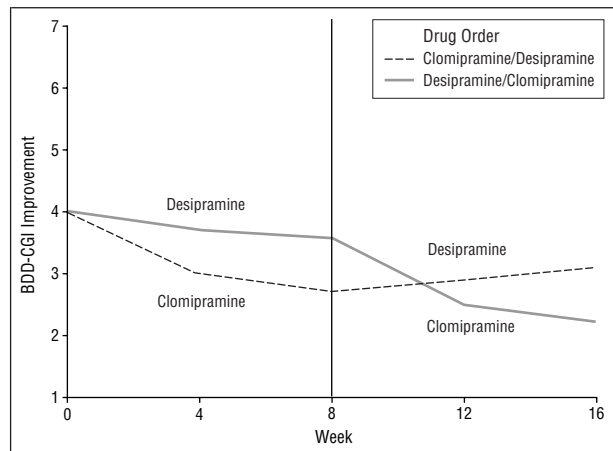


Figure 3. Change in Clinical Global Impression Scale (modified for body dysmorphic disorder) (BDD-CGI) improvement score over time, based on the mean of psychiatrists' and psychologists' ratings ($N=23$, $F_{1,21}=7.28$, $P=.01$).

mine and 22% for desipramine based on a score of 1 or 2 on the BDD-CGI improvement scale ($P=.27$).

Clomipramine was superior to desipramine at the end of phase 1 on 2 of the 3 key measures, BDD-NIMH ($F_{1,22}=12.06$, $P=.002$) and BDD-CGI ($F_{1,21}=5.24$, $P=.03$), but not on the BDD-YBOCS ($F_{1,22}=1.85$, $P=.19$). Clomipramine resulted in significant improvement on all primary outcome measures both at the end of phase 1 and at the clomipramine end point. Results for desipramine were mixed: improvement was not significant on the BDD-NIMH (phase 1 or clomipramine end point) or on the BDD-CGI after phase 1; improvement was significant on the BDD-YBOCS (phase 1 and clomipramine end point) and on the BDD-CGI at clomipramine end point. Overall, clomipramine effected much greater improvement than desipramine.

ADVERSE EFFECTS

Adverse effects for clomipramine and desipramine were similar. They included dry mouth (84% for clomipramine and 62% for desipramine), sedation or tiredness (80% and 52%), constipation (72% and 52%), sweating (44% and 28%), and tremor (44% and 14%). Desipramine tended to produce greater insomnia (41% vs 28% for clomipramine). None of these differences reached statistical significance. Despite adverse effects, no patients dropped out of the study while receiving clomipramine in either arm; 4 patients dropped out while receiving desipramine owing to adverse effects.

COMORBID DIAGNOSIS AND TREATMENT OUTCOME

Twenty-two (76%) of the 29 subjects randomized into the study had at least 1 current comorbid diagnosis. Eighteen (62%) had at least 1 of the key comorbid diagnoses: 13 (45%) suffered from depression, 7 (24%) had social phobia, and 7 (24%) had OCD (see Table 2).

As predicted, overall comorbid diagnoses (depression, social phobia, OCD, or none) did not affect treatment outcome as measured by the BDD-CGI. In addition,

the severity of comorbid symptoms at baseline was not related to clomipramine treatment efficacy. Specifically, there was no correlation between post-clomipramine BDD-CGI improvement ratings and baseline severity of depression, obsessions and compulsions, or social anxiety.

However, there were some important specific differences in treatment efficacy for comorbid symptoms. Depressive symptoms were reduced more by clomipramine treatment than by desipramine treatment ($t_{21}=2.43$, $P=.02$); mean (SD) HAM-D scores were 9.33 (6.75) vs 14.00 (7.99) at end point and 18.06 (9.38) at baseline. For patients with comorbid diagnoses of depression, clomipramine also reduced depressive symptoms more than desipramine ($t_{11}=2.54$, $P=.03$); HAM-D scores were 10.85 (6.93) vs 18.00 (6.28) at end point, and 21.27 (10.19) at baseline. Obsessive-compulsive symptoms also decreased more on clomipramine than desipramine ($t_{21}=3.01$, $P=.007$); YBOCS scores were 15.88 (8.88) vs 21.25 (7.73) at end point and 25.69 (7.13) at baseline.

DEGREE OF INSIGHT AND TREATMENT OUTCOME

Clomipramine was more effective than desipramine among both delusional and nondelusional patients; however, there is a statistically significant interaction suggesting that clomipramine was slightly more effective among patients who had no insight while the reverse was true for desipramine. This interaction was found for all 3 primary outcome measures and was independent of baseline severity (Table 3). The more delusional the patient was at baseline, the more he or she improved after clomipramine treatment (significant negative correlation between baseline delusional and BDD-CGI improvement after clomipramine treatment: $r=-0.56$, $P=.007$).

Compared with baseline, clomipramine resulted in significant improvement in fixity of beliefs both after phase 1 ($t_{10}=2.50$, $P=.03$) and at clomipramine end point ($t_{21}=2.961$, $P=.007$); desipramine did not significantly improve fixity of beliefs at either time point.

Table 3. Interaction Between Delusional Beliefs and Drug Treatment*

Measure	After Clomipramine†		After Desipramine†		ANCOVA, Drug × Insight Interaction
	Nondelusional	Delusional	Nondelusional	Delusional	
BDD-CGI improvement	2.85 (0.75)	2.13 (0.69)	3.20 (1.30)	3.50 (1.09)	$F_{1,18} = 4.21, P = .05$
BDD-NIMH	6.00 (2.12)	5.25 (1.59)	7.50 (2.82)	8.71 (3.42)	$F_{1,18} = 5.37, P = .03$
BDD-YBOCS	16.90 (7.73)	15.67 (9.82)	19.25 (8.46)	23.33 (7.32)	$F_{1,18} = 5.98, P = .03$

*Data are presented as mean (SD) unless otherwise indicated. ANCOVA indicates analysis of covariance; BDD-CGI, Clinical Global Impression Scale modified for body dysmorphic disorder; BDD-NIMH, National Institute of Mental Health Global Obsessive-Compulsive Scale modified for body dysmorphic disorder; and BDD-YBOCS, Yale-Brown Obsessive Compulsive Scale Modified for BDD.

†After clomipramine treatment, all measures were lower for delusional than nondelusional patients. After desipramine treatment, all measures were lower for nondelusional than delusional patients.

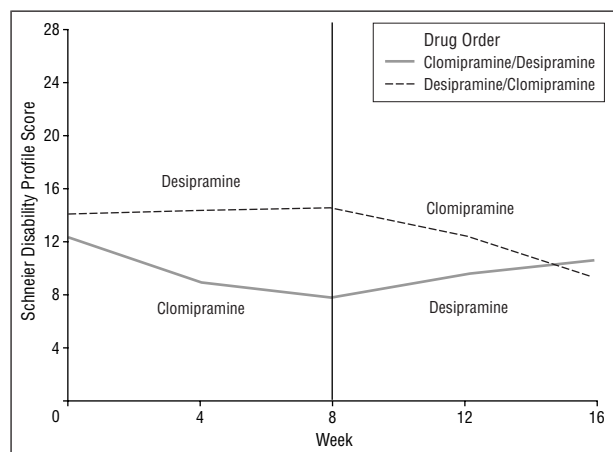


Figure 4. Change in functional impairment over time as measured by the Schneier Disability Profile score ($N = 20, F_{14,18} = 17.43, P = .001$).

EFFECT OF TREATMENT ON FUNCTIONAL DISABILITY

Clomipramine was more effective than desipramine in improving functional disability as measured by the Schneier Disability Profile (**Figure 4**): mean (SD) scores were 8.6 (6.1) after clomipramine treatment, 12.4 (6.9) after desipramine treatment, and 13.2 (6.6) at baseline. There was a significant relationship between baseline and final Schneier Disability Profile scores (covariate effect: $F_{1,17} = 13.29, P = .002$).

COMMENT

The potent SRI clomipramine was significantly superior to the selective norepinephrine reuptake inhibitor desipramine on all primary outcome measures of BDD severity and symptoms.

Fixity of BDD beliefs did not limit treatment outcome; while receiving clomipramine delusional patients improved at least as much as nondelusional patients and perhaps more. This is of clinical importance, suggesting that delusional patients may not require neuroleptic treatment and thus might be spared possible adverse effects associated with long-term neuroleptic use. This extends the work of Phillips et al,²¹ who found that 71% of delusional patients responded to open fluvoxamine treatment vs 61% of nondelusional patients, and that delusionality responded to treatment. We also found

that clomipramine significantly improved fixity of beliefs whereas desipramine did not. Note that item 1 of the BDD Fixity of Beliefs Scale needs to be validated as the OCD version has been. These delusionality findings deserve further investigation.

This study is strengthened by the use of desipramine, an active control, which serves not only to protect the double-blind (since both agents have similar adverse effect profiles) but also controls for nonspecific antidepressant and anxiolytic effects. However, desipramine is not a perfect control. Although it is unlikely that BDD would respond to placebo, since it is not responsive to a broad range of other treatments (including tricyclics, neuroleptics, monoamine oxidase inhibitors, and benzodiazepines), a trial vs placebo, the “gold standard” control, would clearly establish that clomipramine is not simply better than desipramine. In addition, while a crossover design is a strong one since patients serve as their own controls, there are also problems inherent in crossover designs, such as potential carryover effects. Notably, our results were confirmed based on the study’s first arm alone and so cannot be attributed to crossover-design artifacts. It would be valuable to follow up this research with a placebo-controlled parallel-design study. It is also possible that a longer trial would lead to an even greater reduction in symptoms and a greater percentage of responders with clomipramine. Lack of a maintenance phase after the acute crossover trial is also a limitation. Thus, a longer trial and long-term maintenance data would be useful. Also, the mean (SD) dose of clomipramine, 138 (87) mg/d, was rather low owing to flexible dosing to minimize adverse effects. Higher doses might have resulted in a greater percentage of treatment responders to clomipramine but at the cost of more dropouts. Although patients experienced adverse effects typical of tricyclic antidepressants while receiving clomipramine, they tolerated these well and no patients dropped out while receiving clomipramine.

Because clomipramine was superior to desipramine in alleviating BDD symptoms, the data demonstrate that clomipramine has a specific anti-BDD effect; patients’ BDD does not improve simply because of clomipramine’s antidepressant and anti-anxiety effects. This is further supported by the absence of an effect of baseline comorbidity or severity on BDD outcome. These findings are similar to the selective efficacy for SRIs in OCD treatment²² and differ from findings for other mood and

anxiety disorders. Along with overlap in clinical symptoms, course of illness, and comorbidity, our results suggest that BDD may be closely related to OCD. The greater effectiveness of clomipramine compared with desipramine in treating depression in patients with BDD suggests that their depression may be secondary to their BDD.

There is also evidence for greater improvement of functional disability with clomipramine treatment than with desipramine treatment. This is noteworthy given the very high level of functional disability inherent in BDD, especially when demonstrable over such a short time period.

In conclusion, the positive findings of this first controlled study in BDD are a significant initial step in establishing the efficacy of clomipramine in the treatment of this debilitating disorder, even among delusional patients.

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