Combined Dialectical Behavior Therapy and Fluoxetine in the Treatment of Borderline Personality Disorder

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Background: This study examines the therapeutic effect of fluoxetine, a selective serotonin reuptake inhibitor, added to dialectical behavior therapy (DBT), an empirically supported psychosocial therapy, for the treatment of borderline personality disorder.

Method: This is a 12-week, randomized, double-blind, placebo-controlled study of patients with borderline personality disorder (identified using the Structured Clinical Interview for DSM-IV Axis II Disorders). All subjects received individual and group DBT. Of the 20 subjects that completed treatment, 9 were randomly assigned to receive up to 40 mg/day of fluoxetine and 11 were randomly assigned to the placebo condition. Subjects were evaluated at baseline and at week 10 or 11 on self-report measures of depression, anxiety, anger expression, dissociation, and global functioning. The study was conducted between January 1998 and February 2000.

Results: Time-by-group interaction effects revealed no significant group differences in scores from pretreatment to posttreatment on any measure. However, within the DBT/placebo group, there were significant pretreatment/posttreatment differences in the direction of improvement on all measures. No significant pretreatment/posttreatment differences were found within the DBT/fluoxetine condition.

Conclusion: The data suggest that adding fluoxetine to an efficacious psychosocial treatment does not provide any additional benefits. Further studies with larger sample sizes are warranted.

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Expeditious and effective treatment for borderline personality disorder remains a compelling need. Borderline personality disorder is associated with 20% of inpatient admissions,[1] predicts failure of treatment of concomitant Axis I disorders,[2] and has a rate of completed suicide of about 9%.[3] The convergence of descriptions of serotonergic dysfunction with the symptoms of the disorder (e.g., depression, affective lability, suicidality, and hostility) has focused investigative efforts on the selective serotonin reuptake inhibitors (SSRIs) as likely candidates for efficacy.[4] In the American Psychiatric Association's (APA) Practice Guideline for the Treatment of Patients With Borderline Personality Disorder,[5] SSRIs are the first-line pharmacologic treatment for affect dysregulation and impulse-behavioral symptoms of borderline personality disorder.

Since 1989, there have been at least 8 open-label studies testing SSRIs in borderline personality disorder or a mixed sample of borderline personality disorder and other personality disorders: 5 using fluoxetine[6–10]; 2, sertraline[11,12]; and 1 using a partial SSRI drug, venlafaxine.[13] All produced promising results, with benefits usually described in depression, general functioning, and aggression. Despite these early indications, there have been very few placebo-controlled double-blind trials of SSRIs for borderline personality disorder. Only fluoxetine has been examined in randomized, double-blind, placebo-controlled trials for borderline personality disorder.

One double-blind, placebo-controlled study[14] examined 22 subclinical subjects, recruited through newspaper advertisements, who met criteria for borderline personality disorder or had significant borderline personality disorder traits. Potential subjects with concurrent Axis II disorders, recent suicidal or self-mutilating behaviors, or previous psychiatric hospitalization were excluded. None of the subjects had co-occurring Axis I disorders. The dose of fluoxetine was titrated to a maximum dose of 60 mg/day. A mean daily dose of 40 mg was maintained for 12 weeks, targeting dysphoria, anger, and rejection sensitivity. There was a robust placebo response. In fact, the treatment condition was significantly superior on only 2 of 5 measures, with improvements noted in depression and anger among fluoxetine recipients.

Markovitz[11] examined a more symptomatic group in which all participants met criteria for borderline personal-

ity disorder and had an average of 3 Axis I diagnoses. The dose of fluoxetine was advanced to 80 mg/day in the first 3 weeks of the study, and treatment continued for 14 weeks. The medication condition was superior to placebo on global functioning, depression, anxiety, and global psychopathology measures. Parasuicide was also monitored with impressive reductions. There was little change of any kind in the placebo condition. The results seem to suggest that longer treatment with higher doses may be necessary for reliable benefit to emerge.

In the studies described briefly herein, there is scant information offered about what type of psychotherapy may have accompanied the medication trials, if any, in spite of psychotherapy being the first line of treatment for borderline personality disorder as indicated by APA's Practice Guidelines.[5] Dialectical behavior therapy (DBT) is a modification of standard cognitive-behavioral treatment that addresses the needs of chronically suicidal, self-injurious borderline women.[15] Therapy consists of weekly individual psychotherapy coupled with group skills training and a fixed hierarchy of treatment targets (life-threatening behavior, behavior that interferes with the conduct or progress of the therapy, and behavior that, although not immediately lethal, limits one's quality of life, such as depression or drug addiction). The targets are monitored daily by the patient on a diary card and reviewed weekly by the therapist to set the agenda for a given session. In a year-long randomized trial comparing DBT and treatment as usual, DBT was significantly more effective at reducing parasuicide, treatment dropout, and inpatient admissions.[16,17] The DBT patients demonstrated more improvement in global adjustment, and results were maintained a year after termination. However, there was no significant reduction in depressive symptomatology.

To embed a medication trial within a stable, efficacious psychotherapy would offer a number of benefits. It would standardize a major component of treatment, reducing the effect of a potentially confounding variable. Additionally, both placebo and medication conditions would provide active treatment, allowing the inclusion of suicidal patients and a more clinically relevant study population. The present investigation is a 12-week, randomized, double-blind, placebo-controlled trial of fluoxetine added to DBT. We predict that, compared with subjects receiving DBT and placebo, those in the experimental condition would report reductions on measures of depression, anger, aggression, and parasuicidal behavior at the end of the clinical trial.

METHOD

Subjects

Participants were recruited from all admissions to the Women's Partial Program, a 5-day DBT-based partial hospital program, using a brief self-report questionnaire. Follow-up interviews and assessments excluded those with a primary diagnosis of substance dependence, a seizure disorder, unstable medical conditions, a lifetime history of schizophrenia or bipolar disorder, monoamine oxidase inhibitor treatment in the prior 2 weeks, or a previous adequate trial of fluoxetine. Women who were pregnant, lactating, or unwilling to use effective birth control were also excluded. Administration of the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) identified those meeting criteria for borderline personality disorder.[18] The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) identified co-occurrent Axis I disorders.[19] All diagnoses were confirmed in weekly team meetings, which included the treating psychiatrist. Twenty-five female patients entered the study and were randomly assigned to a treatment condition. After complete description of the study to the subjects, written informed consent was obtained.

Design

This study was double-blind and placebo-controlled, with randomized block assignment comparing 12 weeks of DBT plus fluoxetine with DBT plus placebo after a 1-week placebo run-in. Although DBT has been empirically tested as a 12-month treatment, major treatment gains were made before the first assessment at 4 months.[17] A shortened time frame was chosen to keep the study comparable with other fluoxetine studies. The randomized block assignment minimized the possible confound of comorbid Axis I presentations expected to respond to fluoxetine by assignment of an equal number of patients with major depressive disorder, posttraumatic stress disorder, or both to each treatment condition. A suggested strategy for increasing homogeneity among borderline personality disorder samples is to focus on subtypes of borderline personality disorder behavioral clusters such as affective, impulsive, or identity symptom clusters.[4] Because fluoxetine was not expected to improve symptoms of identity disturbance, participants had to meet at least 1 borderline personality disorder criterion pertaining to affective instability (e.g., lability or anger) and 1 pertaining to impulsivity. The study proposed was critiqued and approved by the institutional review board of Butler Hospital (Providence, RI). The study was conducted between January 1998 and February 2000.

Assessment

The dependent measures were chosen for their demonstrated adequate psychometric properties and sensitivity to change in studies of medical or psychosocial treatments for borderline personality disorder. The assessment battery was administered prior to treatment and at week 10 and included the following self-report instruments: Beck Depression Inventory (BDI),[20] State-Trait Anxiety Inventory (STAI),[21] Overt Aggression Scale-Modified (OAS-M),[22]

Table 1. Demographics and Pretreatment Variables in the Study of Combined Dialectical Behavior Therapy and Fluoxetine in Borderline Personality Disorder

	Completers		Dropouts	
Characteristic	Fluoxetine (N = 9)	Placebo (N = 11)	Fluoxetine (N = 3)	Placebo (N = 2)
Mean (SD) age, y	39.78 (9.81)	32.73 (10.76)	30.33 (9.07)	36.50 (6.36)
Education, N (%)				
High school diploma	5 (56)	6 (55)	3 (100)	0 (0)
College	3 (33)	2 (18)	0 (0)	2 (100)
Postgraduate	1 (11)	3 (27)	0 (0)	0 (0)
Marital status, N (%)				
Single/never married	3 (33)	7 (64)	1 (33)	2 (100)
Married	3 (33)	0 (0)	2 (67)	0 (0)
Divorced/separated	2 (22)	1 (9)	0 (0)	0 (0)
Living with significant other	1 (11)	3 (27)	0 (0)	0 (0)
Ethnicity, N (%)				
African American	2 (22)	1 (9)	1 (33)	1 (50)
White	6 (67)	10 (91)	1 (33)	1 (50)
Native American	1 (11)	0 (0)	1 (33)	0 (0)
Number of SCID-II items endorsed, mean (SD)	5.78 (0.83)	6.18 (1.25)	6.67 (0.58)	7.00 (2.83)
Present MDD diagnosis, N (%)	5 (56)	6 (55)	2 (67)	2 (100)
Present PTSD diagnosis, N (%)	4 (44)	4 (36)	1 (33)	2 (100)
Number of psychotropic medications, mean (SD)	2.33 (1.37)	2.00 (1.00)	3.00 (2.00)	2.50 (0.71)

Abbreviations: MDD = major depressive disorder, PTSD = posttraumatic stress disorder, SCID-II = Structured Clinical Interview for DSM-IV Axis II disorders.

Dissociative Experiences Scale (DES),[23] and the State-Trait Anger Expression Inventory (STAXI).[24] A Global Assessment of Functioning scale (GAF)[1] rating based on DSM-IV Axis V was administered by both the therapist and the psychiatrist. The posttreatment assessment was conducted during week 10 to minimize the influence of "termination issues" expected to affect this population.

Treatment

All subjects received twelve 1-hour sessions of individual DBT psychotherapy and participated in a weekly 2-hour skills group for the 13 weeks of the study. They could remain in the skills groups for an additional 12 weeks after completion of the study, but the individual component was terminated and referrals were made to community therapists. All study therapists and psychiatrists had undergone intensive training in DBT.

Study participation began in week 0 with a 30-minute orientation meeting with the assigned psychiatrist, inaugurating the 1-week placebo washout period. Any remnants of prior psychotropic regimens were tapered to discontinuation during this week as well. The only other psychotropic medication allowed was 50 to 100 mg/day of trazodone for insomnia. The study drug was begun at week 1 at 20 mg/day and the dose was advanced to the maximum anticipated dose of 40 mg/day at week 3. No patient required dosage adjustment due to side effects. Subsequent 15-minute medication management meetings were held during weeks 3, 5, 7, 9, and 11. Diary card records of pill ingestion were reviewed, and pill counts were made as a compliance measure.

A non-treating study psychiatrist was available to break the blind in the event of a clinical emergency, but no such emergency occurred. In addition, individual therapists were available to the patients for round-the-clock emergency consultation as a component of DBT treatment. All decisions regarding clinical care, ongoing participation in the study, and other treatment or research issues were made in weekly consultation team meetings as part of DBT, but modified in the service of the research program.

RESULTS

Twenty-five subjects were assessed, randomized (13 to placebo and 12 to fluoxetine), and began treatment. Eleven in the placebo group and 9 in the fluoxetine group completed all treatment and assessments. The 3 dropouts in the fluoxetine condition left treatment in the first 2 weeks, citing a negative experience of the placebo washout period, which led to a reversal of their willingness to tolerate a potential assignment to the placebo condition. The 2 placebo-condition dropouts left at week 6 and 8, respectively. One participant sought hospitalization outside the study at another facility, and the treating physician was unwilling to continue the study drug during her stay. The second participant terminated due to an intolerable lack of improvement in her condition. A midpoint assessment was available for this participant and was included in post hoc analyses.

Table 1 depicts demographic and pretreatment variables in the 2 treatment conditions, including completers

Table 2. Mean Pretreatment and Posttreatment Scores on Primary Outcome Measures for Participants in Each Treatment Condition

									Treatment Effects					
	Fluoxetine (N = 9)		Placebo (N = 11)		Group Differences				DBT/Fluoxetine			DBT/Placebo		
Measure	Mean	(SD)	Mean	(SD)	F	df	p	Effect Size	t	df	p	t	df	p
BDI														
Pre	32.11	(10.93)	32.09	(11.76)	2.76	1,18	NS	.133	1.16	8	NS	5.44	10	< .001
Post	25.00	(18.04)	13.91	(9.54)										
STAI														
Pre	119.22	(13.56)	121.82	(10.02)	0.28	1,18	NS	.02	1.34	8	NS	3.34	10	< .008
Post	101.33	(38.06)	96.18	(28.83)										
STAXI (anger exp)														
Pre	25.78	(16.00)	33.73	(14.09)	0.05	1,18	NS	.003	1.30	8	NS	3.60	10	< .005
Post	20.56	(12.19)	27.64	(12.36)										
DES														
Pre	18.89	(16.78)	20.67	(9.18)	4.83	1,18	< .04*	.23	0.07	8	NS	3.42	10	< .007
Post	18.69	(15.39)	12.66	(12.00)										
OAS-M (aggression)														
Pre	12.56	(22.88)	11.18	(12.44)	0.71	1,18	NS	.04	1.34	8	NS	1.29	10	NS
Post	2.56	(3.81)	7.45	(10.05)										
OAS-M (self-injury)														
Pre	11.33	(34.00)	21.00	(62.76)	0.21	1,18	NS	.012	0.48	8	NS	0.79	10	NS
Post	7.00	(12.37)	6.55	(12.64)										
OAS-M (suicidality)														
Pre	2.63	(3.78)	2.09	(1.04)	0.19	1,18	NS	.08	0.34	8	NS	2.30	10	< .05*
Post	2.13	(3.48)	1.00	(1.18)										
GAF														
Pre	49.39	(9.10)	46.58	(5.90)	0.23	1,17	NS	.013	–2.53	8	< .04*	–5.48	9	< .001
Post	59.92	(13.15)	59.30	(7.17)										

*Values listed are significant by conventional standard of .05 but did not meet our a priori determined significance level of .01.
Abbreviations: BDI = Beck Depression Inventory, DBT = dialectical behavior therapy, DES = Dissociative Experiences Scale, GAF = Global Assessment of Functioning scale, NS = not significant, OAS = Overt Aggression Scale, STAI = State-Trait Anxiety Inventory, STAXI = State-Trait Anger Expression Inventory.

and dropouts. The overall mean (SD) age of participants was 35.3 (10.13) years. With regard to ethnicity, 72% of the sample could be characterized as white, 20% as African American, and 8% as Native American. The majority of our sample (56%) did not have a college degree, but 48% had taken college courses. Approximately half are currently single and have never married, 20% are currently married, 16% live with significant others, and 12% are divorced or separated. One-way analysis of variance (ANOVA) determined no significant group differences on any of the demographic variables.

Since randomization was blocked on present diagnoses of major depressive disorder and/or posttraumatic stress disorder, the proportion of participants with these diagnoses was comparable across treatment groups. Furthermore, each group had 2 patients who reported current substance abuse. There were no significant group differences in the mean number of SCID-II borderline personality disorder items endorsed, with an overall mean (SD) of 6.16 (1.18) among all participants. Similarly, the mean number of pretreatment psychotropic medications was relatively comparable across all groups, with the mean number of medications being 2.33 across the entire sample. Based on 1-way ANOVA, there were no significant group differences in baseline scores on the BDI, the STAI, the STAXI, the DES, the OAS-M, or the therapist-rated GAF. Psychiatrist-rated GAF scores, however, were significantly higher (by approximately 10 points) for those in the fluoxetine group than for those in the placebo group ($F = 5.01$, $p = .037$). Primary analysis involving the GAF utilizes the combined means of the therapist-rated GAF and the psychiatrist-rated GAF, which was not statistically different between groups.

Repeated measures ANOVA on continuous outcome measures (BDI, STAI, STAXI, DES, OAS-M, and GAF) assessed at pretreatment and posttreatment was utilized to determine placebo versus fluoxetine group differences among those who completed 12 weeks of treatment. To control for multiple comparisons, we chose .01 as the level of significance for each of the primary measures. As depicted in Table 2, an examination of the time × group interaction effects reveals no significant group differences in scores from pretreatment to posttreatment. While the interaction was near significance for the DES ($F = 4.83$, $df = 1,18$; $p < .04$), the direction was in contrast to our hypothesis. In fact, an examination of mean scores at pretreatment and posttreatment reveals a greater decrease in symptomatology among those in the placebo group across all continuous outcome measures, although these differences are not statistically significant.

To assess the effect of each treatment independently, we conducted paired sample t tests using pairs of an individual's pretreatment and posttreatment scores on each of the continuous measures. To control for multiple

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post hoc comparisons, we used a stringent Bonferroni corrected α of .004 as the level of significance. As indicated in Table 2, among those in the fluoxetine group, there were no significant differences between pretreatment and posttreatment scores. However, significant differences between pretreatment and posttreatment scores on the BDI ($t = 5.44$, $df = 10$, $p < .001$) and the GAF ($t = –5.48$, $df = 9$, $p < .001$) were found among those in the placebo condition. These results suggest a decrease in self-report depressive symptomatology and an increase in therapist/psychiatrist-rated global functioning among those who received 12 weeks of DBT therapy and placebo medication. Furthermore, there were near-significant decreases in self-report anxiety ($t = 3.34$, $df = 10$, $p < .008$), anger expression ($t = 3.60$, $df = 10$, $p < .005$), and dissociation ($t = 3.42$, $df = 10$, $p < .007$) among participants in the placebo condition.

To further clarify the nature of our unexpected findings, we analyzed data from those patients who terminated treatment prior to completion of the study. Within the fluoxetine condition, there were no significant differences between dropouts and completers on any of the demographic or pretreatment variables. Among those in the placebo condition, only the mean GAF scores differed significantly between completers and dropouts, with those in the latter group being rated as less functional. Even when the placebo-condition subject who dropped out was included in the analysis, using midtreatment scores as posttreatment scores, there were no significant changes in the findings.

Since midtreatment scores were available for only 1 of the dropouts, we also analyzed the results by using the baseline scores as the posttreatment scores for those who terminated the study. As in the previous analyses, inclusion of all dropouts did not result in a significant group × time interaction on any of the continuous outcome measures in a repeated ANOVA. Furthermore, among the fluoxetine group (completers and dropouts), paired sample t tests revealed no significant pretreatment and posttreatment score differences on any measure. The significant differences in pretreatment and posttreatment scores on the BDI and GAF for the placebo group were preserved even when the baseline scores for the placebo dropouts were used ($t = 3.64$, $df = 12$, $p < .003$), and STAI changes in placebo participants were also significant ($t = 3.78$, $df = 12$, $p < .003$). In sum, the initial findings survive the inclusion of the most recent assessment of all dropouts.

Finally, in an effort to compare pretreatment and posttreatment differences among positive responders, we analyzed the data, omitting the 3 subjects in the fluoxetine condition whose BDI scores increased at the end of the study. Compared with all subjects in the placebo condition, repeated measures ANOVA still found no significant time × group interactions on any of the outcome measures in spite of this substantial manipulation.

DISCUSSION

In this double-blind study, fluoxetine did not surpass placebo on any outcome measure. Although there was no statistically significant difference between the 2 study groups, results from within-group pretreatment and posttreatment comparisons were strikingly different. The placebo group showed significant improvement in clinician-rated global functioning and depression and clinically meaningful reductions in anxiety and dissociation. In contrast, there were no significant pretreatment-posttreatment changes on any measure for the fluoxetine group.

Unlike previous open[6–13] and double-blind, placebo-controlled trials,[11,14] the present findings suggest that adding fluoxetine to a stable, efficacious psychotherapy is not an effective treatment to reduce anger, depression, and anxiety or to improve global functioning in patients with borderline personality disorder. This study differs from previous work in that it controlled for the psychosocial treatment using DBT, a therapy with demonstrated efficacy in borderline personality disorder. All study therapists were experienced in treating borderline personality disorder and intensively trained in the use of DBT. The therapy itself may have been so powerful as to overwhelm any impact of medication, and, at a minimum, may have contributed to the significant pretreatment/posttreatment differences observed among those in the placebo condition. However, in the absence of a non-DBT condition, the true efficacy of the therapy itself cannot be determined.

There is also the possibility that the sample in the present study was biased toward medication nonresponders. Each participant was willing to discontinue her current medications and to risk assignment to placebo. It is noteworthy that several dropped out because of unwillingness to tolerate a nonmedicated condition. All 3 dropouts in the fluoxetine condition terminated within the first 2 weeks of the study, while the 2 dropouts in the placebo condition terminated after 6 and 8 weeks of treatment. Therefore, our analyses in which the most recent observation was carried forward should be interpreted with caution. However, the post hoc analyses, which excluded nonresponders from both groups, yielded similar findings of a significant pretreatment-posttreatment difference in the placebo group but not in the fluoxetine group. This disparity suggests that even among patients who responded positively to treatment, those in the placebo condition had more significant improvements compared with those in the fluoxetine condition.

Reasons for inconsistent findings across studies are obscure, but certain factors may play a role. Even given the frequently observed heterogeneity of patients meeting borderline personality disorder criteria,[25] the study populations varied considerably across investigations. Salzman et al.[14] examined subjects with mild-to-moderate borderline personality disorder symptoms without Axis I diag-

noses or any history of psychiatric hospitalization. The current study recruited from patients already hospitalized with comorbid Axis I pathology. Markovitz's[11] subjects were more similar to those in the present study with a mean of 3 Axis I diagnoses, but Markovitz obtained opposite results. Although bipolar disorder was an exclusion criterion in the present study, it is possible that some nonresponders had an undetected subclinical presentation of bipolar disorder, which would worsen with antidepressant treatment. Some researchers have noted a subclinical presentation that frequently co-occurs with borderline personality disorder and have advocated a spectrum approach to conceptualizing bipolar disorder.[26,27] One such study asserts that 44% of its borderline personality disorder sample belongs to the bipolar spectrum and that most subjects responded negatively, i.e., with hostility and agitation, to antidepressants.[26] While comorbid Axis I conditions often obfuscate the findings of clinical trials aimed at one disorder, diagnostic co-occurrence in a clinical personality disorder sample is the norm rather than the exception.[28] Thus, it can be argued that our sample is more representative of the prototypic borderline personality disorder clinical population. In fact, our inclusion of subjects with diagnostic comorbidities who may even be suicidal in a randomized clinical treatment trial is an advantage over comparable pharmacologic studies that exclude such individuals.

Another possible explanation for our unexpected findings is that daily fluoxetine dosages across studies varied from 20 mg to 80 mg. It is possible that 40 mg/day as administered in the present study was insufficient. However, Salzman et al.[14] found no difference in response rates with doses above 40 mg. The intent of limiting the dosage to 40 mg in the current study was to maximize therapeutic impact while minimizing side effects that might lead to premature termination from the study. Since the subjects in Salzman's study were nonclinical, it is possible that a lower dosage is sufficient in reaching a ceiling effect of improvement that would not necessarily occur among a more severe or clinical sample. Future studies that have flexible dosing and allow for higher dosages are warranted to determine whether a clinical sample may benefit from higher doses than the 40 mg/day that were prescribed in the current study. While this relatively low dosage is a potential limitation of the current study, it still does not account for the improvement found among subjects in the placebo condition and lack of comparable improvement among subjects in the fluoxetine condition.

The limited length of treatment might also have affected the study outcome. While a 12-week duration was selected to be comparable to other randomized, double-blind fluoxetine trials, few clinicians expect rapid success with the borderline personality disorder population. In fact, 12 weeks is a considerably shorter treatment trial than any published study of DBT. The final assessment of the present study occurred even earlier, during week 10 or 11, to minimize the interference of therapeutic termination in the posttreatment assessment. In the present study, there was a trend toward improvement in most of the fluoxetine subjects, which could have become more pronounced over time. In a recent long-term pharmacologic treatment trial,[10] borderline personality disorder patients taking fluoxetine had a good outcome at 6 months.

In addition, there is no evidence to suggest that the course of improvement from either fluoxetine or DBT is linear. It is possible that the benefits from DBT fluctuate after the "honeymoon effect" of a new therapeutic relationship wears off. Clearly, longer and larger controlled trials with multiple assessment points are needed to elucidate these findings. Multiple assessment points would yield important information with regard to minimum length of time for a therapeutic response to occur. A larger sample size is necessary, not only to confirm or disconfirm the present findings, but to allow for finer statistical analyses of whether different diagnostic subgroups experience differential effects.

In sum, the overall conclusion from this study is that recommendations for the use of SSRIs in the treatment of borderline personality disorder and concurrent Axis I disorders may be premature and further double-blind, randomized clinical trials are warranted. More rigorous trials of manualized pharmacotherapy with provisions for adherence and compliance checks are needed. There have been few placebo-controlled, double-blind studies in patients with borderline personality disorder, and evidence from those extant is not conclusive. The present study is the first to control for concomitant psychosocial therapy in addition to pharmacotherapy. Some agreement on how to identify and characterize meaningful subgroups of borderline personality disorder and which symptoms to assess and which instruments to employ would foster more informative comparison of results across studies. Publication of all methodologically sound studies, including those with negative findings, is necessary to develop an accurate understanding of which medications and dosages are effective for symptoms associated with borderline personality disorder.

Drug names: fluoxetine (Prozac and others), sertraline (Zoloft), trazodone (Desyrel), venlafaxine (Effexor).

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