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THE IMPACT OF DEPRESSIVE PERSONALITY DISORDER ON TREATMENT OUTCOME FOR CHRONIC DEPRESSION

by

RACHEL E. MADDUX

Under the Direction of Lawrence P. Riso

ABSTRACT

Our conceptualization and empirical understanding of the course of depression is beginning to change. This is largely a result of recent epidemiological and clinical data that suggest depression has a chronic course for many individuals. Treatment studies for chronic depression have found that response rates are consistently less robust than in studies of acute, episodic depression. As is such, investigators have begun to examine factors that impede treatment response among these patients. One such factor is the presence of comorbid Axis-II personality disorders. This study examined the moderating effects of Depressive Personality Disorder (DPD) on treatment outcome among 680 outpatients with chronic depression. Results suggest that DPD did not serve as a prognostic indicator of worse outcome after 12 weeks of treatment or at last observation carried forward. This was a secondary analysis of the data presented by Keller and colleagues (Keller, McCullough, Klein, Arnow, Dunner, & Gelenberg, 2000).

INDEX WORDS: Depression, Chronic Depression, Depressive Disorder, Axis-II, Personality Disorders, Depressive Personality, Treatment for Depression

THE IMPACT OF DEPRESSIVE PERSONALITY DISORDER ON TREATMENT OUTCOME FOR CHRONIC DEPRESSION

by

RACHEL ELIZABETH MADDUX

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DEDICATION

For my greatest mentor:

Dr. Bill D. Maddux

TABLE OF CONTENTS

ACKNOWLEDGEMENTS……...……	iii
LIST OF TABLES…….	vi
LIST OF FIGURES……...	vii
LIST OF ABBREVIATIONS……	viii
CHAPTER	
1 INTRODUCTION……	1
Treatment for Depression……...	2
2 SPECIFIC AIMS……..	10
Primary Aim……...	11
Primary Hypothesis……	11
3 METHODS……...	12
Participants……	12
Procedures…….	13
Measures……...	17
4 RESULTS…….	18
5 DISCUSSION……...	41
Strengths of the Current Study……..	47
Limitations of the Current Study……..	48
Future Directions……...	50

Conclusion……	52
REFERENCES……...	54

LIST OF TABLES

Table 1: DSM-IV criteria for Depressive Personality Disorder and Dysthymic Disorder……..	7
Table 2: Criteria for study eligibility……	14
Table 3: Correlations (Pearson r)……..	20
Table 4: Demographics for entire sample (n=681)……...	22
Table 5: Demographics and Clinical Characteristics……	23
Table 6: Descriptive Data for HRSD Outcome at Week 12…….	25
Table 7: Descriptive Data for HRSD Outcome at Last Observation Carried Forward (LOCF)……	26
Table 8: Summary of 2 x 3 factorial ANCOVA for DPD at week 12……..	27
Table 9: Summary of 2 x 3 factorial ANCOVA for DPD at LOCF…….	34
Table 10: Summary of 2 x 3 factorial ANCOVA for any PD at week 12…….	42

LIST OF FIGURES

Figure 1: Treatment Outcome at Week 12 (HRSD)……..	28
Figure 2: Nefazodone Outcome at Week 12 (HRSD)……...	29
Figure 3: Psychotherapy (CBASP) Outcome at Week 12 (HRSD)……..	30
Figure 4: Combination Outcome at Week 12 (HRSD)…….	31
Figure 5: Outcome by Treatment Arm at Week 12……...	32
Figure 6: Treatment Outcome at LOCF (HRSD)……..	35
Figure 7: Nefazodone Outcome at Last Observation Carried Forward (LOCF)……..	36
Figure 8: Psychotherapy (CBASP) Outcome at Last Observation Carried Forward (LOCF)……...	37
Figure 9: Combination Outcome at Last Observation Carried Forward (LOCF)…….	38
Figure 10: Outcome by Treatment Arm at Last Observation Carried Forward (LOCF)……..	39
Figure 11: Impact of Personality Disorder on Treatment Outcome as week 12……...	43

LIST OF ABBREVIATIONS

APD = Avoidant Personality Disorder

ANCOVA = Analysis of Covariance

CBASP = Cognitive Behavioral Analysis System of Psychotherapy

DPD = Depressive Personality Disorder

HRSD = Hamilton Rating Scale for Depression

HRSD.base = Hamilton Rating Scale for Depression at Baseline

HRSD.12 = Hamilton Rating Scale for Depression at Week 12

HRSD.99 = Hamilton Rating Scale for Depression at Last Observation Carried Forward

LOCF = Last Observation Carried Forward

mstatus = Marital Status

OCPD = Obsessive Compulsive Personality Disorder

PD = Personality Disorder

partial η^2 = Partial Eta Squared

Introduction

Extensive clinical and epidemiological data has consistently indicated that Major Depressive Disorder (MDD) is a highly prevalent, often recurrent condition associated with substantial psychosocial dysfunction, morbidity and mortality (Kessler, McGonagle, & Zhao, 1994; Wells, Stewart, & Hayes, 1989; Wells, Golding, & Burnam, 1988; Wells, 1985; Coryell, Noyes, & Clancy, 1982). Point prevalence rates registered by the National Comorbidity Survey (NCS) were estimated at 4.9%, suggesting that over 14 million people in the United States suffer from MDD at any given time (Kessler et al., 1994). Moreover, a World Health Organization (WHO) report ranked unipolar major depression as the leading cause of years lived with disability worldwide in 1990 (Murray & Lopez, 1996). It is estimated that by the year 2020, depression will be the second most disabling condition in the world below ischaemic heart disease, and the *leading* cause of disease burden among women and people in developed countries (Murray & Lopez, 1996). Perhaps the most salient statistics involve the relationship between depression and mortality. Fifteen percent of patients who require hospitalization for severe depression will die by committing suicide (Coryell et al., 1982). Approximately 10% of patients with MDD who attempt suicide will eventually take their own lives. One study found that approximately 50% of individuals who committed suicide had a primary diagnosis of MDD (Barklage, 1991). Taken together, it is strikingly evident that MDD is a serious health problem.

MDD has traditionally been conceptualized as an episodic, remitting condition. However, major epidemiological studies indicate that 3% – 6% of individuals in community samples have experienced a chronic course of depression (at least 2 years in duration) (Robins & Regier, 1991). Data from the National Institute of Mental Health Collaborative Depression Study longitudinal follow-up suggest that over 19% of depressed patients experienced chronic episodes lasting 2 years or more, and 7% of those individuals had not recovered after 8 years (Mueller, Keller, & Leon, 1996). Observations from other large outcome studies including the Zurich Follow-Up Study (Angst, 1986) and the Medical Outcomes Study (Wells et al., 1989) have helped reconceptualize our understanding of MDD from that of an episodic illness toward a disorder that is more chronic in course for many patients. Furthermore, in clinical settings, chronic depression is commonly seen, with a reported 22%-36% of outpatients meeting criteria for Dysthymic Disorder (Klein & Santiago, 2003).

Although no uniform definition of chronic depression exists, depression is broadly regarded as 'chronic' when clinically significant symptomatology and functional impairment extend over several years. Recent attempts to classify chronic depression using longitudinal course specifiers have led to the description of three different forms in the DSM-IV: (1) Dysthymic Disorder, (2) Major Depressive Disorder, chronic type, and (3) recurrent Major Depressive Disorder without full interepisode recovery (American Psychiatric Association, 2000). Additionally, the term 'double depression' is used to describe Dysthymic Disorder with a superimposed major depressive episode (Keller & Shapiro, 1982).

Treatment for Depression: There has been rigorous empirical study over the past 20 years investigating the efficacy of various treatments for MDD. Additionally, the Department of Health and Human Services Agency for Health Care Policy and Research (AHCPR) published a comprehensive report outlining the range of treatments available for patients with MDD (1993). Overall, three common treatment types are available: medication, psychotherapy, and combination treatment. Response rates to a single antidepressant medication were found to be 60%-70%, compared to placebo response rates of 30% (Gitlin, 2002). These figures are somewhat inflated because they exclude those who fail to complete the clinical trial. Overall, this means that many patients significantly improve, but it also indicates that some 30%-40% of patients treated with antidepressants do not get better.

The efficacy of antidepressant medication has been established for the short-term treatment of chronic depressions by randomized, placebo-controlled clinical trials (Kocsis, 2003). Medications found to be superior to placebo include tricyclic antidepressants (TCAs) and serotonin reuptake inhibitors (SSRIs). Unfortunately, however, the response rates among chronically depressed individuals in such trials are substantially lower than those reported in studies of acute major depression, which also demonstrates their refractory nature (Gwirtsman, Blehar, & McCullough, 1997; Khan, Dager, & Cohen, 1991; Stewart, McGrath, & Quitkin, 1993; Kocsis, Frances, & Voss, 1987). Similarly, placebo response rates among this population are also lower than those usually seen for acute major depression (Khan et al., 1991; Brown, Dornseif, & Wernicke, 1988; Fairchild, Rush, & Vasvada, 1986). Eleven controlled trials involving acute treatment of chronically depressed patients yielded intent-to-treat response rates in

the range of only 45%-55% (Kocsis, 2003). Moreover, forty percent (40%) of responders typically did not meet criteria for full remission.

Several studies have also examined the efficacy of targeted psychotherapies for chronic forms of depression (Markowitz, 1994; Rush & Thase, 1999). Most of these studies have been open rather than controlled trials, and nearly all of them assessed psychotherapy as a monotherapy rather than an adjunctive treatment. Cognitive-behavioral therapy (CBT) has been found to have measurable but modest treatment effects among patients with Dysthymic Disorder or chronic major depression, with a mean response rate of approximately 31% (Markowitz, 1996). Interpersonal psychotherapy (IPT) has also been reported to be helpful; however, methodological limitations, such as small sample size, have compromised the usefulness of these results (Mason, Markowitz, & Klerman, 1993).

More recently, researchers have begun to investigate the value of combination treatment. Keller and colleagues designed a large multisite collaborative study to specifically target chronic depression (Keller, McCullough, Klein, Arnow, Dunner, & Gelenberg, 2000). The study compared nefazodone alone (up to 600mg/day) to psychotherapy alone (16 to 20 sessions) to the combination over a 12-week period. Six hundred and eighty one patients (n=681) with chronic MDD, MDD plus Dysthymic Disorder (double depression), or recurrent MDD without interepisode recovery were randomized to one of the three treatment arms. Overall response rates for the intent-to-treat sample were 48% for psychotherapy, 48% for nefazodone, and 73% for the combination. Remission rates were 33% for psychotherapy, 29% for nefazodone, and 48% for the combination. Fifty two percent (52%) of psychotherapy patients, 51% of

nefazodone patients, and 25% of combination patients were considered to have no response to treatment. A secondary analysis of this study is the focus of the proposed investigation.

Despite some evidence for the efficacy of antidepressant medication and psychotherapy for chronic depression, the overall response and remission rates remain relatively low, particularly for monotherapy. Moreover, our ability to predict which patients will respond to any particular treatment, or combination of treatments, remains elusive.

One potentially important factor influencing treatment response is Axis-II comorbidity. High rates of co-occurring personality disorders are frequently found in depressed inpatients and outpatients, with most studies reporting rates from 30%-60% (Flick, Roy-Byrne, & Cowley, 1993; Shea, Widiger, & Klein, 1992). Importantly, Axis-II personality disorders are particularly high for chronic forms of depression, with rates as high as 85% in some studies (Pepper, Klein, & Anderson, 1995; Markowitz, Moran, & Kocsis, 1992; Alnnaes & Torgersen, 1991).

A majority of studies of depressed patients found significant evidence that the presence of a personality disorder is associated with worse outcome (McDermut & Zimmerman, 1998; Shea et al., 1992; Shea, Pilkonis, & Beckham, 1990). This finding is fairly consistent across type of treatment involved, and has been replicated in several patient populations including inpatients, outpatients, those referred from primary care, and the elderly (Rothschild & Zimmerman, 2002). Some studies have found that cluster A (paranoid, schizoid, schizotypal) and cluster C (avoidant, dependent, obsessive-compulsive) personality disorders are related to poorer outcome (Greenberg, Craighead,

& Evans, 1995; Sato, Sakado, & Sato, 1994; Peselow, Fieve, & DiFiglia, 1992) although some studies have not had this finding (Fava, Bouffides, & Pava, 1994; Newman, Ewing, & McColl, 2000). Recently, Papakostas and colleagues examined whether the presence of comorbid Axis I and Axis II disorders predicted clinical response to an open trial of nortriptyline among patients with treatment-resistant depression (Papakostas, Peterson, & Farabaugh, 2003). Forty-two percent (42%) of patients responded to nortriptyline; however, the presence of Avoidant Personality Disorder predicted poorer response to the drug. The response rate was only 16.7% for patients with Avoidant Personality Disorder and 48.6% for patients without Avoidant Personality Disorder.

Evidence of the impact of personality on treatment outcome for depression can be best explained by the pathoplasticity model (Klein, Wonderlick, & Shea, 1993). The pathoplasticity model views personality as having a direct, causal impact on the expression of depression after onset. More specifically, this model suggests that there is a nonetiologic relationship between two psychological disorders, although the presence of one disorder affects the clinical presentation and/or the course of the second disorder. In other words, the comorbid disorder affects the presentation of the other disorder, not the risk for developing the disorder. This includes personality influencing response to treatment among patients with depression (Klein, Durbin, & Shankman, 2002).

Perhaps owing to its status as an appendix diagnosis in the DSM-IV, the impact of Depressive Personality Disorder (DPD) has scarcely been studied. The core features of DPD are excessive, negative, pessimistic beliefs about oneself, others, and the world. These are persons who characteristically display gloominess, cheerlessness, pessimism,

brooding, rumination, and dejection. The DSM-IV provisional criteria set for Depressive Personality Disorder can be found in Table 1.

Table 1. DSM-IV criteria for Depressive Personality Disorder and Dysthymic Disorder

Depressive Personality Disorder	Dysthymic Disorder
A pervasive pattern of depressive cognitions and behaviors beginning by early adulthood and present in a variety of contexts as indicated by five (or more) of the following:	Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least two years. Presence, while depressed, of two (or more) of the following:
(1) usual mood is dominated by dejection, gloominess, cheerlessness, joylessness, unhappiness;	(1) poor appetite or overeating
(2) self-concept centers around beliefs of inadequacy, worthlessness, and low self-esteem;	(2) insomnia or hypersomnia
(3) is critical, blaming, and derogatory toward self;	(3) low self-esteem
(4) is brooding and given to worry;	(4) poor concentration or difficulty making choices
(5) is negativistic, critical, and judgmental toward others;	(5) feelings of hopelessness
(6) is pessimistic;	
(7) is prone to feeling guilty or remorseful.	

Although there is a dearth of treatment outcome data, several papers have investigated the role of DPD and its relationship to depressive disorders (Ryder, Bagby, & Schuller, 2002; Ouimette, Klein, & Pepper, 1996; Huprich, 2001; Klein, 1990). It has been posited that DPD may represent the characterologic core of depression, particularly in patients with chronic forms of depression (Ryder et al., 2002). Support for this notion is provided by recent family-genetic studies (Klein, 1999; Klein, Riso, & Donaldson, 1995). Much of this has been the focus of work done by Klein and colleagues (Klein, 1990; Klein & Miller, 1993). This group has demonstrated an increased rate of mood disorders among first-degree relatives of patients with DPD. Conversely, there is evidence of an increased rate of DPD in the relatives of patients with Major Depressive Disorder (MDD) and early-onset Dysthymic Disorder. In one study, adolescents and young adult offspring of parents with MDD had significantly higher rates of depressive personality than offspring of medical and normal controls (Klein, Clark, & Dansky, 1988) More recently, it was found that relatives of patients with Dysthymic Disorder exhibited a significantly higher rate of depressive personality as compared to the relatives of normal controls (Klein, 1999).

There has been large debate about whether Depressive Personality Disorder can be adequately distinguished from Dysthymic Disorder (Hirschfeld & Holzer, 1994; Clark & Watson, 1999; Bagby & Ryder, 1999; Huprich, 2001). This is because the DSM-IV diagnostic criteria significantly overlap, leading to questions about whether DPD should be conceptualized as a distinct entity (Table 1). Although some investigators posit that DPD cannot adequately be distinguished from Dysthymic Disorder, a field trial by the DSM-IV Mood Disorders Work Group indicated that many patients meet criteria for

DPD but not Dysthymic Disorder (Phillips, Hirschfeld, & Shea, 1995; Widiger, 1999). Conversely, patients with more affective symptoms meet criteria for Dysthymic Disorder but not DPD. Nevertheless, additional research is needed to differentiate between the two disorders and to determine whether DPD is best conceptualized as a personality disorder or an affective disorder.

Given the data on the effects of personality disorders on treatment outcome among patients with depression and evidence of the validity of DPD, we predicted that DPD would have a negative impact on treatment response. Thus, the poor response rates among chronically depressed patients with DPD may represent the difficulty of treating or changing entrenched personality traits. Moreover, this notion fits particularly well with the Papakostas (2003) data which found that Avoidant Personality Disorder was a strong negative predictor of response to treatment. Conversely, if chronically depressed patients with and without DPD are not distinguishable in terms of treatment outcome, this would argue against DPD as a distinct diagnostic category and its usefulness as a prognostic indicator in treatment. To date, there are only scant data on the impact of DPD on treatment outcome among patients with chronic depression. The only data relevant to this issue looked at length of treatment and found that patients with Depressive Personality Disorder spent a mean of 63 months in psychotherapy, which was more than twice as long as other patients with mild but chronic depression (Phillips et al., 1998). Thus, consistent with the National Institute on Mental Health directions for future research on depression vulnerability and resilience, additional research is needed on personality in order to better understand outcomes and interventions intended to improve them (NIMH, Basic Behavioral Science Research for Mental Health, 1995).

Specific Aims:

Our clinical and empirical understanding of depression suggests that effective treatments are imperative to the amelioration of symptoms and to improve quality of life. However, establishing treatment efficacy is more difficult for chronic forms of depression, thus necessitating additional work with this population. Based on past research demonstrating the impact of Axis-II comorbidity on treatment outcome, it is expected that chronically depressed patients with comorbid Depressive Personality Disorder will respond less well to treatment, regardless of modality, than patients without Depressive Personality Disorder. It is also expected that DPD patients receiving mono-treatment (drug alone or psychotherapy alone) will respond less well than DPD patients receiving combination treatment. This is primarily because DPD is defined by cognitive symptoms, and to a lesser extent affective symptoms, thus a cognitive and social skills intervention coupled with pharmacology may provide the most optimum treatment. Additionally, this was the pattern of results found in the larger treatment trial (Keller et al., 2000). Since the symptom criteria for DPD are primarily cognitive, it is also expected that addressing cognition and social problem solving through psychotherapy will achieve a better treatment response than through a physiologically based intervention (drug alone).

This study also aims to add information to the existing debate concerning the nature of Depressive Personality Disorder. Demonstrating the prognostic value of DPD in the treatment of chronic depression would argue for moving DPD from the appendix to Axis-II as a bona-fide personality disorder in the next version of the DSM. The proposed

study will address these issues through a re-analysis of a recent, large trial of 681 chronically depressed patients (Keller et al., 2000).

Primary Aim: The aim of this investigation is to determine whether the presence of Depressive Personality Disorder will moderate treatment outcome among patients with chronic forms of depression.

Primary Hypothesis: Patients with chronic depression and a comorbid diagnosis of Depressive Personality Disorder (DPD) will be less likely to respond to medication, psychotherapy, or combination treatment compared to patients without comorbid Depressive Personality Disorder. Specifically, DPD patients will have a significantly poorer response than non-DPD patients to 3 treatment types:

(1) 12 weeks of treatment with nefazadone (200-600mg flexible dose/daily)

(2) 12 weeks of treatment with Cognitive Behavioral-Analysis System of Psychotherapy (CBASP)(semi-weekly sessions during weeks 1-4, and weekly sessions during weeks 5-12)

(3) 12 weeks of combination treatment (Nefazadone + CBASP)

Based on the above hypothesis, we expect to find a significant main effect for DPD group, with DPD patients showing a significantly poorer response to treatment at week 12 and at last observation carried forward (LOCF) than non-DPD patients across treatment types, as measured by the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1967). We also expect a significant main effect for treatment type (Keller et al., 2000, reported a statistically significant difference between combination treatment

and both mono-treatments. There was not a significant difference between mono-treatments). We also expect to find a significant interaction between DPD group and treatment type, with DPD patients in the combination arm performing better than DPD patients in either mono-treatment group in terms of treatment outcome at week 12 and LOCF. Moreover, we expect that DPD patients receiving psychotherapy alone will respond better than DPD patients receiving nefazodone alone.

Methods

Participants

The present study represents a follow-up analysis to a larger trial for the treatment of chronic depression. This study was previously described in detail by Keller and colleagues (Keller et al., 2000). In the larger trial, outpatients from 12 academic centers were screened for inclusion in this study. All eligible subjects met criteria for one of the following forms of chronic depression:

a) Chronic Major Depression (continuous episode of MDD for 2 years), or
b) Major Depressive Disorder, Single Episode, superimposed on antecedent Dysthymic Disorder, or
c) Recurrent Major Depressive Disorder with incomplete interepisode recovery (total continuous illness duration is 2 years and the patient is currently in an episode of Major Depressive Disorder).

Diagnoses were made according to criteria set forth in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (APA, 2000), and obtained using the Structured Clinical Interview for Axis I DSM-IV Disorders (SCID) (First, Spitzer, &

Gibbon, 1995). In addition to the diagnostic criteria for chronic depression, several other conditions were met for patient eligibility (Table 2).

Procedures

The institutional review board at each site approved the study prior to enrolling subjects. No study specific procedures were conducted until written informed consent was obtained. Patients underwent a preliminary screening for eligibility according to inclusion/exclusion criteria (Table 2). Six hundred eighty one (n=681) patients who remained eligible at the end of a two week evaluation period were randomized in a 1:1:1 ratio for twelve weeks of treatment with nefazadone (n=226), Cognitive Behavioral-Analysis System of Psychotherapy (CBASP) (n=228), or combination treatment (n=227).

Nefazodone: Nefazodone hydrochloride is a synthetically derived phenylpiperazine antidepressant. It is considered a mixed serotonin antagonist reuptake inhibitor, with both serotonin and norepinephrine transporter inhibition as well as antagonism of 5-HT_{2A} and alpha-1-receptors. Nefazodone has demonstrated efficacy in placebo-controlled trials and in numerous double-blind trials of short-term treatment of Major Depressive Disorder (Garlow, Owens, & Nemeroff, 2000). Nefazodone was selected for this trial because, unlike other newer agents, it lacks troublesome side effects, particularly weight gain and sexual dysfunction.

CBASP (McCullough, 1984): The Cognitive Behavioral Analysis System of Psychotherapy (CBASP) was specifically designed to target the pathological characteristics of chronically depressed patients, and has shown promising results in a small, open trial (McCullough, 1991). At present, it is the only therapy model developed specifically for the treatment of chronic depression. This approach was developed by

Table 2. Criteria for study eligibility

Inclusion Criteria

a. Written informed consent.
b. Men or women aged 18-85 years old
c. A score of $\geq$ 20 on the Hamilton Rating Scale for Depression (HRSD)

Exclusion Criteria

a. Pregnant women or women of child bearing potential who are not using a medically accepted means of contraception.
b. Unstable medical illness including cardiovascular, hepatic, renal, respiratory, endocrine, neurologic, or hematologic disease.
c. Clinical or laboratory evidence of hypothyroidism.
d. Uncontrolled seizure disorder.
e. The following DSM-IV diagnoses: 1) organic mental disorders; 2) substance use disorders, including alcohol, active within the last year or patients with a positive urine drug screen; 3) schizophrenia; 4) delusional disorder; 5) psychotic disorders; 6) bipolar disorder; 7) bereavement; 8) adjustment disorder; 9) antisocial personality disorder; 10) panic disorder, social phobia, GAD or OCD.
f. Patients with psychotic features.
g. Patients who are a serious suicide or homicide risk.
h. Current use of other psychotropic drugs.
i. Patients who have been on a course of Nefazadone during the current episode.
j. Patients previously intolerant to Nefazadone or non-responsive to at least 12-weeks of cognitive-behavioral psychotherapy.
k. Patients currently in psychotherapy.
l. Patients who have taken an investigational psychotropic drug within the last year.
m. Patients with a positive toxicology screen.

(Keller et al., 2000)

McCullough and colleagues who suggest that chronically depressed patients are perceptually disconnected from the environment such that behavioral consequences cannot inform behavior. Piagetian preoperational functioning in the social-interpersonal arena maintains the disorder and causes cognitive-emotional-behavioral patterns to remain on an immature level.

In psychotherapy, patients are taught that their interpersonal behavior has specific consequences and, in learning to recognize what these consequences are, patients become perceptually reconnected to their environment and open to feedback from others. This is achieved through three primary techniques: Situational Analysis, the Interpersonal Discrimination Exercise, and in-session Behavioral Skill Training/Rehearsal. In Situational Analysis, the therapist directs the patient's attention to the effect his/her behavior is having upon others, and teaches the individual how his/her interpersonal behavior is affecting the therapist. The Interpersonal Discrimination Exercise shows patients how the therapist differs in comparative ways to maltreating significant others in the individual's life. Behavioral Skill Training/Rehearsal exposes the patient's behavioral deficits. Patients learn to inhibit reflexive, hostile reactions and, instead of reacting impulsively, to wait and see how the situation unfolds and then to react with less affect. Through practice, patients are able to gain control of their emotional outbursts and, thus, achieve a more desirable outcome. A more detailed description of CBASP procedures can be found elsewhere (McCullough, 2003).

Patients randomized to the nefazadone group (n= 226) began an initial dose of 200mg/day (100mg twice a day), with an increase to 300mg/day during the second week. Thereafter, the dose increased in weekly increments of 100mg, to a maximum daily

dosage of 600mg. Patients were tapered down to a minimum of 300mg/day if intolerable side effects occurred. Patients who required a taper below 300mg/day were terminated from the study and referred to appropriate aftercare. Patients randomized to nefazadone were seen once weekly for 12 weeks. Visits for medication were limited to 15 to 20 minutes, and psychopharmacologists were not permitted to make formal psychotherapeutic interventions.

Patients randomized to the Cognitive Behavioral-Analysis System of Psychotherapy (CBASP) group (n=228) had semi-weekly sessions during weeks 1-4, and weekly sessions during weeks 5-12. All psychotherapists (Ph.D. or MD degree required) attended a two day training workshop and met the criteria for mastery of treatment procedures involved in CBASP, as assessed by evaluation of performance during two videotaped pilot cases. All psychotherapy cases were videotaped and reviewed weekly by supervisors.

Patients randomized to the combination treatment group (nefazadone + CBASP) (n=227) had twice weekly CBASP sessions during weeks 1-4, and weekly sessions during weeks 5-12. These patients also began an initial regimen of nefazadone 200mg/day, and increased to 300mg/day during the second week. Thereafter, dose was increase 100mg/day, to a maximum daily dosage of 600mg. Patients were tapered down to a minimum of 300mg/day if intolerable side effects occurred. Patients who needed to be tapered below 300mg/day were terminated from the study and referred to appropriate aftercare.

Measures

Diagnosis of chronic depression was assessed using the Structured Clinical Interview for DSM-IV Axis-I Disorders: Patient Edition (SCID-I/P) (First et al., 1995). Several studies have demonstrated superior reliability and validity of the SCID (Williams, Gibbon, & First, 1992; Skre, Onstad, Torgersen, & Kringlen, 1991; Zanarini & Frankenberg, 2001; Zanarini, Skodol, & Bender, 2000, Basco, Bostic, & Davies, 2000, Kranzler, Kadden, & Babor, 1996; Shear, Greeno, & Kang, 2000; Steiner, Tebes, & Sledge, 1995). This clinician-rated SCID proceeds by modules to the different DSM-IV Axis I disorders. Answers are generally rated on a scale of 1-3 (1= doubtful, 2= probable/subthreshold, 3= definite/ symptom endorsed), and based on the number of positive answers, a diagnosis is determined. This measure was administered at the screening visit to confirm or rule out a diagnosis of chronic depression.

To determine the presence or absence of Depressive Personality Disorder, the Structured Clinical Interview for DSM-IV Axis-II Personality Disorders (SCID-II) (First, Gibbon, & Spitzer, 1997) was employed. High reliability and validity of the SCID-II have been demonstrated in several studies (First, Spitzer, & Gibbon, 1995; Dreessen & Arntz, 1998; Maffei, Fossati, & Agostoni, 1997; Weiss, Najavits, & Muenz, 1995; Skodol, Rosnick, & Kellman, 1988). This clinician-rated SCID proceeds by modules to the different DSM-IV Axis II disorders. Answers are generally rated on a scale of 1-3 (1=doubtful, 2=probable/subthreshold, 3=definite/symptom endorsed), and based on the number of positive answers, a diagnosis is determined. This measure was also administered at the screening visit to confirm or rule out a diagnosis of a DPD.

Depression severity was rated by the Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1967). The HRSD is the most widely studied instrument for depression, and its reliability and validity are high (Schwab, Bialon, & Holzer, 1967). This instrument was completed by the clinician, based on his/her assessment of the patient's depressive symptoms. The HRSD quantifies the degree of depression in patients who already have a diagnosis of depressive disorder. Questions focus on depressive symptoms experienced over the past 7 days. The HRSD is a useful tool for measuring the progress of a patient during the course of treatment. Answers to questions are rated on a scale of 0-4 or 0-2, with higher scores indicating more severe pathology. This measure was administered at screen and baseline to determine patient eligibility, and subsequently at each clinic visit for enrolled patients to determine changes in depression symptom severity over 12 weeks.

Results

Prior to conducting statistical analyses, the data were examined for missing cases for the HRSD baseline, HRSD week 12, and HRSD last observation carried forward (LOCF) variables. Patients with incomplete or missing data for any of these variables were discarded from the analysis. Complete HRSD baseline data included 681 patients (n=681). The primary analyses were based on 484 patients with week 12 HRSD scores, and secondary analyses were conducted on 647 patients.

Because this sample was selected from a clinical population of chronically depressed individuals and not from a normal population, HRSD baseline, HRSD week 12, and HRSD LOCF distributions were examined for problematic skew. Frequency distribution tables and histograms were created to assess the shape of each distribution

and detect skew. Problematic skew was further defined as a skew statistic > 1.96. Because all three variables revealed positive skew, the data were transformed using a square root transformation in an attempt to improve normality. The mathematical modification did not produce a skew statistic within the range of $\pm$ 1.96, thus the original raw data were accepted for analysis. Due to restrictive entry criteria (HRSD $\geq$ 20) and a maximum rating scale total (HRSD = 70), outliers were not found.

Potential confounds for this population have been identified based on previous literature (Klein & Santiago, 2003). The effects of age, gender, race, marital status and depression severity were intercorrelated and individually correlated with the dependent measures (HRSD week 12, HRSD LOCF) to determine influence on treatment outcome. Depression severity at baseline (HRSD) was significantly correlated with both HRSD week 12 and HRSD LOCF ($r=.121$, $p <.01$, $r=.185$, $p <.01$), as was race ($r=.092$, $p < .05$, $r=.112$, $p <.01$). When the baseline data are highly correlated with the endpoint data, the reliability of change scores is significantly problematic (Lord, 1956). Therefore, difference scores were not used as a dependent measure. While age, gender, and marital status did not significantly correlate with either outcome variable, previous literature suggests they may account for some variance in the model (Klein & Santiago, 2003). Thus the effects of all potential confounds, including age, gender, race, marital status, and depression severity at baseline were entered as covariates to statistically control for their effects in the first step of the regression model. Additionally, the effects of other comorbid personality disorders, other than DPD, were controlled for in order to best isolate the unique effects of depressive personality. The full correlation matrix can be found in Table 3.

Table 3: Correlations (Pearson r)

	hrsd.1	hrsd.9	hrsd.bas	gender	race	age	mstatu
hrsd.12	----	**.917****	**.121****	-.005	**.092***	.005	-.044
hrsd.99	**.917****	---	**.185****	.031	**.122****	-.017	-.021
hrsd.bas	**.121****	**.185****	----	**.104****	.013	.010	-.003
gender	-.005	.031	**.104****	----	.008	.033	.015
race	**.092***	**.122****	.013	.008	----	-.026	**.075***
age	.005	-.017	.010	.033	-.026	----	**.180****
mstatus	-.044	-.021	-.003	.015	**.075***	**.180****	----

* p < .05, ** p< .01

Note.

hrsd.12 = Hamilton Rating Scale for Depression at week 12
hrsd.99 = Hamilton Rating Scale for Depression at LOCF
hrsd.base = Hamilton Rating Scale for Depression at baseline
mstatus = marital status
The cell sizes vary slightly due to missing data.

Nearly two-thirds of the sample was female with a mean age in the early forties. The great majority of the sample was Caucasian with less than ten percent being Black, Asian, Hispanic or other racial or ethnic background. With respect to marital status, most patients were married, single, or divorced, while less than twelve percent of the sample reported being separated, widowed, or living together with someone. (Table 4).

To prepare to test the primary hypothesis, patient data was split into those patients meeting criteria for a comorbid diagnosis of Depressive Personality Disorder and those patients not meeting criteria for a comorbid diagnosis of Depressive Personality Disorder. Of the 681 total patients, information on the presence or absence of DPD was not available for 1 case. This case was discarded, reducing the sample to 680 (n=243 with DPD, n=437 without DPD). Categorical variables (gender, race, marital status) were analyzed using chi-square and continuous variables (age, HRSD baseline) were analyzed using independent sample t-tests. Preliminary analysis found no statistical differences between groups, suggesting that they were highly similar with respect to basic clinical and demographic characteristics. In terms of other Axis-II comorbidity, 79% of patients with DPD (n=193) had an additional Axis-II diagnosis as compared to 27% of patients without DPD (n=117). This difference was statistically significant (X^2 (1) = 55.347, $p<.001$). Comparisons on demographic and clinical data for those with versus without DPD can be found in Table 5. No statistically significant differences were found for any other clinical variable or demographic characteristic.

It was hypothesized that the presence of comorbid DPD would negatively impact response to three types of treatment for depression (grouped together), resulting in significant differences between patients with and without DPD. Treatment outcome was

Table 4: Demographics for entire sample (n=681)

Age	range: 19-74	mean: 43.3 (10.71)
Gender		
	Male	236 (34.7%)
	Female	445 (65.3%)
Race		
	White	616 (90.5%)
	Black	23 (3.4%)
	Asian	8 (1.2%)
	Hispanic	22 (3.2%)
	Other	12 (1.8%)
Marital Status		
	Single	185 (27.2%)
	Married	257 (37.7%)
	Widowed	14 (2.1%)
	Divorced	160 (23.5%)
	Separated	31 (4.6%)
	Living with someone	34 (5.0%)

Table 5: Demographic and Clinical Characteristics

		DPD (n=243)	**no DPD** (n=437)
Baseline HRSD		mean: 27.92 SD: 5.23	mean: 26.24 SD: 4.75
Comorbid PD		193 (79%)	117 (27%)*
	Avoidant	108 (44%)	60 (14%)
	Dependent	8 (3%)	2 (0.5%)
	OCPD	50 (21%)	45 (10%)
	Schizotypal	0 (0%)	0 (0%)
	Borderline	27 (11%)	9 (2%)
Age		range: 19-72 mean: 45.5	range: 20-74 mean: 47
Gender			
	Male	92 (37.9%)	143 (32.7%)
	Female	151 (62.1%)	294 (67.3%)
Race			
	White	220 (90.5%)	396 (90.6%)
	Black	9 (3.7%)	14 (3.2%)
	Asian	2 (0.8%)	6 (1.4%)
	Hispanic	8 (1.2%)	14 (3.2%)
	Other	4 (1.6%)	7 (1.6%)
Marital Status			
	Single	73 (30%)	112 (25.6%)
	Married	99 (40.7%)	158 (36.2%)
	Widowed	2 (0.8%)	12 (2.7%)
	Divorced	45 (18.5%)	114 (26.1%)
	Separated	13 (5.3%)	18 (4.1%)
	Living with someone	11 (4.5%)	23 (5.3%)

* $p < .001$

Note.
HRSD = Hamilton Rating Scale for Depression
SD = standard deviation
DPD = Depressive Personality Disorder
PD = personality disorder
OCPD = Obsessive Compulsive Personality Disorder

measured using HRSD week 12 completer data (Table 6). It was further hypothesized that the presence of comorbid DPD would negatively impact response to treatment within each treatment arm separately. As mentioned previously, HRSD week 12 completer data was the primary outcome measure. These hypotheses were simultaneously tested using a mixed 2 x 3 factorial ANCOVA design. This analysis was repeated using an alternate outcome variable, HRSD last observation carried forward (LOCF) (baseline + at least one additional treatment visit)(Table 7).

Results of the primary analysis found no significant main effect for DPD, suggesting that there is not a significant difference between patients with comorbid DPD and patients without comorbid DPD in terms of treatment outcome at week 12 ($F(2,469) = 0.151$, $p = .860$) (Figure 1). As expected, there was a significant main effect for treatment group (published previously in Keller et al., 2000). Results from the original study revealed a significant difference between combination treatment and both monotherapies, with combination treatment reducing depression severity at week 12 significantly more than either therapy alone ($F(2,469) = 9.409$, $p = .00$). There was no significant difference detected between drug alone and psychotherapy alone. Further, there was no significant interaction between DPD and treatment group, which suggests that treatment outcome among patients with and without DPD is not significantly different depending upon treatment type ($F(4,469) = 0.612$, $p = .654$) (Figure 2, 3, 4, 5; Table 8). When re-analyzed without controlling for the effects of other personality disorders, the overall statistical outcomes remained the same. Therefore, the hypothesis that patients with a comorbid diagnosis of DPD would differentially respond to treatment, as a whole and/or within each treatment arm, was not supported. Thus, in this sample,

Table 6: Descriptive Data for HRSD Outcome at Week 12

		n	Mean HRSD	SD
Overall (n=484)				
	No DPD	316 (65%)	12.91	8.76
	DPD	168 (35%)	13.07	9.70
Nefazodone (n=154)				
	No DPD	97 (63%)	14.39	8.66
	DPD	57 (37%)	15.00	10.59
Psychotherapy (CBASP) (n=157)				
	No DPD	104 (66%)	14.79	9.27
	DPD	53 (34%)	14.51	10.68
Combination (n=173)				
	No DPD	115 (66%)	9.79	7.47
	DPD	58 (34%)	9.84	6.73

Note.
HRSD = Hamilton Rating Scale for Depression
SD = standard deviation
DPD = Depressive Personality Disorder
CBASP = Cognitive Behavioral Analysis System of Psychotherapy

Table 7: Descriptive Data for HRSD Outcome at Last Observation Carried Forward

	n	Mean HRSD	SD
Overall (n=647)			
No DPD	412 (64%)	14.01	9.48
DPD	235 (36%)	14.43	10.35
Nefazodone (n=214)			
No DPD	132 (62%)	15.11	9.31
DPD	82 (38%)	16.72	10.83
Psychotherapy (CBASP) (n=215)			
No DPD	140 (65%)	15.54	9.51
DPD	75 (35%)	16.16	10.81
Combination (n=218)			
No DPD	140 (64%)	11.29	9.09
DPD	78 (36%)	10.35	8.02

Note.
HRSD = Hamilton Rating Scale for Depression
SD = standard deviation
DPD = Depressive Personality Disorder
CBASP = Cognitive Behavioral Analysis System of Psychotherapy

Table 8: Summary of 2 x 3 factorial ANCOVA for DPD at week 12

Variable	df	F	partial η^2
HRSD baseline	1	9.958**	.021
Race	1	2.697	.006
Age	1	.169	.000
Gender	1	.127	.000
Marital status	1	1.110	.002
Comorbid PD	1	3.893*	.008
Treatment group	2	9.409**	.039
DPD	2	.151	.001
Treatment group x DPD	4	.612	.005

* $p < .05$, ** $p < .01$

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression
partial η^2 = partial eta squared

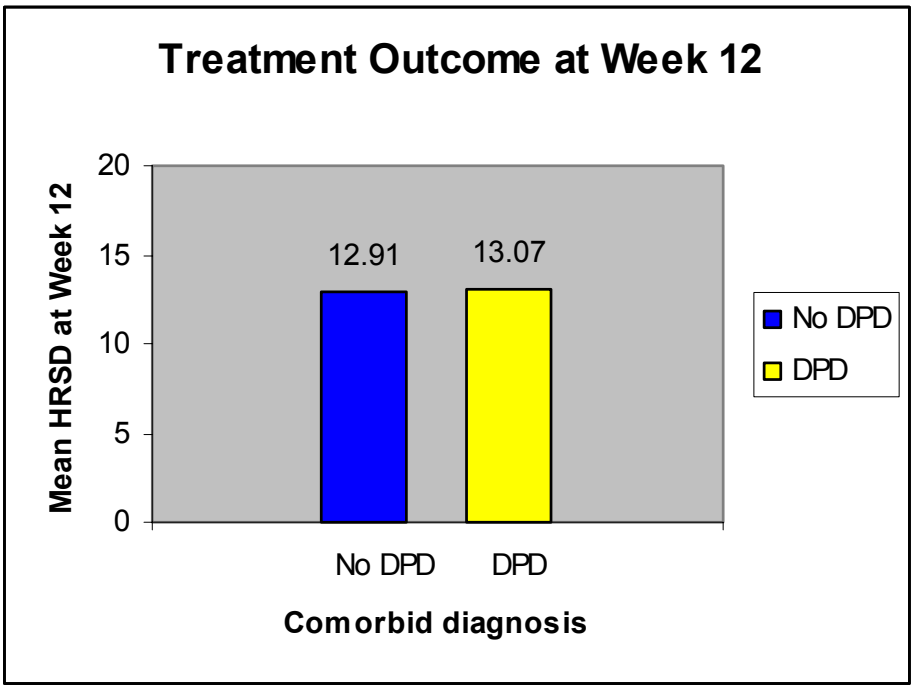

Figure 1: Treatment Outcome at Week 12 (HRSD)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

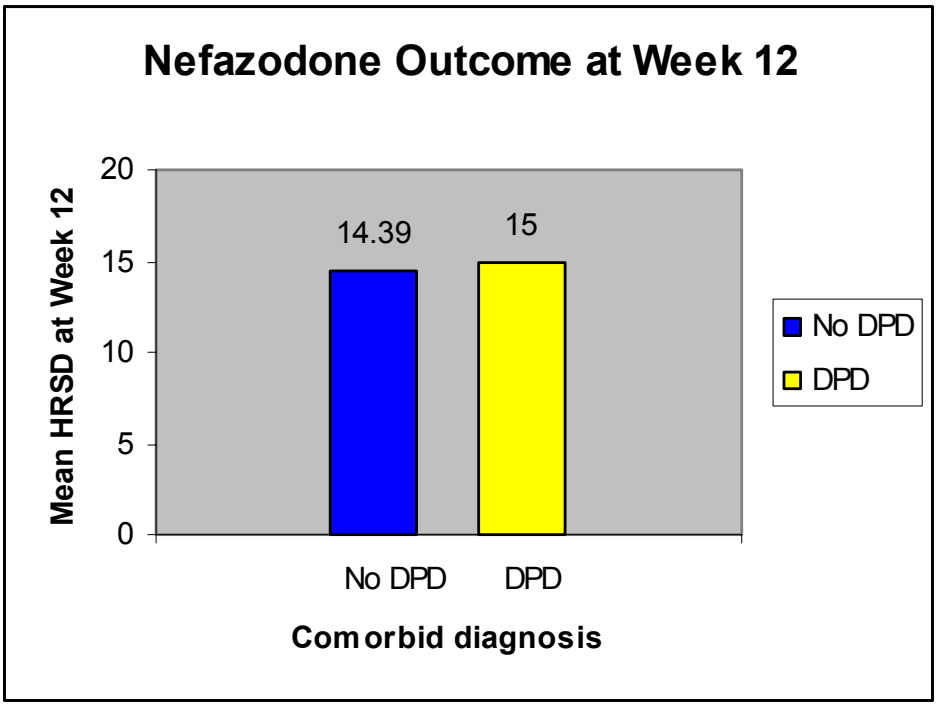

Figure 2: Nefazodone Outcome at Week 12 (HRSD)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

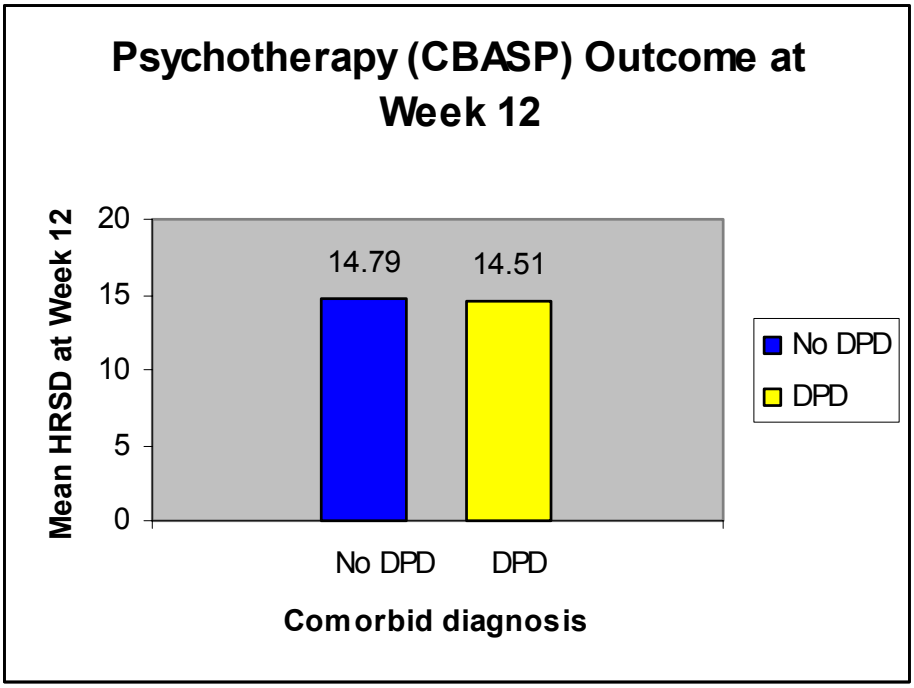

Figure 3: Psychotherapy (CBASP) Outcome at Week 12 (HRSD)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression
CBASP = Cognitive Behavioral Analysis System of Psychotherapy

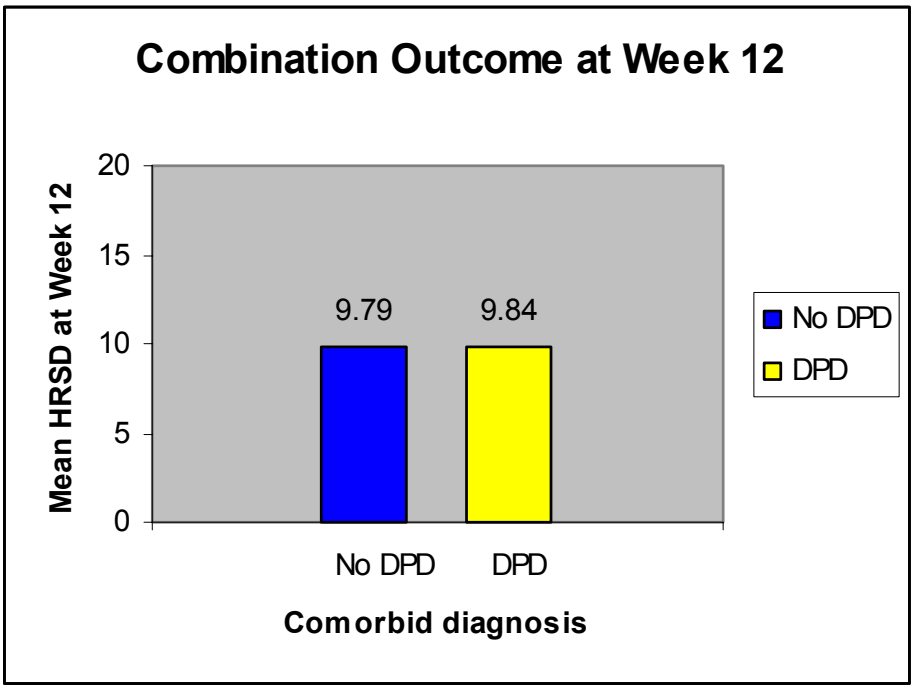

Figure 4: Combination Outcome at Week 12 (HRSD)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

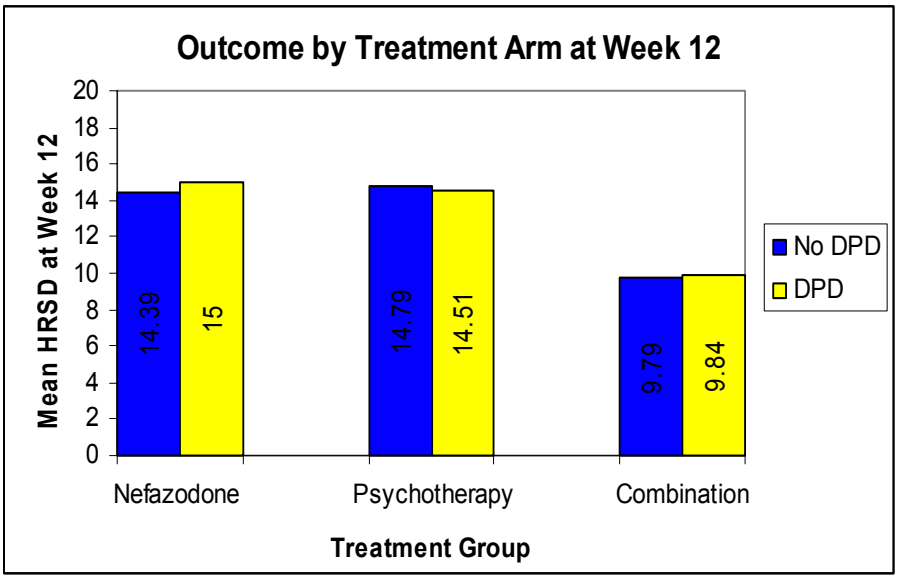

Figure 5: Outcome by Treatment Arm at Week 12

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

the presence of DPD was not a prognostic indicator of worse treatment outcome for patients with chronic depression as measured by the HRSD at week 12.

Results of the secondary analysis, in which the HRSD last observation carried forward (LOCF) was examined as the dependent measure, were similar to the primary analysis. There was no significant main effect for DPD suggesting that there is not a significant difference between patients with comorbid DPD and patients without comorbid DPD in terms of treatment outcome at LOCF ($F(2,632) = 0.073$, $p = .930$)(Figure 6). As expected, there was a significant main effect for treatment group (published previously in Keller et al., 2000). Results from the original study revealed a significant difference between combination treatment and both monotherapies, with combination treatment reducing depression severity at last observation carried forward (LOCF) significantly more than either therapy alone ($F(2,632) = 11.730$, $p = .00$). There was no significant difference detected between drug alone and psychotherapy alone. Further, there was no significant interaction between DPD and treatment group, which suggests that treatment outcome among patients with and without DPD is not significantly different depending upon treatment type ($F(4,632) = 0.477$, $p = .753$) (Figure 7, 8, 9, 10; Table 9). When re-analyzed without controlling for the effects of other personality disorders, the overall statistical outcomes remained the same. As before, the hypothesis that patients with a comorbid diagnosis of DPD would differentially respond to treatment, as a whole and/or within each treatment arm, was not supported. Thus, in this sample, the presence of DPD was not a prognostic indicator of worse treatment outcome for patients with chronic depression as measured by the HRSD last observation carried forward (LOCF).

Table 9: Summary of 2 x 3 factorial ANCOVA for DPD at LOCF

Variable	df	F	partial η^2
HRSD baseline	1	29.124**	.044
Race	1	8.621*	.013
Age	1	.033	.000
Gender	1	.316	.001
Marital status	1	.421	.001
Comorbid PD	1	1.810	.003
Treatment group	2	11.730**	.036
DPD	2	.073	.000
Treatment group x DPD	4	.477	.003

* $p < .01$, ** $p < .001$

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression
partial η^2 = partial eta squared

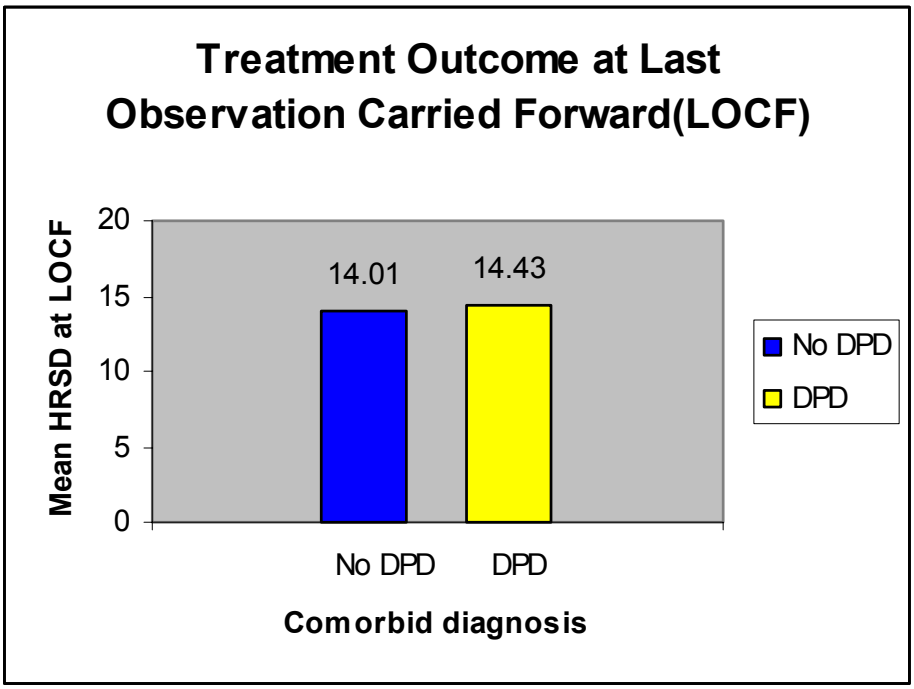

Figure 6: Treatment Outcome at LOCF (HRSD)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

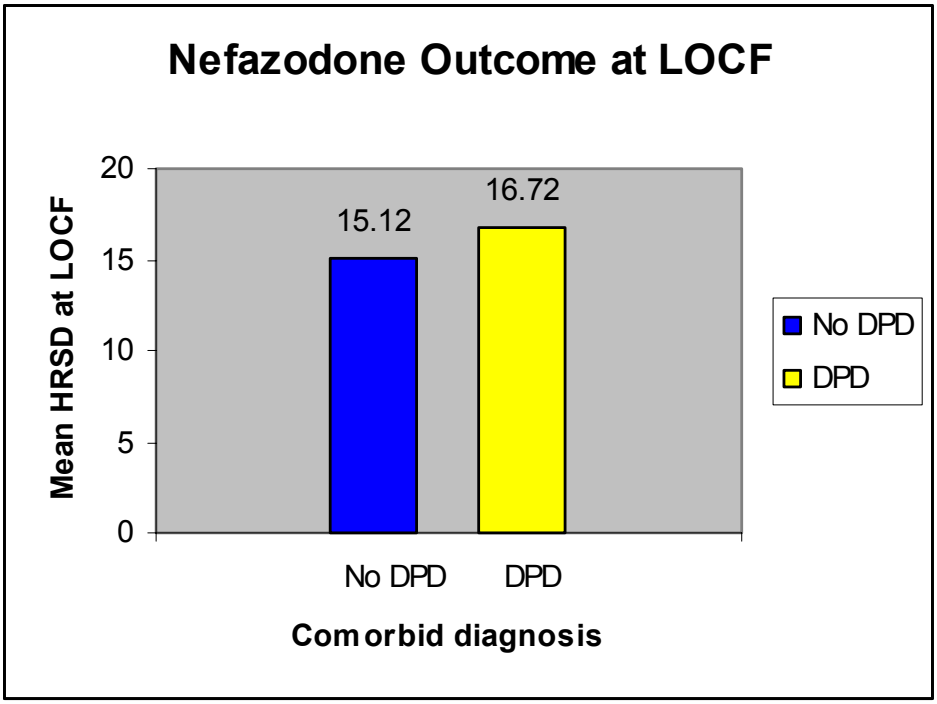

Figure 7: Nefazodone Outcome at Last Observation Carried Forward (LOCF)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

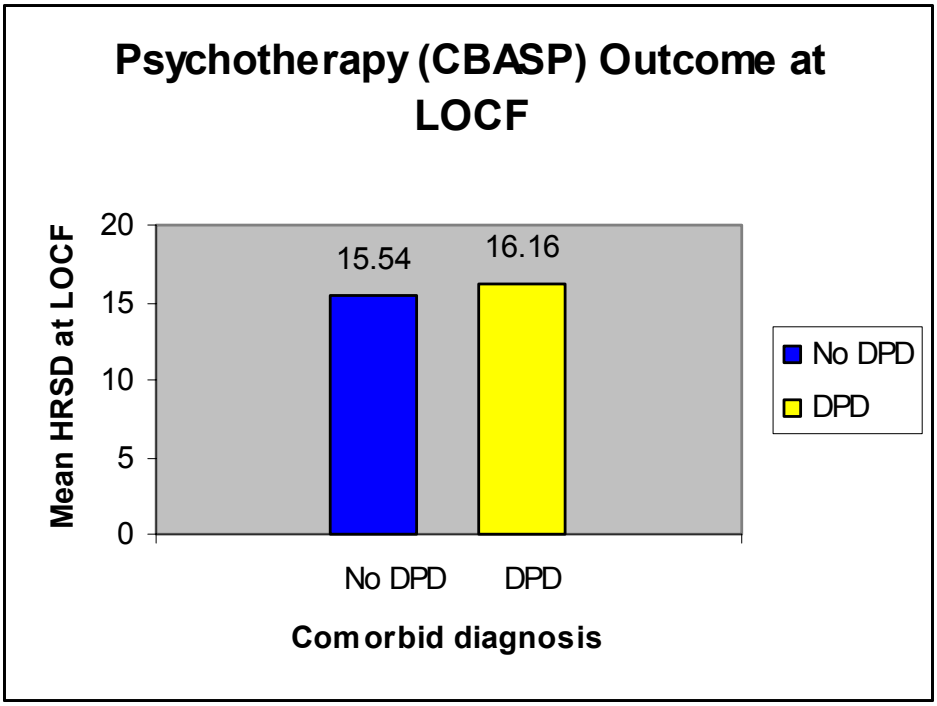

Figure 8: Psychotherapy (CBASP) Outcome at Last Observation Carried Forward (LOCF)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression
CBASP = Cognitive Behavioral Analysis System of Psychotherapy

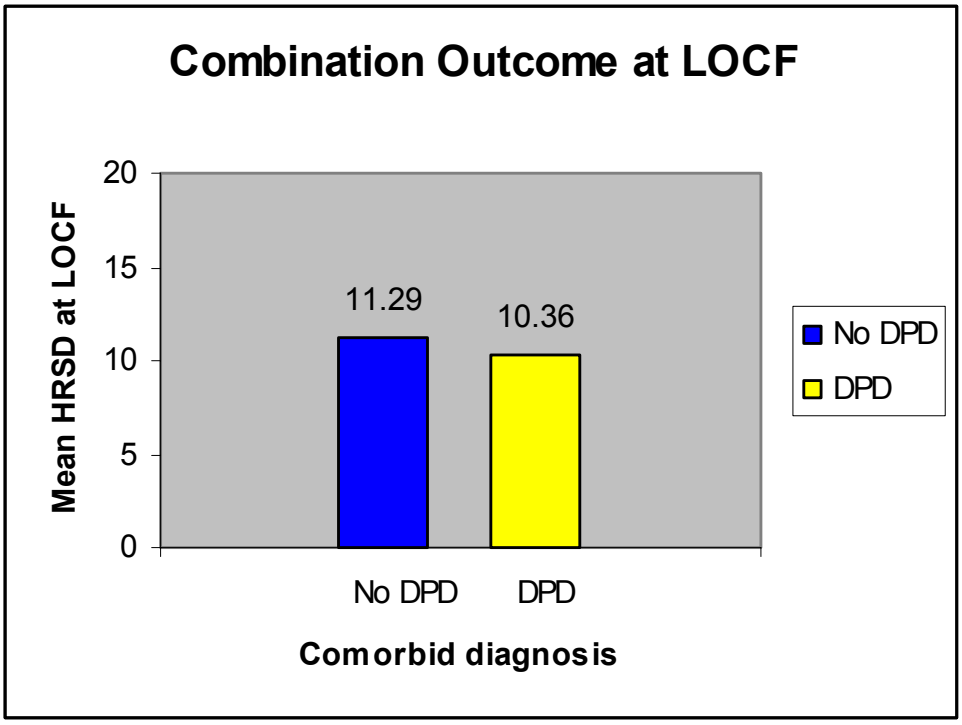

Figure 9: Combination Outcome at Last Observation Carried Forward (LOCF)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

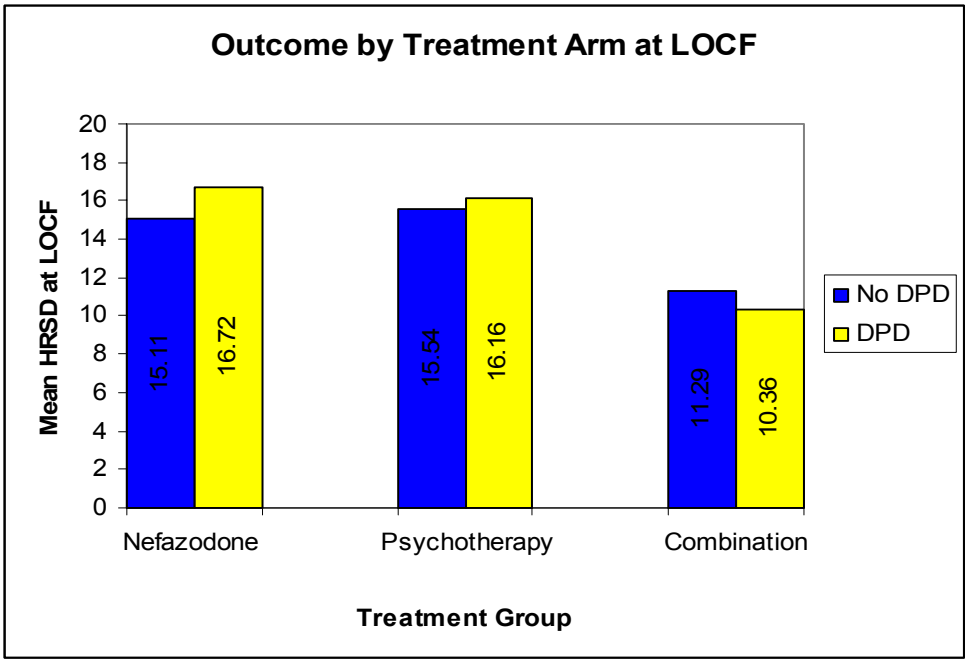

Figure 10: Outcome by Treatment Arm at Last Observation Carried Forward (LOCF)

Note.
DPD = Depressive Personality Disorder
HRSD = Hamilton Rating Scale for Depression

These unanticipated results prompted further investigation of the impact of personality disorders, other than DPD, to determine which, if any, would show differential response to treatment as suggested by the pathoplasticity model of personality and depression (Klein et al., 2002). However, small numbers of positive comorbid diagnoses for dependent personality disorder (n=10), schizotypal personality disorder (n=0), and subthreshold borderline personality disorder (n=36) prohibited analyses due to lack of power to detect effects.

A mixed 2 x 3 factorial ANCOVA was performed for Avoidant Personality Disorder (APD). Twenty five percent of patients (n=168) were positively diagnosed with comorbid APD as compared to 75% of patients (n=512) who were not. There was no significant main effect for APD suggesting that there is not a significant difference between patients with comorbid APD and patients without comorbid APD in terms of treatment outcome at week 12 (F, (2,469) = 1.215, p = .298) or at LOCF (F (2,632) = 0.243, p = .785). Likewise, there was no significant interaction between APD and treatment group for either dependent measure, which suggests that treatment outcome among patients with and without APD is not significantly different depending upon treatment type (HRSD week 12: F (4,469) = 1.298, p = .270; HRSD LOCF: F (4,632) = .577, p = .680). When re-analyzed without controlling for the effects of other personality disorders, the overall statistical outcomes remained the same. Therefore, the presence of APD was also not a prognostic indicator of worse treatment outcome for patients with chronic depression.

A mixed 2 x 3 factorial ANCOVA was also performed for Obsessive Compulsive Personality Disorder (OCPD). Fourteen percent of patients (n=95) were positively

diagnosed with comorbid OCPD as compared to 86% of patients (n=584) who were not. There was no significant main effect for OCPD, suggesting that there is not a significant difference between patients with comorbid OCPD and patients without comorbid OCPD in terms of treatment outcome at week 12 (F, (2,469) = .268, p = .765) or at LOCF (F (2,631) = 0.077, p = .926). Similarly, there was no significant interaction between OCPD and treatment group for either dependent measure, which suggests that treatment outcome among patients with and without OCPD is not significantly different depending upon treatment type (HRSD week 12: F (4,469) = .577, p = .680; HRSD LOCF: F (4,631) = .167, p = .955). When re-analyzed without controlling for the effects of other personality disorders, the overall statistical outcomes were similar. As before, the presence of OCPD was not predictive of worse treatment outcome for patients in this sample.

In a final analysis, the presence of any personality disorder, regardless of type, was examined in terms of impact on treatment outcome at week 12 and LOCF using a series of mixed 2 x 3 factorial ANCOVAs. At week 12, there was a significant main effect for personality disorder (F(1,473) = 3.894, p < .05). Contrary to our predictions, those with a personality disorder actually had lower HRSD scores at week 12. (Table 10; Figure 11). However, there was no significant interaction which demonstrates that this difference does not depend on treatment type (F(2,473) = .882, p = .415). No significant findings were revealed at LOCF.

Discussion

The fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) included a provisional set of criteria placed in Appendix B. Here, Depressive Personality Disorder (DPD) was included as a diagnostic category needing further

Table 10: Summary of 2 x 3 factorial ANCOVA for any PD at week 12

Variable	df	F	partial η^2
HRSD baseline	1	11.113*	.023
Race	1	2.567	.005
Age	1	.153	.000
Gender	1	.107	.000
Marital status	1	1.445	.003
Treatment group	2	17.677**	.070
PD	2	3.894*	.008
Treatment group x PD	4	.882	.004

* $p < .05$, ** $p < .01$

Note.
PD = Personality Disorder
HRSD = Hamilton Rating Scale for Depression
partial η^2 = partial eta squared

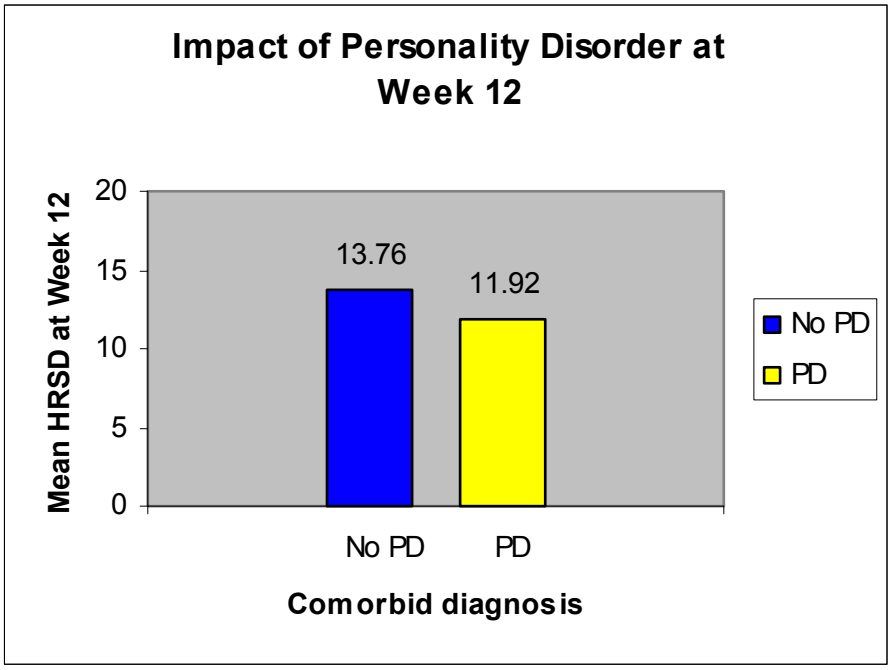

Figure 11: Impact of Personality Disorder on Treatment Outcome at week 12

Note.
PD = Personality Disorder
HRSD = Hamilton Rating Scale for Depression

evaluation. A large amount of theory has been generated on the validity of DPD which has ignited discussion about whether DPD should be allied with mood or personality disorders. However, there is little empirical literature available to aid in its evaluation.

The primary aim of this research was to determine whether patients with chronic depression and a comorbid diagnosis of DPD would respond differentially to three treatment types as compared to chronic patients without comorbid DPD. This aim has implications not only for the treatment of chronic depression, but for the validity of the depressive personality diagnosis. If DPD should stymie treatment response as hypothesized, this would bolster support for this diagnosis which is awaiting further data.

Results of these analyses indicated that the presence of DPD did not moderate treatment outcome at week 12 or at last observation carried forward (LOCF) as predicted. This was the case both for treatment as a whole as well as within each treatment arm individually. Moreover, in a series of ancillary analyses, neither comorbid Avoidant Personality Disorder (APD) or comorbid Obsessive Compulsive Personality Disorder (OCPD) served as a prognostic indicator of worse treatment outcome at week 12 or LOCF. Taken together, these findings suggest that comorbid personality abnormalities may not be a clinically useful indicator of worse treatment outcome, at least among patients with chronic forms of depression in this sample. Notably, in one analysis, the presence of any one personality disorder actually predicted a better response after 12 weeks of treatment with either nefazodone, targeted psychotherapy, or combination treatment.

One explanation for this result may lie in the findings of other empirical work examining treatment effects for personality disorders. Several investigators have found

that antidepressants may be helpful in the treatment of personality disorders regardless of change in depression (Fava, Farabaugh, Sickinger, Wright, Alpert, Sonawalla, Nierenberg, & Worthington, 2002; Kapfhammer & Hippius, 1998; Markovitz, Calabrese, Schultz, & Meltzer, 1991). Treatment, in any modality, may be accompanied by significant changes in behaviors and attitudes that are a part of personality disorders and independent of changes in depression severity. In this study, psychotherapy (CBASP) was designed specifically to target such issues. Moreover, Shea and colleagues have suggested that the added distress of depression among patients with personality disorders may actually serve as a motivator to comply with treatment and modify the behaviors that contribute to their difficulties (Shea et al., 1992).

Another possibility is that patients with personality disorders may have had a different illness than patients without personality disorders. Those with the comorbid conditions may have a form of depression that is secondary to the personality disorder and more amenable to clinical intervention. On the other hand, those with a primary diagnosis of chronic depression that was not secondary to a personality disturbance maybe more refractory. Finally, there is also the possibility that those with a personality disorder were more likely to negatively distort the reports of their history of depression and, in fact, did not have as severe a mood disturbance as the pure, chronically depressed group.

While the pathoplasticity model of personality and depression may predict that DPD would negatively impact treatment response as compared to patients without the comorbid diagnosis, there is also a body of literature to suggest that the presence of comorbid personality disorders does not influence response to treatment (Fava et al.,

1994; Newman et al., 2000). Thus, the results from this research lend support to this evidence base. However, it is important to note that there is a relative dearth of empirical information pertaining to treatment outcomes among patients with chronic forms of depression and comorbid personality disorders. The majority of published studies which have examined the impact of personality disorders have been performed on samples of acutely depressed patients (McDermut & Zimmerman, 1998; Sato et al., 1994; Shea et al., 1992; Shea et al., 1990). As distinguished earlier in the paper, chronic forms of depression may represent a distinct subset of patients. Thus, it is important to consider that the pathoplastic effects of personality disorders may not apply to persistent, severe forms of depression.

Secondly, it is possible that the chronic and severe nature of this sample led to mood state effects on the assessment of personality disorder. That is, ratings of personality disorders could have been distorted by the depressive episode. Thus, personality abnormalities may be concomitant with chronic depression and return only to nonsymptomatic levels after recovery (Klien et al., 2002). As discussed by Klein and colleagues, mood state effects are particularly problematic when trying to disentangle comorbid diagnoses. It is complicated to determine whether the comorbid problem is a consequence of the mood state or if it existed as an independent, pre-morbid condition. In the former case, it would make sense that the alleviation of mood symptoms would also alleviate other comorbid symptoms, such as those recognized and diagnosed as personality disorders. If it were the case that the personality abnormality existed outside of the depressive episode, then treatment for the mood disorder would not be expected to ameliorate the pre-morbid personality symptoms. In our sample, it was unknown

whether or not the symptoms of depressive personality existed prior to, and/or were independent of, the depressive episode. The results of this study, interestingly, suggest that whether or not the personality disorder was pre-morbid or existed as a consequence of mood state, treatment of the mood disorder was not hampered by the presence of DPD or any of the other personality disorders assessed.

Third, because DPD presently resides in the appendix of the DSM-IV as a condition requiring further study, there is relatively little empirical data to determine whether or not it should be construed as a bona-fide personality disorder. Because the clinical symptomatology required for a diagnosis of DPD greatly overlap with those required to diagnose Dysthymic Disorder, there has been large debate in the recent psychological and psychiatric literature about the validity of DPD as a distinct condition (Hirschfeld & Holzer, 1994; Clark & Watson, 1999; Bagby & Ryder, 1999; Huprich, 2001). In this sample, DPD was considered a personality disorder which was separate from the mood episode. However, as mentioned previously, missing pre-morbid and/or post-treatment assessment prevents any reliable conclusion to be drawn about the true nature of DPD.

Strengths of the current study

There are a number of strengths of the present study that warrant recognition. First, the sample selected for this study was based on rigorous recruitment at twelve clinical sites in the United States. Not only did this large sample size include patients from diverse geographic locations, it contributed to very high-power research. Second, careful diagnoses were captured by trained clinicians using structured interviews. Such strict assessment was used both in screening patients for eligibility as well as ensuring a

high rate of inter-rater reliability and, thus, a high level of internal validity. Moreover, clinical outcomes were assessed at each clinic visit using the Hamilton Rating Scale for Depression, the mostly widely recognized instrument for detecting depressive symptomology and severity among severely depressed patients.

Third, two different outcome variables were employed for analysis in this study. Data evaluated from week 12 completer patients permitted examination of treatment outcomes among individuals who received the same course of treatment. Conversely, evaluation of patients who terminated early from the study allowed for comparisons to be made to those who completed, and to assess their differential outcomes. Further, including last observation carried forward (LOCF) data ensured that all patient data, regardless of treatment course, were considered for analysis and not discarded.

Lastly, this clinical trial was conducted using highly manualized treatment approaches. This helped guarantee consistent treatment delivery across clinical site and maximized the internal validity of the research. Further, all study clinicians assessing patients, at any time-point, were required to have a Ph.D. or M.D. degree. Psychotherapists involved in the Cognitive Behavioral System Analysis of Psychotherapy (CBASP) attended a mandatory, two day training workshop and met the criteria for mastery of treatment procedures. This was assessed through evaluation of performance during two videotaped pilot cases, and all subsequent psychotherapy cases were videotaped and reviewed weekly by supervisors.

Limitations of the current study

There are several limitations to the current research to consider. First, the demographics of the sample were overwhelmingly comprised of Caucasian individuals

(90%) and nearly two thirds (65.3%) of patients were female. Although a more racially diverse sample would improve the generalizability of the results, the gender ratio closely approximates epidemiological estimates of depression in community samples (Kessler et al., 1994; Kornstein, 1997). With respect to inclusion criteria for study entry, patients with severe borderline personality disorder and/or antisocial personality disorder were excluded, as were acutely suicidal patients. These ineligible patients may have provided important, clinically relevant data when considering a cohort of individuals with chronic depression. In addition, some Axis-II diagnoses were never assessed including paranoid, schizoid, histrionic, and narcissistic personality disorders. Thus, patients with these personality abnormalities may have been present in this sample, yet remained unaccounted for.

Secondly, inclusion criteria for the trial required the presence of "chronic" depression; however, patients with three types of depression were admitted for study: patients with a pre-existing Dysthymic Disorder and a superimposed major depressive episode, patients in a current major depressive episode, and patients with residual symptoms of depression. While all patients were similar in terms of episode course, this complicated the moderation analysis of comorbid DPD such that all primary diagnoses were amalgamated. While this is considered a limitation, it should be noted that no single definition of chronic depression exists in our current nosology; that is, the DSM-IV regards several depressions as having the longitudinal course specifier of chronicity, as opposed to one, distinct diagnosis of chronic depression.

Third, assessment of DPD was captured only at the screen and baseline visits. While this information is relevant and required for the present research, there is no way to

determine whether personality pathology existed independent of, and/or prior to, the mood episode. As mentioned previously, it is unknown whether the presence of DPD was a distinct Axis-II condition or if it was simply a concomitant mood state effect. Further, because DPD was not reassessed at treatment endpoint, it is not possible to decipher whether the symptoms of depressive personality were affected by treatment.

Future directions

The limitations of the present research have provided a number of pathways for future research. Beginning with the first limitation, it would be potentially useful to recruit subjects that are more demographically representative of the overall population. This would not only increase the external validity of the results, but would provide useful clinical data for effectively treating diverse populations.

Second, given that various personality disorders were either excluded or were not assessed, it is critical that future research aim to more carefully account for Axis-II comorbidity. Conventions should be implemented regarding the types of personality pathology that will be allowed for study, and these patients should represent a collective sub-sample. This would ensure that Axis-II pathology is captured and evaluated properly, thereby increasing the validity of the research and the conclusions that are drawn.

Third, because several types of mood disorders (double depression, chronic MDD, MDD in incomplete remission) were pooled into one group (chronic depression) based only on longitudinal course, it seems necessary and prudent to research the various types of chronic depression separately or in head-to-head comparison trials. For example, a diagnosis of “double depression” is warranted when Dysthymic Disorder has been

present for at least 2 years and is subsequently followed by a superimposed major depressive episode. This means that the original disorder is characterized by an early, insidious onset, while "MDD chronic" is a full-blown and severe mood episode, while patients with MDD in incomplete episode recovery are, presumably, in the maintenance phase of treatment. Thus, the problematic admixture of this sample may be reduced through more diagnostically homogeneous samples to allow for greater specificity in measurement, treatment, and outcome analysis associated with these various forms of depression.

Fourth, because we can draw only tentative conclusions about the impact of DPD on treatment outcome due to unavailable pre-morbid data, there is a critical need for alternate research designs such that personality and depression are adequately distinguished from one another. This is the only way to be certain that the personality disorder being studied is, in fact, a personality disorder and not a concomitant mood state bias. One way this could be tested is through cross-sectional studies of patients in remission, or through longitudinal studies assessing patients when they are in an episode and again after they have recovered. If personality abnormalities persist after remission, it would suggest that they are trait markers rather than complications of the depressed state. To our knowledge, only 2 studies have tested personality measures in depressed individuals before and after a major depressive episode. However, each of these projects aimed to examine personality traits (neuroticism/extraversion) and not personality disorders (Kendler, Neale, Kessler, Heath, & Eaves, 1993; Shea, Leon, Mueller, Solomon, Warshaw, & Keller, 1996).

Potentially useful data could also be garnered from family, twin, and adoption studies. Demonstrating that never depressed relatives of patients with mood disorders have higher levels of personality disorder than healthy relatives of controls would provide some support for personality pathology existing independent of mood state. Further support could be offered if relatives of never depressed patients with personality abnormalities had an elevated rate of mood disorders (Klein, 2002). The most compelling approach, however, is to conduct longitudinal studies of individuals with no prior history of mood disorder and trace the development and impact of personality vulnerabilities as the patient waxes and wanes through mood episodes. Thus, future research should seek to examine more closely pre-morbid personality to make certain personality pathology existed prior to the mood episode, if it is concomitantly present as a mood state effect, or if it exists as a consequence of the mood episode. If these groups could be disentangled, then followed through treatment, we would have a better idea of the clinical prognostic value of personality disorder at the time of treatment.

Conclusion

Chronic depression, in one form or another, accounts for about twenty percent of all depression (Mueller, Keller, & Leon, 1996). In all cases, including this sample, the full syndrome of major depression exists for 2 years or longer which means that these patients suffer from continuous emotional and functional impairment. Moreover, high rates of comorbid Axis-II disorders are frequently seen, thus significant adaptation is required on the part of patients and their families to cope with the illness.

Given that chronic forms of depression are often associated with personality disorders and frequently result in poorer clinical outcomes, investigation into the impact

of Axis-II disorders on treatment outcome is highly warranted. The purpose of this study was to examine the effects of DPD on treatment outcome for patients with chronic depression. In this sample, the presence of comorbid DPD did not impact response to any of the three treatment types. Moreover, the presence of Avoidant Personality Disorder and Obsessive Compulsive Personality Disorder in particular, or any of several personality disorders as a general comorbid condition, did not predict worse treatment outcome. While these empirical findings were not significant in terms of differential response to treatment, the clinical implications are highly important. That is, among patients with persistent forms of depression, a comorbid personality disorder diagnosis did not make treatment for these patients more difficult. While it is often assumed that patients with personality disorders are challenging to treat, the findings from this work suggest that they responded as well as patients without co-existing personality disorder.

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