Delusionality and Response to Open-Label Fluvoxamine in Body Dysmorphic Disorder

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Background: Available data suggest that the delusional variant of body dysmorphic disorder (BDD), a type of delusional disorder, may respond to serotonin reuptake inhibitors (SRIs) and that delusionality (lack of insight) in BDD may improve with SRI treatment. However, this research has been hampered by the lack of a reliable and valid scale to assess delusionality.

Method: Thirty subjects (21 women, 9 men; mean age = 33.3 ± 9.0 years) with DSM-IV BDD were prospectively treated with open-label fluvoxamine for 16 weeks. Subjects were assessed at regular intervals with the Brown Assessment of Beliefs Scale (BABS), the Yale-Brown Obsessive Compulsive Scale Modified for BDD (BDD-YBOCS; a measure of BDD severity), and other instruments. The BABS is a reliable and valid 7-item, semistructured, clinician-administered scale that assesses current delusionality.

Results: In this prospective, open-label study, 63% of BDD subjects responded to fluvoxamine. Delusional and nondelusional subjects had similar improvement in BDD symptoms. In addition, insight significantly improved in both delusional and nondelusional subjects. Baseline BABS scores did not contribute significantly to endpoint BDD-YBOCS scores in a regression analysis.

Conclusion: Degree of delusionality did not predict fluvoxamine response, and delusionality significantly improved. These findings are preliminary and require confirmation in controlled trials. The implications of these findings for other types of delusions requires investigation.

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While antipsychotic medications are considered the mainstay of pharmacotherapy for delusions, much of the available literature suggests that delusional disorder does not respond well to these medications.[1] However, the treatment of delusional disorder has received surprisingly little investigation, with virtually no controlled treatment studies having been conducted.[1]

In this study, we investigate the treatment response of body dysmorphic disorder (BDD), a preoccupation with a nonexistent or slight defect in appearance. BDD is characterized by a spectrum of insight ranging from good to absent,[2–4] with a significant percentage of patients being delusional and having ideas or delusions of reference.[5] Delusional BDD is classified in DSM-IV as a psychotic disorder, a type of delusional disorder, somatic type (nondelusional BDD is classified as a somatoform disorder).

Although several reports[6,7] suggest that pimozide is effective for delusional BDD, more recent case reports[8–11] and a clinical series[12] suggest that delusional BDD may respond to serotonin reuptake inhibitors (SRIs) and may not respond to antipsychotics alone. In the clinical series (N = 100),[12] delusional patients were as likely to respond to an SRI (as assessed by the Clinical Global Impressions scale [CGI][13]) as nondelusional patients (with response rates of 75% of 29 trials in delusional patients vs. 66% of 32 trials in nondelusional patients, a nonsignificant difference). Furthermore, clinical observations suggest that delusionality (lack of insight) in BDD may improve with SRIs—that is, some patients appear to develop a more realistic view of their appearance and experience resolution of their ideas or delusions of reference.[4]

However, this evidence, as well as research on the treatment of delusions in general, has been limited by the lack of a reliable and valid scale to assess delusionality. Available scales that assess delusions, insight, or other psychotic symptoms[14,15] do not focus on delusions per se, have not been shown to be reliable and valid, or are not suitable for use in disorders such as BDD that are not characterized by formal thought disorder (e.g., loosening of associations). Furthermore, existing scales do not provide both dimensional and categorical ratings of delusionality.

In the present study, we use a reliable and valid measure of delusionality (the Brown Assessment of Beliefs

Scale [BABS][16]) to investigate the relationship between delusionality and SRI response in BDD. This 16-week open-label fluvoxamine trial is the first pharmacotherapy study of BDD to use reliable and valid outcome measures specific to BDD.[17] It is also the first study to systematically and prospectively examine the effect of SRIs on delusions using a reliable and valid delusionality scale. The questions we address are whether delusionality predicts response to an SRI; in other words, are subjects with delusional BDD as likely to respond to fluvoxamine as nondelusional subjects? In addition, does delusional thinking improve or resolve with SRI treatment?

METHOD

Subjects

Thirty outpatients (21 women, 9 men; mean ± SD age = 33.3 ± 9.0 years; range, 20–53 years) participated in the 2-site study.[17] All subjects met DSM-IV criteria for BDD: (A) preoccupation with an imagined defect in appearance; if a slight physical anomaly is present, the concern is markedly excessive; (B) the preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning; and (C) the preoccupation is not better accounted for by another mental disorder (e.g., dissatisfaction with body shape and size in anorexia nervosa). Patients with delusional BDD, who would receive a diagnosis of delusional disorder, were included in the study. According to DSM-IV, the delusional and nondelusional variants of BDD may be double coded, reflecting the possibility that they are the same disorder. The subjects' demographic and clinical features were similar to those of other series of patients with BDD,[3,12] with the most common areas of preoccupation the skin (e.g., facial acne or scarring, in 19/30 [63%]), hair (e.g., balding or hair texture, in 16/30 [53%]), and nose (9/30 [30%]).

Inclusion criteria were (1) DSM-IV diagnosis of BDD or its delusional disorder variant for at least 6 months, (2) age 18–65 years, (3) a score of ≥ 5 on the first 3 items of the Yale-Brown Obsessive Compulsive Scale Modified for BDD (BDD-YBOCS),[18] and (4) a score of ≥ 7 on the National Institute of Mental Health Global Obsessive Compulsive Scale,[19] which was adapted to BDD. Exclusion criteria were (1) unstable medical illness or clinically significant laboratory, electrocardiogram, or physical examination abnormalities; (2) history of seizures; (3) current pregnancy or lactation, or inadequate contraception in women of childbearing potential; (4) need for a drug that might interact adversely with or obscure the action of the study medication; (5) recent clinically significant suicidality; (6) history of DSM-III-R bipolar disorder type I, schizophrenia, or dementia; (7) DSM-III-R substance abuse or dependence within the past 6 months; (8) initiation of psychotherapy or behavior therapy from a mental health professional within 3 months of study baseline; (9) past treatment with fluvoxamine; (10) treatment with investigational medication, depot neuroleptics, or electroconvulsive therapy within 3 months, with fluoxetine within 6 weeks, or with other psychotropics within 2 weeks of study baseline. All subjects signed statements of informed consent.

Assessments

Delusionality was assessed with the BABS, a 7-item, semistructured, clinician-administered scale that assesses delusionality during the past week.[16] The BABS rates delusionality dimensionally and also categorizes beliefs as delusional or nondelusional. BABS items are (1) conviction (how convinced the patient is that his or her belief is accurate), (2) perception of others' views (how certain the patient is that most people think the belief makes sense), (3) explanation of differing views (the patient's explanation for the difference between his or her and others' views of the belief), (4) fixity (whether the patient could be convinced that the belief is wrong), (5) attempt to disprove beliefs (how often the patient attempts to disprove the belief), (6) insight (recognition that the belief has a psychiatric etiology), and (7) ideas/delusions of reference (how certain the patient is that others take special notice of him or her in relation to the belief). BABS items are scored on a 5-point scale; scores range from 0 to 24, with higher scores indicating more delusional thinking (item 7 is not included in the total score). A total score of 18 or higher plus a score of 4 on item 1 (conviction) classifies a belief as delusional. The BABS has good interrater and test-retest reliability (intraclass correlative coefficient for total score = 0.96 and 0.95, respectively) as well as internal consistency (Cronbach α coefficient = 0.87).[16] Correlations between each item and the total score minus that item were significant and ranged from 0.38 to 0.85. Total BABS score was significantly positively correlated with items and scores of other delusionality scales, but was not significantly correlated with symptom severity scores. Factor analysis identified one factor accounting for 56.1% of the variance. Using an expert clinician's global ratings of delusionality as the gold standard, a cut point for delusional thinking in BDD had a sensitivity of 100% and a specificity of 86%.

The major outcome measures of BDD severity were the BDD-YBOCS[18] and the CGI.[13] The BDD-YBOCS is a 12-item, semistructured, clinician-administered scale that assesses BDD severity during the past week. This scale, adapted from the Yale-Brown Obsessive Compulsive Scale,[20,21] assesses obsessional preoccupation with the perceived defect (time occupied, interference with functioning, distress, resistance against and control over the preoccupation), associated compulsive behaviors (time spent, interference, distress if the behavior is prevented, resistance against and control over the behaviors),

delusionality, and avoidance. The scale has good interrater and test-retest reliability, internal consistency, and factor structure; preliminary data also support its convergent and discriminant validity.[18] Scores range from 0 to 48. Response on the BDD-YBOCS was defined as 30% or greater decrease in total score. BDD was diagnosed with a reliable semistructured diagnostic instrument for DSM-IV BDD[22] modeled after the Structured Clinical Interview for DSM-III-R.[23,24] Other study ratings are described elsewhere.[17]

Procedures

After completing all baseline evaluations, subjects began receiving unblinded fluvoxamine, 50 mg/day, for 16 weeks. A fixed/flexible dosing schedule was used, with an attempt to increase the dose to 50 mg b.i.d. on day 5 and to 150 mg/day on day 9 for 6 days. The dose was then further increased weekly by 50-mg/day increments to a maximum of 150 mg b.i.d. if tolerated. No other psychotropic medications were taken except chloral hydrate, 0.5 to 2.0 gm/day, if needed for insomnia. Psychotherapy (including cognitive-behavioral therapy) was not initiated during the study. Subjects were evaluated with the BABS at baseline and at weeks 4, 8, 12, and 16. The BDD-YBOCS, CGI, and other ratings were administered at baseline and weekly for the first 4 weeks of the study and then every other week for the remainder of the study.

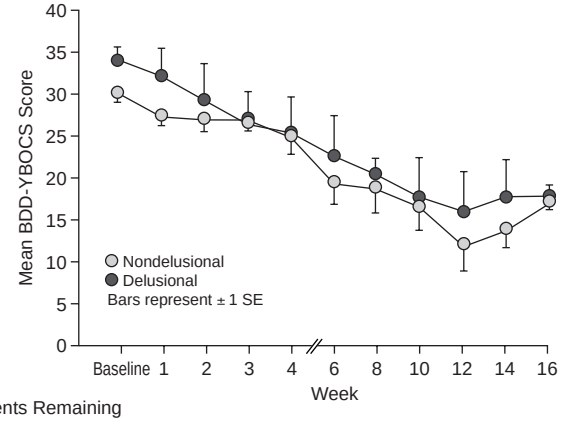
Statistical Analyses

To compare baseline scores with subsequent scores on continuous study measures, 2-tailed paired t tests were used. Analysis of covariance (ANCOVA) was also used to compare groups at endpoint while controlling for baseline differences. A repeated-measures ANCOVA was used to further test for a time effect in BDD-YBOCS score between groups. The Fisher exact test was used for comparisons of categorical variables. Correlations between BABS scores and BDD-YBOCS scores were examined using the Pearson product moment correlation coefficient. A simple linear regression analysis was conducted to evaluate the relationship between BABS scores and endpoint BDD-YBOCS scores. All analyses are intent-to-treat with last observation carried forward.

RESULTS

Of the 30 subjects, 18 (60%) completed the 16-week study. No significant differences were found between completers and dropouts on baseline BABS or BDD-YBOCS total scores.[17] BDD-YBOCS scores decreased by at least 30% in 19 subjects (63.3%) (mean ± SE = 31.1 ± 5.4 at baseline, 16.9 ± 11.8 at termination for all subjects; t = 6.7, df = 29, p < .001). Similarly, on the CGI, 19 subjects (63.3%) were responders, with 10 (33.3%) much improved and 9 (30.0%) very much improved. The mean time to response on the BDD-YBOCS was 6.1 ± 3.7 weeks (range, 1–16 weeks); survival analysis yielded a mean time to response of 8.4 ± 5.4 weeks. The mean dose of fluvoxamine at termination was 238.3 ± 85.8 mg/day (range, 50–300 mg/day).

Figure 1. Scores Over Time on the Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS) for 7 Delusional and 23 Nondelusional Subjects Receiving Fluvoxamine for Body Dysmorphic Disorder



Patients Remaining							
Nondelusional	23	23	18	16	13	13
Delusional	7	6	6	6	5	5

The correlation between baseline delusionality as assessed by the BABS (mean ± SE BABS total score = 14.5 ± 4.4) and change in BDD severity as assessed by the change in BDD-YBOCS score from baseline to week 16 was nonsignificant (r = 0.19, p = .33). Correlations between individual baseline BABS items and change in BDD-YBOCS scores were also all nonsignificant, ranging from r = −0.05 to 0.30, with the exception of the BABS ideas/delusions of reference item (r = 0.41, p < .05). Baseline BABS scores did not contribute significantly to endpoint BDD-YBOCS scores in a regression analysis (t = 0.30, p = .77).

Controlling for baseline differences in delusionality, both groups improved on the BDD-YBOCS across time (F = 34.3, df = 1,28; p = .000) (Figure 1). ANCOVA indicated no significant group differences; delusional subjects were as likely as nondelusional subjects to respond to fluvoxamine. Specifically, among delusional subjects mean ± SE BDD-YBOCS scores decreased by 47.3%, from 34.1 ± 3.3 to 17.7 ± 12.4; among nondelusional subjects BDD-YBOCS scores decreased by 45.0%, from 30.2 ± 5.7 to 16.6 ± 11.9. Five (71.4%) of 7 delusional subjects versus 14 (60.9%) of 23 nondelusional subjects were fluvoxamine responders (not significant). When the preceding analyses were repeated excluding the BDD-YBOCS delusionality item, the results were similar.

Delusionality significantly improved, with mean ± SE total BABS score decreasing from 14.5 ± 4.4 at baseline

Figure 2. Scatterplot of the Correlation Between Change in Total Score on the Brown Assessment of Beliefs Scale (BABS) and Yale-Brown Obsessive Compulsive Scale Modified for Body Dysmorphic Disorder (BDD-YBOCS)

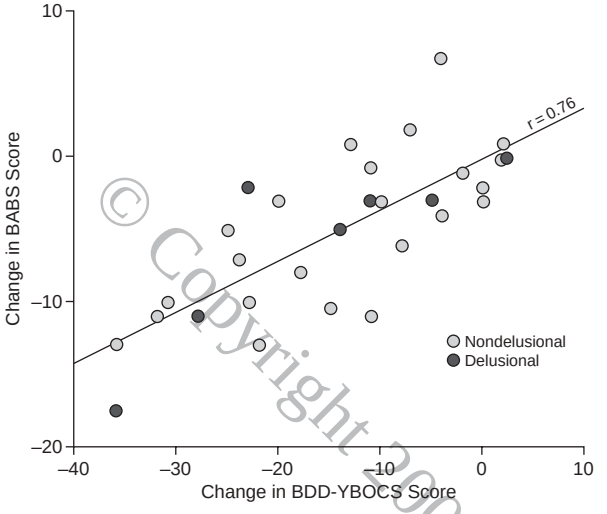
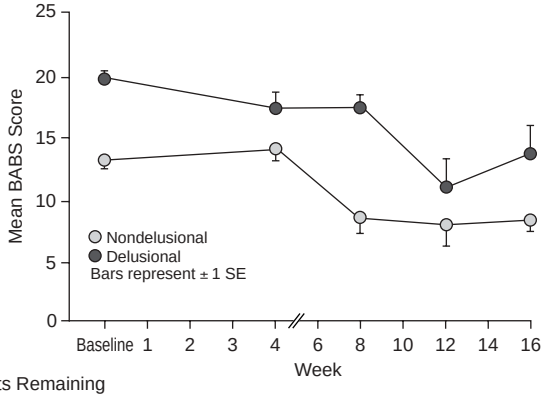


Figure 3. Scores Over Time on the Brown Assessment of Beliefs Scale (BABS) for 7 Delusional and 23 Nondelusional Subjects Receiving Fluvoxamine for Body Dysmorphic Disorder



Patients Remaining

Nondelusional	23	23	18	16	13	13
Delusional	7	6	6	6	5	5

(poor insight) to 9.5 ± 5.8 (good-to-fair insight) at termination ($t = 5.0$, $df = 29$, $p < .001$). Change in total BABS scores and in total BDD-YBOCS scores was significantly correlated ($r = 0.76$, $p < .001$; Figure 2). Correlations between change in individual BABS items and change in total BDD-YBOCS scores were also significant with the exception of the BABS insight item ($r = 0.30$, $p = .11$). BABS scores significantly decreased by study week 8; at the time each individual demonstrated response on the BDD-YBOCS, there was also a statistically significant decrease in BABS scores from baseline ($t = 3.1$, $df = 18$, $p < .01$). Delusionality significantly improved in the subgroup of patients who responded to fluvoxamine, with total BABS score in this group decreasing from 15.1 ± 3.8 at baseline (poor insight) to 7.6 ± 5.1 at endpoint (good insight) ($t = 6.6$, $df = 18$, $p < .001$). Scores on each individual BABS item significantly decreased in fluvoxamine responders: conviction ($t = 5.5$, $df = 18$, $p < .001$), perception of others' views ($t = 2.7$, $df = 18$, $p < .05$), explanation of differing views ($t = 6.1$, $df = 18$, $p < .001$), fixity ($t = 4.4$, $df = 18$, $p < .001$), attempt to disprove ideas ($t = 6.6$, $df = 18$, $p < .001$), insight ($t = 2.3$, $df = 18$, $p < .05$), and ideas/delusions of reference ($t = 3.9$, $df = 18$, $p < .01$). The correlation between change in total BABS and BDD-YBOCS scores in fluvoxamine responders was 0.66 ($p < .01$). Delusionality did not significantly improve in fluvoxamine nonresponders; the mean total BABS score in this group was 13.5 ± 5.4 at baseline and 12.6 ± 5.6 at endpoint ($t = 0.8$, $df = 10$, $p = .46$). None of the individual BABS item scores significantly changed in this group, and the correlation between change in total BABS and BDD-YBOCS scores was nonsignificant ($r = 0.17$, $p = .62$). However, an ANCOVA found no significant differences between the 2 groups at study endpoint.

As shown in Figure 3, delusionality significantly decreased in both delusional and nondelusional subjects (mean ± SE BABS baseline score in delusional subjects = 19.6 ± 1.5, termination score = 13.7 ± 6.1, $t = 2.5$, $df = 6$, $p < .05$; baseline score in nondelusional subjects = 12.9 ± 3.8, termination score = 8.3 ± 5.2, $t = 4.0$, $df = 22$, $p < .01$). ANCOVA indicated no significant differences between the 2 groups at study endpoint.

DISCUSSION

In this study, delusionality did not predict fluvoxamine response; delusional subjects were as likely as nondelusional subjects to respond to this SRI, consistent with findings from our clinical series.[3,12] In addition, delusionality significantly improved—that is, many subjects became aware that the defect was not as ugly or abnormal in appearance as they had previously considered it to be. While delusions are generally thought to respond only to antipsychotics, these findings suggest that at least some types of psychosis may respond to SRIs alone. One likely interpretation of these findings is that insight (delusionality) is a dimensional construct and that delusional and nondelusional symptoms do not differ qualitatively.[4]

It is our clinical impression that delusionality was sometimes accompanied by, or perhaps due to, resolution of a likely abnormality in visual processing. Some fluvoxamine responders stated that after treatment, the defect had visually improved or was even no longer visible, with most recognizing that their previous view of their appear-

ance was inaccurate. One subject, for example, said "I look completely different, like a different person. My skin looks clearer, and my face is more proportionate. . . . I look normal, but I didn't used to. . . . What I see now is the correct view." Another said that he had discovered that fluvoxamine makes hair grow, stating that he actually saw more hair on his head. Such reports are consistent with the theory that some delusions may arise from anomalous sensory, or perceptual, experiences[25,26] and with evidence that the visual system appears to be modulated by serotonin.[27] These clinical observations require investigation in psychophysical studies in which perception in BDD is accurately and precisely measured.

Delusionality did not improve in all fluvoxamine responders, however. Several subjects worried less about the defect and were less distressed and impaired by it, but were just as certain that it was ugly and unacceptable in appearance. Why some treatment responders, but not others, experience a decrease in delusionality is unknown. In our clinical experience, amelioration of delusionality tends to enhance treatment compliance and is an important component of overall improvement in BDD. An important question that requires investigation is whether antipsychotic augmentation of an SRI might decrease delusionality in patients whose delusionality has not improved or only partially improved with an SRI alone. Also needing study is the question of whether antipsychotics alone are effective for delusional BDD. Although available data suggest that they may not be, most data are retrospective and limited to a small number of cases.[2,12]

Our study has several important limitations. The major limitation is that the study was uncontrolled, and the findings should therefore be considered preliminary. In addition, the BABS was administrated only monthly, which limits conclusions about the time course of change in delusionality. While the BABS appears to have good psychometric properties, confirmatory work is needed; in particular, the cut point for delusionality requires further study. Despite these limitations, our findings raise intriguing questions about the treatment of delusions and suggest that SRIs alone may be effective for certain types of psychosis. Further research is needed to confirm these findings in BDD in controlled studies and to determine whether other disorders characterized by delusional thinking may respond to SRIs alone.

Drug names: fluoxetine (Prozac), fluvoxamine (Luvox), pimozide (Orap).

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