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Pretreatment Depression Severity in Breast Cancer Patients and Its Relation to Treatment Response to Behavior Therapy

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Objective: Major depressive disorder is prevalent in breast cancer patients. There is a paucity of research on variables associated with depression severity and the link between depression severity and response to psychotherapy. To provide optimal mental health services to breast cancer patients, examining correlates of depression severity and its relation to treatment response is critical. ***Method:*** In the context of a randomized trial of behavior activation and problem-solving therapy for depressed breast cancer patients, this study evaluated demographic (marital status, age, education), psychosocial (social support, environmental reward, anxiety, number of coexistent anxiety disorders), and cancer-related (bodily pain, length of diagnosis, cancer stage) variables associated with pretreatment depression severity. Second, the relation of pretreatment depression severity with posttreatment and 12-month response and remission was assessed. ***Results:*** For pretreatment depression severity, the overall regression model accounted for 40% of the variance, $F(5, 74) = 9.87$, $p < .001$. Less environmental reward and greater somatic anxiety were significantly and uniquely associated with depression severity. Depression severity was unrelated to treatment remission but was a significant moderator of treatment response at posttreatment and 12-month follow-up; individuals with higher depression severity were more responsive to therapy. For patients treated with behavior activation, environmental reward significantly mediated the relationship between pre- and posttreatment depression. ***Conclusions:*** Consistent with behavioral models of depression, less environmental reward and greater anxiety might influence depression severity in breast cancer patients. Data support the efficacy of behavior therapy for breast cancer patients, particularly those with more severe depression.

Keywords: Behavior therapy, breast cancer, depression, depression severity, treatment response

The lifetime prevalence of major depressive disorder (MDD) is approximately 21%, and adequate treatment occurs for less than 50% of individuals with MDD (Kessler et al., 2005; Wang et al., 2005). MDD is the most common psychiatric disorder in cancer patients, with prevalence rates ranging from 8%–49% depending on cancer type, method of assessing depression, and treatment phase (Krebber et al., 2014; Massie, 2004; Mitchell et al., 2011; Walker et al., 2014). Together with pancreatic, lung, and oropharyngeal cancers, individuals with breast cancer are at high risk of developing MDD (16%–25%: Krebber et al., 2014; Mitchell et al., 2011), particularly in the first year following cancer diagnosis (Kangas, Henry, & Bryant, 2005; Krebber et al., 2014). Relative to nondepressed breast cancer patients, depressed breast cancer patients have poorer physical health, more pain and fatigue, more anxiety and substance use, poorer quality of life, marital spouses with elevated depression, impaired sexual functioning, sleep disorders, poorer immune system functioning, more rapid progression of cancer, higher levels of proinflammatory cytokines, and possibly higher mortality (Evans et al., 2005; Fortner et al., 2002; Hopko, Bell, et al., 2008; Miller, Maletic, & Raison, 2009; Mitchell, Ferguson, Gill, Paul, & Symonds, 2013; Reddick, Nanda, Campbell, Ryman, & Gaston-Johansson, 2006; Spiegel & Giese-Davis, 2003; Williamson, 2000; Young, Bruno, & Pomara, 2014). MDD also is associated with poor recovery from breast cancer treatment in that depression is linked with reduced optimism about medical interventions, maladaptive coping styles, and poorer adherence to breast cancer treatment regimens (Cohen, de Moor, & Amato, 2001; Evans et al., 2005; Miller, O'Hea, Lerner, Moon, & Foran-Tuller, 2011). Given the prevalence and correlates of MDD in individuals with breast cancer, the importance of evaluating the impact of depression severity on treatment outcome is a pressing need (Hart et al., 2012; Hopko, McIndoo, Gawrysiak, & Grasetti, 2014). Primary aims of this study were to (a) examine demographic, psychological, and cancer-related variables associated with higher depression severity in breast cancer patients, and (b) as a follow-up to a recent randomized trial of behavioral activation (BA) and problem-solving therapy (PST; Hopko et al., 2011), determine whether depression severity was associated with treatment response and remission.

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Several clinical trials have examined the efficacy of psychosocial treatments for breast cancer patients with depressive symptoms. Importantly, the overwhelming majority of these studies included breast cancer patients with subsyndromal depressive symptoms rather than patients with systematically diagnosed MDD (Hart et al., 2012; Hopko et al., 2014). As such, the extent to which positive effects of interventions extend beyond nonclinical samples toward MDD patients is unclear, the latter population being more difficult to treat (Cuijpers, Smit, Bohlmeijer, Hollon, & Anderson, 2010). Although pharmacological treatments may effectively reduce depressive symptoms (Kissane, Maj, & Sartorius, 2011), they are sometimes ineffective or potentially dangerous to use with breast cancer patients (Kelly et al., 2010; Kissane et al., 2011). Accordingly, psychological treatment options are necessary because of potentially dangerous side effects of medications, recommendations that medication is not optimal for patients with lower depression severity (Fournier et al., 2010), patient preferences for psychotherapy (Kwan, Dimidjian, & Rizvi, 2010), and accumulating evidence that a majority of breast cancer patients do not receive necessary psychological services (Jacobsen & Wagner, 2012).

A number of meta-analyses examined the efficacy of psychotherapy for breast cancer patients with depressive symptoms (Fann et al., 2008; Hart et al., 2012; Lepore & Coyne, 2006; Newell, Sanson-Fisher, & Savolainen, 2002; Williams & Dale, 2000). To summarize, interventions generally effectively reduce symptoms of depression, anxiety, and pain in breast cancer patients. Although almost exclusively incorporating samples of breast cancer patients with subsyndromal depression, the most empirically supported interventions are supportive-expressive group therapy, cognitive–behavioral therapy, BA, PST, and mindfulness-based stress reduction (Hart et al., 2012; Hopko et al., 2014). In a recent randomized trial of BA and PST in breast cancer patients with MDD (Hopko et al., 2011), across both interventions, results revealed strong treatment integrity, excellent treatment satisfaction, low attrition, and significant treatment gains across depression, anxiety, quality of life, social support, and medical outcomes (i.e., bodily pain, general health). Environmental reward, or pleasurable affective experiences based on response-contingent positive reinforcement deemed essential toward decreasing depression (Lewinsohn, 1974), also increased significantly. On the basis of response and remission criteria, 70% of patients exhibited clinically significant improvement, and treatment gains were maintained at 12-month follow-up. Pertinent to current study aims, this clinical trial did not examine factors associated with higher depression severity in breast cancer patients or whether depression severity was systematically related to treatment response.

These empirical questions are critical to explore in that cognitive–behavioral treatment outcome research for MDD is controversial in terms of whether depression severity is associated with a negative (or limited) treatment response (Driessen, Cuijpers, Hollon, & Dekker, 2010; Forand & Derubeis, 2013). Indeed, moderating effects of depression severity may be critical toward interpreting the relative efficacy of interventions. For example, in a recent randomized controlled trial comparing cognitive therapy, BA, and antidepressant medication (i.e., Paroxetine), although there were no differences across treatments for less depressed patients, the latter two interventions were more effective than cognitive therapy for severely depressed patients (Dimidjian et al., 2006). Minimal research has examined moderators of treatment outcome in cancer patients, and patient samples problematically largely consist of individuals with subsyndromal depression. This limitation noted, more social support, empathic couple-based communication, practitioner expertise, higher depression severity, shorter latency from cancer diagnosis to initiation of psychotherapy, and less severe cancer stage are associated with more favorable treatment outcome (Baucom et al., 2009; Heron-Speirs, Baken, & Harvey, 2012; Schneider et al., 2010; Tamagawa, Garland, Vaska, & Carlson, 2012; Zimmermann, Heinrichs, & Baucom, 2007). In the only studies examining predictors of BA treatment outcome in breast cancer patients with MDD, fewer coexistent anxiety disorders (Hopko, Robertson, & Colman, 2008) and greater compliance with structured activities (using the current database) were associated with positive treatment response (Ryba, Lejuez, & Hopko, 2014). Finally, being married, not being concurrently in cancer treatment, and having a history of psychotherapy were associated with positive treatment outcome (Hopko et al., 2015). Two highly significant limitations of these studies were that no assessment of variables associated with pretreatment depression severity was examined (Dobson & Dozois, 2008), and the impact of pretreatment depression severity on treatment response and remission was not evaluated (Driessen et al., 2010).

The important issue addressed in this study is that depression treatment outcome research is at a stage where it is increasingly critical to examine moderators of outcome to inform treatment selection, assess strengths and weaknesses of interventions, and examine the efficacy of psychological treatments as a function of depression severity (Driessen et al., 2010; Forand & Derubeis, 2013). These pressing initiatives are largely unexamined among cancer patients with MDD, and therefore, this study was designed to investigate the potential moderating effects of depression severity on treatment outcome for depressed breast cancer patients. Prior to addressing this question, and exploring a clinically significant research question also unexamined, the objective was to assess demographic, psychological, and cancer-related variables associated with higher pretreatment depression severity in breast cancer patients. Primary hypotheses were that depression severity would be related to being single, younger, and less educated, as well as having less social support, less environmental reward, more somatic anxiety, a greater number of coexistent anxiety disorders, cancer severity (i.e., higher staging), more bodily pain, and shorter latency since being diagnosed with breast cancer. Second, consistent with the extant psychotherapy outcome literature on individuals with MDD, including individuals with cancer (Driessen et al., 2010; Heron-Speirs et al., 2012; Schneider et al., 2010; Tamagawa et al., 2012), breast cancer patients with higher pretreatment depression severity were expected to have higher response and remission rates to behavior therapy (i.e., BA and PST).

Method

Participants

Participants were 80 women with a principal diagnosis of MDD who were treated at the University of Tennessee Medical Center's Cancer Institute. All participants provided informed consent prior to study enrollment, and the institutional review board approved

the study. Patients were recruited through clinic screening (n = 16; 20%), brochures (n = 9; 11%), and oncologist referral (n = 55; 69%). Patients were approached by clinical psychology doctoral students and asked to complete the Harvard National Depression Screening scale (HANDS; Baer et al., 2000), a 10-item measure assessing symptoms of MDD (*DSM–IV*; American Psychiatric Association, 1994). The HANDS has a score range of 0–30, with a cutpoint of 9 or greater having diagnostic sensitivity of 95% (Baer et al., 2000). Patients who had breast cancer and met this criterion were asked to participate in a comprehensive pretreatment diagnostic assessment. This assessment included administration of the Anxiety Disorders Interview Schedule–IV (ADIS-IV; Brown, Di Nardo, & Barlow, 1994) and self-report instruments outlined below. Advanced doctoral students conducted psychological assessments and were supervised by the principal investigator (DRH) in the context of audiotape review and discussion, resulting in a consensus diagnosis. Inclusion criteria were older than 18 years, diagnosed with breast cancer, and a principal diagnosis of MDD. In terms of breast cancer diagnosis, women were eligible for inclusion regardless of when they had been diagnosed and treated for breast cancer, as long as they were active patients at the Cancer Institute (e.g., follow-up appointments and assessments). Approximately 13% of patients were actively receiving chemotherapy or radiation therapy. For purposes of generalizability, antidepressant and antianxiety medication usage was not exclusionary. Participants were included if not taking antidepressant medication (n = 38; 48%) or, if they were taking medication, had been stabilized at a *consistent* dosage for 8 weeks prior to study assessment (n = 38; 48%). Due to ethical considerations with regard to withholding treatment, patients also were included who had initiated taking medication but were not stabilized (n = 4; 4%). A total of 80 patients were included and randomized to eight sessions of BA or PST. A total of 65 patients completed treatment, resulting in an overall attrition rate of 19%. Patient attrition did not differ as a function of treatment condition, $\chi^2(1) = 1.48$, $p = .26$.

The majority of patients were Caucasian (93%; 7% African American), with a mean age of 55.4 years (SD = 11.9), and patients had a mean education of 14.8 years (SD = 2.3). Marital status was as follows: married (56%), single (29%), divorced (11%), or separated (4%). Approximately 42% of the sample was employed either full- or part-time, and the remaining patients were unemployed (28%) or retired (30%). The mean time since breast cancer diagnosis was 3.2 years (SD = 3.9). Patients of all cancer stages were included: Stage 0 (lobular carcinoma in situ, ductal carcinoma in situ: 26%), Stage I (28%), Stage II (32%), Stage III (11%), and Stage IV (3%). During the study, no patient participated in adjunctive psychotherapy. Coexistent psychiatric diagnoses included generalized anxiety disorder (n = 35; 44%), social phobia (n = 9; 11%), posttraumatic stress disorder (n = 5; 6%), specific phobia (n = 3; 4%), and panic disorder (n = 2; 3%). Based on analyses of variance for continuous variables and chi-square analyses for categorical variables, treatment groups did not statistically differ on demographic, cancer-related, or psychological variables.

Assessment Measures

The Beck Depression Inventory–II (BDI-II; Beck, Steer, & Brown, 1996) consists of 21 items rated on a 4-point Likert scale. The instrument has excellent reliability and validity data with depressed younger and older adults (Beck et al., 1996; Dozois, Dobson, & Ahnberg, 1998). The psychometric properties of the BDI-II also have been studied in cancer patients and a diverse primary care sample, with the instrument having strong predictive validity as it pertains to a diagnosis of clinical depression, strong internal consistency (α = .94), and adequate item-total correlations (range = .54–.74; Arnau, Meagher, Norris, & Bramson, 2001; Katz, Kopek, Waldron, Devins, & Tomlinson, 2004; for the present study: α = .84; range = 14–60; M = 27.0, SD = 8.5). For the purpose of data analyzing the relation of depression severity to treatment outcome and remission, patients were categorized based on their pretreatment BDI-II score (BDI-II $<$ 30 = low severity; BDI-II $\geq$ 31 = high severity). These are the traditional cut-scores determined to have good psychometric properties in both the original development of the BDI-II (Beck et al., 1996) and thereafter by other researchers (Hautzinger, Keller, & Kühner, 2006; Sprinkle et al., 2002).

The Environmental Reward Observation Scale (EROS; Armento & Hopko, 2007) is a 10-item measure that assesses exposure to environmental rewards deemed essential for increasing response-contingent positive reinforcement (RCPR; Lewinsohn, 1974). RCPR is defined as positive or pleasurable outcomes or rewards that follow behaviors—that is, extrinsic (e.g., social, monetary) or intrinsic (e.g., physiological, feeling of achievement)—and increase the likelihood of those behaviors occurring in the future. Decreased RCPR is a central predictor of increased depression (Lewinsohn, 1974). Higher scores on the EROS suggest increased environmental reward. Sample items include "the activities I engage in usually have positive consequences," and "lots of activities in my life are pleasurable." Based on psychometric research with three independent college samples, the EROS has strong internal consistency (α = .85–.86), shows excellent test–retest reliability (r = .85), and correlates strongly with other psychometrically sound measures of depression (r = −.63 to −.69) and anxiety (Armento & Hopko, 2007). In this study, internal consistency was adequate (α = .78; M = 22.7, SD = 4.6).

The Beck Anxiety Inventory (BAI; Beck & Steer, 1993) is a 21-item measure designed to distinguish cognitive and somatic symptoms of anxiety from those of depression. Good psychometric properties have been demonstrated among community, medical, and psychiatric outpatient samples (Morin et al., 1999; Wetherell & Areán, 1997; α = .88; M = 16.8, SD = 9.5).

The Medical Outcomes Study Short Form (SF-36; Ware & Sherbourne, 1992) assesses health and functional status and includes eight subscales. In this study, only the bodily pain scale was relevant to hypotheses and data analysis. The bodily pain scale is a global assessment of pain that is nonspecific to breast cancer. Higher scores indicate more optimal functioning. The SF-36 has a stable factor structure and adequate psychometric properties (Dexter, Stump, Tierney, & Wolinsky, 1996; Ware & Sherbourne, 1992; α = .80 for this study). Factor structure, strong internal consistency, and good discriminant validity were demonstrated in a sample of patients with laryngeal cancer (Mosconi et al., 2000).

The Multidimensional Scale of Perceived Social Support (Zimet, Dahlem, Zimet, & Farley, 1988) is a 12-item scale that assesses adequacy of social support from family, friends, and significant others, with higher scores indicating poorer social support. The instrument has adequate psychometric properties in

clinical and nonclinical samples of adults (Stanley, Beck, & Zebb, 1998; Zimet et al., 1988; $\alpha = .87$; $M = 32.9$, $SD = 17.8$).

Study Interventions and Treatment Fidelity

Behavioral activation for depression (BA) focuses on increasing overt behaviors to bring patients into contact with reinforcing environmental contingencies and corresponding improvements in thoughts, mood, and quality of life (Hopko, Lejuez, Ruggiero, & Eifert, 2003; Lejuez, Hopko, & Hopko, 2001). Patients randomized to PST were treated based on a structured manual (Mynors-Wallis, 2005). For both treatments, initial sessions involved motivational exercises, depression psychoeducation, understanding the relationship between depression and breast cancer, and introduction of the treatment rationale. In BA, patients then engaged in behavioral self-monitoring, followed by identifying values and goals in primary life areas, construction of an activity hierarchy, and structured behavioral activation. Goals of PST were to (a) increase understanding of the connection between depression symptoms with everyday problems, (b) increase the ability to define current problems, (c) learn a specific problem-solving method to address life problems, and (d) create more positive experiences through improved abilities to solve problems. Patients in both treatments received eight weekly 1-hr individual psychotherapy sessions.[1] Six advanced clinical doctoral students were therapists in this study.[2] As reported (Hopko et al., 2011), therapist adherence and competence as rated by an independent evaluator were excellent, with no significant differences as a function of intervention.

Response and remission criteria. Consistent with methods highlighted in previous clinical trials of cognitive–behavioral therapy (Dimidjian et al., 2006; Hopko et al., 2011), response represented significant symptomatic improvement (i.e., 50% reduction from baseline BDI-II score), whereas remission represented improvement to the point of being asymptomatic within normal range (BDI-II $\leq$ 10).

Procedure

Following recruitment procedures, eligible participants were administered the ADIS-IV and self-report measures. All psychological assessments and treatment sessions were conducted at the Cancer Institute. Advanced doctoral students in clinical psychology conducted comprehensive assessments. At the time of these assessments, examiners were blind to the potential treatment condition of the patient if included in the study. If included following the comprehensive assessment, based on a preestablished randomization chart, patients were randomized to BA or PST. Patients subsequently engaged in their 8-week (one-on-one) treatment. For the purpose of this study, treatment groups were collapsed into a single group (i.e., behavior therapy) to increase statistical power for data analyses.

Results

Bivariate Correlations

All data analyses were conducted using SPSS version 21. Correlations among demographic, psychological, and cancer-related variables with depression severity were examined using Pearson product moment correlations and are presented in Table 1. Significant correlations were noted among variables such that higher depression severity (BDI-II) was associated with less education ($r = -.30$, $p < .01$), less environmental reward (EROS: $r = -.47$, $p < .001$), greater somatic anxiety (BAI: $r = .44$, $p < .001$), more coexistent anxiety disorders (ADIS-IV: $r = .36$, $p < .01$), and more bodily pain (SF-36: $r = -.23$, $p < .05$). Interestingly, higher education in breast cancer patients was associated with mental health benefits beyond lower depression severity, including more environmental reward, fewer anxiety disorders, and less bodily pain. Finally, more somatic anxiety as reported on the BAI was associated with a greater number of coexistent anxiety disorders, more bodily pain, and more severe cancer diagnosis (i.e., higher stage).

Linear Regression Analysis

For the linear regression analysis examining variables most associated with pretreatment depression severity, only the (five) variables identified as significant in bivariate analyses were included in the regression equation. The statistical program G*Power 4 was used to assess statistical power (Cohen's f^2) for multiple regression analysis. Using a medium effect size ($f^2 = 0.2$) and setting alpha error probability at .05 and power at 0.85, the total sample size required to detect an effect was 78 (five independent variables). As such, the conclusion was reached that the sample size allowed for reasonable statistical power to correctly reject the null hypothesis if it was false.

Pretreatment Depression Severity

A linear regression analysis was conducted to examine relations between pretreatment depression severity and significantly associated demographic (i.e., education), psychological (i.e., environmental reward, somatic anxiety, more coexistent anxiety disorders), and cancer-related variables (i.e., more bodily pain). For this analysis, pretreatment depression severity was the (continuous) criterion variable, and all other variables were simultaneously entered as predictor variables. Based on the statistical literature (Asteriou & Hall, 2011), collinearity statistics were within the acceptable range (tolerance values range = .73–.87, variable inflation factor range = 1.15–1.38). Linear regression analysis results are presented in Table 2. The overall regression model was significant, $F(5, 74) = 9.87$, $p < .001$, and accounted for 40% of the variance in depression severity. As indicated in Table 2, standardized coefficients and associated t tests indicated that less environmental reward, $t = -3.74$, $p < .001$, and greater somatic anxiety, $t = 3.42$, $p < .01$, were the only variables that emerged as significantly associated with pretreatment depression severity.

[1] Both treatment manuals are available from the first author on request.

[2] Post hoc data analysis indicated rates of treatment response and remission did not significantly differ as a function of therapist or whether patients were medicated during the study.

Table 1
Correlations Among Depression Severity and Demographic, Psychological, and Cancer Variables (N = 80)

Subscale	1	2	3	4	5	6	7	8	9	10	11
1. Depression (BDI-II)											
2. Martial status	−.06										
3. Age	−.16	−.01									
4. Education	−.30**	.16	.04								
5. MSPSS	.17	.25*	.01	−.18							
6. EROS	−.47***	−.07	.09	.32**	−.38***						
7. BAI	.44***	−.03	−.06	−.10	.05	−.13					
8. COEX_ANX	.36**	.03	−.08	−.28*	.13	−.25*	.34**				
9. Bodily pain	−.23**	.10	−.20	.42**	−.04	.12	−.22*	−.18			
10. Length of diagnosis	.07	.04	−.02	−.09	.32**	−.06	−.09	−.03	.03		
11. Cancer stage	−.18	.04	−.06	−.10	−.08	.02	.39***	−.05	.03	.09	

Note. BDI-II = Beck Depression Inventory; MSPSS = Multidimensional Scale of Perceived Social Support; EROS = Environmental Reward Observation Scale; BAI = Beck Anxiety Inventory; COEX_ANX = number of Anxiety Disorders Interview Schedule–IV coexistent anxiety disorders.
* $p < .05$. ** $p < .01$. *** $p < .001$.

Depression Severity and Relation to Treatment Outcome

For these analyses, BDI-II–defined response (50% BDI-II decrease from baseline) and remission (BDI-II ≤ 10) were examined as categorical dependent variables. As reported (Hopko et al., 2011), combined rates of response and remission based on the BDI-II were 70% ($n = 29$) in behavioral activation treatment for depression and 81% ($n = 31$) in PST (entire sample 75%: $n = 60$), with no significant difference across treatments in response, $\chi^2(1) = 2.29$, $p = .20$, or remission, $\chi^2(1) = 0.68$, $p = .49$. Given the absence of between-group differences and to increase statistical power, we collapsed data across treatment groups. As indicated in Figure 1, pretreatment depression severity was not significantly related to treatment remission, $\chi^2(1) = 0.21$, $p = .81$, at posttreatment. As presented in Figure 2, however, pretreatment depression severity was significantly related to treatment response, $\chi^2(1) = 5.50$, $p = .02$, at posttreatment such that individuals with high depression severity were more likely to achieve treatment response relative to those with low depression severity. As a follow-up to these analyses, the relation between pretreatment depression severity and response and remission at 12-month follow-up was assessed. Similar to posttreatment outcome data, at 12-month follow-up, depression severity was significantly related to treatment response, $\chi^2(1) = 5.56$, $p = .02$, but not remission, $\chi^2(1) = 0.58$, $p = .46$.[3]

Mediation Analyses

Given significant associations of decreased environmental reward and increased somatic anxiety with pretreatment depression severity, as well as the moderating effect of depression severity on treatment outcome, post hoc mediation analyses were conducted to assess whether change in somatic anxiety and environmental reward mediated the relations of either intervention on depression reduction (from pretreatment to posttreatment and from pretreatment to 12-month follow-up). A bootstrapping method (Preacher & Hayes, 2008) with $k = 5{,}000$ resamples and 95% bias-corrected and accelerated confidence intervals (CIs) was used to evaluate indirect effects (i.e., equivalent to significance testing at $p < .05$). CIs containing zero are interpreted as nonsignificant. Mediation analyses were conducted separately by treatment condition. In the first analysis, pretreatment depression (BDI-II) was the predictor variable, pre- to posttreatment environmental reward change (EROS) was the mediator, and posttreatment depression (BDI-II) was the outcome variable. For breast cancer patients treated with BA, environmental reward significantly mediated the relationship between pre- and posttreatment depression (95% CI [−0.26, −0.03]; $B = 0.14$, $SE = .05$), although this effect was not maintained at 12-month follow-up (95% CI [−0.14, 0.01]; $B = 0.05$, $SE = .03$). When pre- to posttreatment change in somatic anxiety (BAI) was examined as a mediator of depression reduction in the BA group, it was not a significant mediator at either posttreatment (95% CI [−0.23, 0.02]; $B = 0.05$, $SE = .04$) or 12-month follow-up (95% CI [−0.08, 0.02]; $B = 0.01$, $SE = .01$). For patients treated with PST, environmental reward did not significantly mediate depression reduction at either posttreatment (95% CI [−0.36, −0.16]; $B = 0.07$, $SE = .10$) or 12-month follow-up (95% CI [−0.28, 0.08]; $B = 0.04$, $SE = .05$). Similar to the BA group, change in somatic anxiety was not a significant mediator at either posttreatment (95% CI [−0.21, 0.05]; $B = 0.03$, $SE = .05$) or 12-month follow-up (95% CI [−0.17, 0.03]; $B = 0.02$, $SE = .03$).

Discussion

Supporting the primary hypothesis, results indicated that education, environmental reward, pretreatment anxiety, coexistent anxiety disorders, and bodily pain were significantly correlated with depression severity. Most provocatively, less environmental reward and greater somatic anxiety were the only variables that emerged as having significant associations with depression severity. This finding is consistent with behavioral models of depression

[3] When these analyses were conducted independently for the BA and PST groups (i.e., data noncollapsed), the same pattern of findings emerged across both interventions.

Table 2
Depression Severity in Breast Cancer Patients (N = 80)

Depression (BDI-II)	Standardized coefficient	*SE*	*r*	*t*	Tolerance	VIF
Demographic						
Education	−.10	.39	−.30	−.98	.73	1.38
Psychological						
Environmental reward (EROS)	−.36	.18	−.47	−3.73**	.87	1.15
Pretreatment anxiety (BAI)	.33	.09	.44	3.42*	.85	1.18
Number of coexistent anxiety disorders	.12	1.19	.36	1.16	.79	1.24
Cancer related						
Bodily pain	−.04	.03	−.23	−.44	.79	1.26

Note. BDI-II = Beck Depression Inventory; VIF = Variable Inflation Factor; EROS = Environmental Reward Observation Scale; BAI = Beck Anxiety Inventory.
* $p < .01$. ** $p < .001$.

that highlight decreased RCPR and aversive (anxiety) experiences as predictive of depression severity (Ferster, 1973; Lewinsohn, 1974; Hopko, Robertson, & Lejuez, 2006). Indeed, breast cancer patients experience a number of challenges throughout the process of being diagnosed and treated for cancer, as well as beyond treatment when in remission. Such challenges may include coping with stress and worries (e.g., death, significant others), working through chemotherapy, radiation therapy and associated side effects that can be debilitating, possible bodily changes (e.g., mastectomy) and feelings of decreased femininity, changing psychosocial needs and desires, experiential avoidance, and time restrictions related to ongoing health care. Such cognitive and behavioral experiences may greatly interrupt established routines and behaviors that historically have elicited environmental reward or pleasure, the result being greater depression and anxiety.

Although this conceptualization is highly plausible, other alternatives should be considered. For example, it is conceivable that higher depression severity is a precursor rather than a consequence of less environmental reward and higher anxiety. In other words, particularly if depression is conceptualized as a largely organic disorder (Russo & Nestler, 2013), behavioral avoidance and anhedonia related to biologically based depression may limit access to RCPR, increasing depressive affect further. Given the predominant cross-sectional data analyses in this study, causal inferences are admittedly difficult to determine. However, the finding of environmental reward as a significant mediator of depression reduction in the behavior activation group provides at least some support that decreased environmental reward is causally related to depression.

As a second study limitation, given the data collection process, many important variables were not systematically assessed and thus cannot be ruled out as important predictors of depression severity in breast cancer patients (e.g., exposure to trauma, physical and sexual abuse, highly stressful and adverse life events, maladaptive cognitive styles, family history of depression, insecure parental attachments, genetic predispositions; Dobson & Dozois, 2008). Third, although regression to the mean is a potential explanation of the relation of pretreatment depression severity and treatment response in this trial, findings of several recent meta-analyses of controlled trials help rule out this explanation (Heron-Speirs et al., 2012; Schneider et al., 2010; Tamagawa et al., 2012). Fourth, only the BAI was used to assess anxiety, meaning that

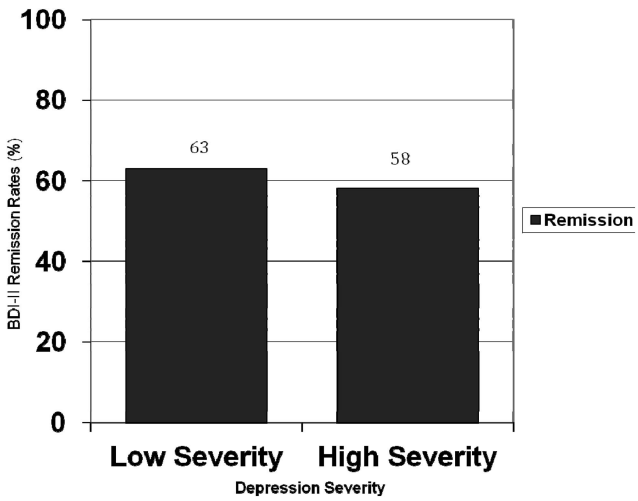

Figure 1. Depression remission rates as a function of depression severity. BDI-II = Beck Depression Inventory.

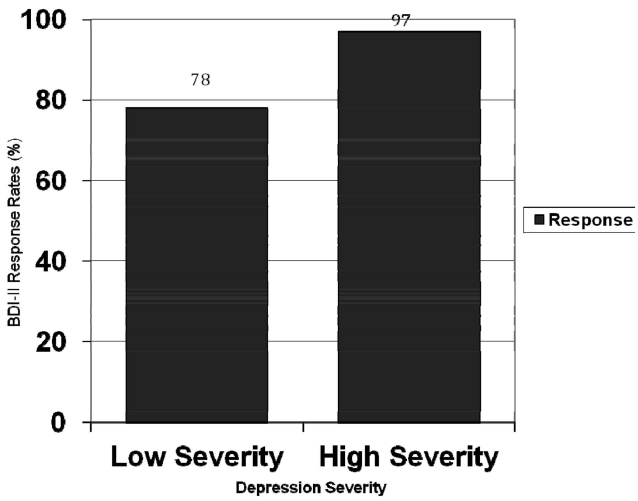

Figure 2. Depression response rates as a function of depression severity. BDI-II = Beck Depression Inventory.

somatic anxiety was assessed at the exclusion of both cognitive and behavioral manifestations of anxiety. In addition, because many symptoms assessed on the BAI could be related to somatic problems more associated with the diagnosis and treatment of breast cancer (rather than anxiety unassociated with breast cancer), this distinction will need to be further examined. Future research should therefore include a more multimodal assessment of anxiety dimensions toward assessing depression severity in breast cancer patients. Fifth, continued efforts should be made to examine important mediators and moderators of the relation between breast cancer and depression severity, including demographic, psychological (e.g., helplessness, optimism, hopelessness, perceptions of social support), and cancer-related variables.

Despite these limitations, the study convincingly demonstrates that breast cancer patients experiencing greater depression severity are simultaneously less exposed to environmental reward and, whether or not directly associated with the breast cancer diagnosis, present with more somatic anxiety. From a clinical perspective, prompt assessment and identification of patients with more severe depression are indicated so that interventions that directly target environmental reward and physiological symptoms can be implemented. Supported by study findings, increasing environmental reward through behavior activation seems especially effective toward depression reduction in breast cancer patients.

The second major finding of the study was that behavior therapy was effective in treating breast cancer patients across the spectrum of depression severity—both milder and more severe depression. This result is encouraging and provocative, particularly in the context of research indicating that prominent therapies such as cognitive therapy (Dimidjian et al., 2006; Elkin et al., 1995) and antidepressant medications (Fournier et al., 2010) may not be as effective for patients with more severe clinical depression. Indeed, although there were no differences in treatment remission as a function of depression severity, more severely depressed breast cancer patients actually had significantly more favorable outcomes in terms of treatment response. This finding is consistent with previous research and further supports the notion that behavior therapy may be particularly useful for cancer patients with more severe depression (Heron-Speirs et al., 2012; Schneider et al., 2010; Tamagawa et al., 2012). Moreover, study results are consistent with a recent meta-analysis suggesting that depression severity moderation is most likely found under conditions highly consistent with the current study design: when efficacious treatments are compared with one another and the sample contains both more and less severely depressed patients (Driessen et al., 2010). In closing, this is only the second study demonstrating the efficacy of behavioral activation for severely depressed patients (Dimidjian et al., 2006) and the first identifying the intervention as effective in a difficult-to-treat cohort of patients with a coexistent cancer diagnosis and severe MDD. Pragmatically, these results suggest that relatively uncomplicated and time-efficient interventions such as behavioral activation and problem-solving therapy show promise for patients with complicated and severe diagnostic presentations. As the study sample was primarily Caucasian, exclusively female, well educated, actively recruited, and composed entirely of breast cancer patients, examining generalizability to other patient samples is indicated.

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