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Randomized Trial of Behavioral Activation, Cognitive Therapy, and Antidepressant Medication in the Acute Treatment of Adults with Major Depression

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Abstract

Antidepressant medication is considered the current standard for severe depression and cognitive therapy is the most widely investigated psychosocial treatment for depression. However, not all patients want to take medication and cognitive therapy has not demonstrated consistent efficacy across trials. Moreover, dismantling designs have suggested that behavioral components may account for the efficacy of cognitive therapy. The present study tested the efficacy of behavioral activation by comparing it to cognitive therapy and antidepressant medication in a randomized placebo-controlled design with adults with major depressive disorder (n = 241). In addition, it examined the importance of initial severity as a moderator of treatment outcome. Among more severely depressed patients, behavioral activation was comparable to antidepressant medication, and both significantly outperformed cognitive therapy. The implications of these findings for the evaluation of current treatment guidelines and dissemination are discussed.

Key words: Behavioral Activation; Cognitive Therapy; Antidepressant Medication; Major Depression

Behavioral Activation, Cognitive Therapy, and Antidepressant Medication in the Acute Treatment of Major Depression

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Antidepressant medications are the standard of treatment of depression, particularly more severe major depression (American Psychiatric Association, 2000), and represent the most common form of treatment for major depression (Olfson et al., 2002). However, antidepressant medication is not useful for every depressed person and not all individuals want to take medications, particularly given the side effects that often accompany their use (American Psychiatric Association, 2000).

Of the psychosocial treatments for depression, cognitive therapy has been the most extensively studied, with numerous outcome studies documenting its efficacy (Hollon, Thase, & Markowitz, 2002). However, in the largest and best-known controlled treatment trial, the NIMH Treatment of Depression Collaborative Research Program (TDCRP), cognitive therapy was less effective than antidepressant medication and no more effective than placebo among more severely depressed participants (Elkin et al., 1995). While this study had considerable influence on the field, questions have been raised about the adequacy with which the cognitive therapy was implemented (Jacobson & Hollon, 1996). Furthermore, a subsequent mega-analysis pooling data from the TDCRP and other relevant studies failed to find significant differences between antidepressant medication and cognitive therapy among more severely depressed participants (DeRubeis, Gelfand, Tang, & Simons, 1999). Nonetheless, the uncertainty surrounding the relative efficacy of cognitive therapy and antidepressant medication highlights the importance of studies that include controls and ensure that the interventions are adequately implemented.

The emergence of cognitive therapy over the past two decades eclipsed more behavioral approaches; however, findings from a component analysis of cognitive therapy suggested that the behavioral components alone worked as well as the full package and may hold greater public health relevance (Jacobson et al, 1996). Specifically, the behavioral activation component alone produced as much change in depressive symptoms as the full cognitive therapy condition during acute treatment and evidenced no more relapse than cognitive therapy over a two-year follow-up (Gortner, Gollan, Dobson, & Jacobson, 1998). These data were consistent with other process oriented research on cognitive therapy, suggesting that a focus on creating cognitive changes about interpersonal relationships was associated with worse functioning after cognitive therapy, whereas a focus on creating *actual* interpersonal change was associated with improvement (Hayes, Castonguay, & Goldfried, 1996). These findings provided additional support for behaviorists, who had long questioned whether the cognitive interventions in cognitive-behavioral therapies were essential to its success (Jacobson, Martell, & Dimidjian, 2001). These data also revitalized interest in purely behavioral treatments for depression and led to the development of a more fully realized behavioral intervention based on a contextual approach (Martell, Addis, & Jacobson, 2001).

Whereas the earlier model of behavioral activation tested in the component analysis study was defined primarily by the proscription of cognitive interventions, the fundamental principle of the expanded behavioral activation model is the use of idiographic functional analysis for the understanding of depressive behavior and contextual interventions for its remediation. The BA approach is conceptually compatible with the behavioral tradition established by Ferster (1973) and Lewinsohn (1974), both of whom identified the link between avoidant behavior and depression, and recommended activation strategies to undermine punishment and increase

positive reinforcement from the environment (see also Rehm, 1977). The expansion of the BA component treatment was an attempt to renew focus on the purely behavioral aspects of these traditions, which were largely overlooked in recent decades.

The current study was developed as a replication and extension of both the TDCRP and the component analysis study, addressing the principal criticisms and methodological shortcomings of each. It also paralleled many features of the DeRubeis et al. study (2005), which compared antidepressant medication and cognitive therapy. The current study compared behavioral activation and cognitive therapy to antidepressant medication in the context of a placebo controlled trial and included careful steps to ensure the fidelity of the respective treatments. The present study had two primary aims. First, it tested the relative efficacy of behavioral activation in the acute treatment of major depression by comparing it both to cognitive therapy alone and antidepressant medication in the context of a placebo controlled trial. Second, it tested whether either psychosocial treatment was a viable alternative to antidepressant medication in the treatment of moderate to severe depression. Primary predictions specified a significant advantage for antidepressant medication over placebo for severely depressed participants and no significant differences between the active treatments. No differences were expected with the less severely depressed participants among all four conditions.

Method

Participants

The University of Washington Institutional Review Board approved the protocol.[1] All participants provided written informed consent prior to enrollment in the study. Participants consisted of 241 individuals between the ages of 18 and 60 years who met criteria for major depression according to the *Diagnostic and Statistical Manual of Mental Disorders* (4th edition;

American Psychiatric Association, 1994), and scored 20 or higher on the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996) and 14 or greater on the 17-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960). All DSM-IV diagnoses were made using the Structured Clinical Interview for the DSM-IV (First, Spitzer, Gibbon, & Williams, 1997). Recruitment occurred between 1998 and 2001; the majority of participants were recruited from media advertisements (*n* =150; 62%); a substantial minority by referral from local agencies (*n* = 64; 27%); and, the rest by "word of mouth" or other referral sources (*n* = 27; 11%).

Participants were excluded if they had a lifetime diagnosis of psychosis or bipolar disorder, organic brain syndrome, or mental retardation. Additional exclusion criteria included the following: substantial and imminent suicide risk; a current (e.g., within the past six months) or primary diagnosis of alcohol or drug abuse or dependence, or a positive toxicology screen; a primary diagnosis of panic disorder, obsessive-compulsive disorder, psychogenic pain disorder, anorexia, or bulimia; or presence of antisocial, borderline, or schizotypal personality disorders. In addition, participants who had not responded favorably within the preceding year to an adequate trial of either cognitive therapy or paroxetine also were excluded.

Because medications were administered in the trial, individuals also were required to have satisfactory results from a physical examination, laboratory screen (complete blood count, complete metabolic panel, thyroid screen including TSH, T3, T4, and urinalysis), and electrocardiogram (if over 40 years of age). Participants were excluded if they had an unstable medical condition, were using any medication that would complicate the administration of paroxetine, or had a known allergy to paroxetine. Moreover, women were not enrolled if pregnant or lactating or not using suitable contraception if capable of becoming pregnant.

Procedure

Participants who passed an initial diagnostic telephone screen were scheduled for an on-site clinical evaluation to provide informed consent and ascertain study eligibility. If eligible, participants then completed a medical evaluation to assess possible medical contraindications. Once eligibility was determined, participants were then assigned by the study coordinator to one of four treatment conditions using a computer generated randomization list: behavioral activation (BA), cognitive therapy (CT), antidepressant medication (ADM), or pill-placebo (PLA). Twice as many participants were assigned to the ADM condition in order to accommodate the design of the continuation phase of the study. Following the TDCRP, severity was used as a stratification variable during randomization (Elkin et al., 1989). Scores on the pre-treatment HRSD were used to form two groups: high severity (HRSD $\geq$ 20) and low severity (HRSD $\leq$ 19). Participants were assigned to therapists within modality based on therapist availability.

Participants completed standard comprehensive outcome assessments at mid- and post-treatment, approximately 8 and 16 weeks from the start of treatment, and at non-standard time points as clinically indicated (e.g., at early termination) by evaluators blind to treatment assignment. The HRSD was also administered to ADM/PLA participants as part of each treatment session by the treating pharmacotherapist, who was blind to whether participants were receiving active medication.

Therapists

BA was provided by two licensed psychologists and a licensed clinical social worker; on average, they were in clinical practice for approximately 7 years. Dr. Neil Jacobson provided initial training in BA. Therapists received individual off-site supervision via telephone from two of the current authors (MEA and KSD) and participated in an on-site consultation meeting chaired by Dr. Neil Jacobson, before his death, and by Dr. Christopher Martell thereafter.

CT was provided by three licensed psychologists, who had been in clinical practice for an average of 14 years. Two had extensive training in CT prior to outset of the trial, including training by the Beck Institute, and had served as cognitive therapists in earlier studies on depression by our group. The third had received specialized training in CT focused on the treatment of anxiety disorders. All were certified by the Academy of Cognitive Therapy during the course of the study. Two study authors (SDH and KSD) oversaw initial training and provided individual supervision off-site via telephone. The therapists also participated in an on-site consultation meeting chaired by Dr. Sandra Coffman.

Five pharmacotherapists provided ADM/PLA; all were board-certified with an average of approximately 12 years of clinical experience. Training and supervision was provided by one of the authors (DLD), an experienced pharmacotherapy researcher who has conducted numerous controlled clinical trials.

Treatments

Behavioral Activation (BA). The BA treatment condition employed in the study was an expanded version of the approach used in the component analysis study, which was based exclusively on the behavioral interventions recommended by Beck and associates (Beck, Rush, Shaw, & Emery, 1979). The expanded BA model was based on a conceptualization of depression that emphasized the relationship between activity and mood and the role of contextual changes associated with decreased access to antidepressant reinforcers. The model highlighted the centrality of patterns of avoidance and withdrawal (e.g., of interpersonal situations, occupational or daily life routine demands, distressing thoughts or feelings, and so forth). Because contacting potential antidepressant reinforcers is often immediately punishing, avoidance of contact minimizes distress in the short term but is associated with greater long-term difficulty, both by

reducing opportunities to contact potentially antidepressant environmental reinforcers and by creating or exacerbating new problems secondary to the decreased activity. Increased activation was presented as a strategy to break this cycle. In general, BA sought to identify and promote engagement with activities and contexts that were reinforcing and consistent with an individual's long-term goals. Specific behaviorally focused activation strategies included self-monitoring; structuring and scheduling daily activities; rating the degree of pleasure and accomplishment experienced during engagement in specific daily activities; exploring alternative behaviors related to achieving participant goals; and using role playing to address specific behavioral deficits. In addition, the expanded BA model included an increased focus on the assessment and treatment of avoidance behaviors, establishing or maintaining regularized routines, and behavioral strategies for targeting rumination, including an emphasis on the function of ruminative thinking and on moving attention away from the content of ruminative thoughts toward direct, immediate experience.

Although BA and CT shared certain elements (e.g., session structure, emphasis on collaborative relationship with the participant, use of homework, etc.), the use of specific cognitive interventions was clearly proscribed in the BA condition. Information on BA is available in the published treatment manuals (Jacobson et al., 2001; Martell et al., 2001). Participants in the BA condition received a maximum of 24 50-minute sessions over 16 weeks, with sessions were held twice weekly for the first 8 weeks and once weekly for the next 8 weeks.

Cognitive Therapy (CT). CT was provided in a manner consistent with standard cognitive therapy for depression as specified by Beck et al. (1979) and Beck (1995). CT therapists used three broad classes of interventions targeting the following areas: 1) behavioral dysfunction, 2) situation specific negative thinking and cognitive distortions, and 3) underlying dysfunctional

beliefs or cognitions that were assumed to be related to the participant's current depression and risk of future depression. These components were implemented in an integrative fashion, in contrast to the sequential manner used in the component analysis study (Jacobson et al., 1996). CT therapists were able to use the full range of behavioral activation strategies outlined in the CT texts cited above, but did not utilize the strategies added as part of the expanded BA model previously described. Participants in the CT condition followed the same frequency, schedule, and allotment of treatment sessions as BA participants.

Pharmacotherapy. Both the ADM and PLA conditions were administered in a triple-blind manner during the first eight weeks of the study (i.e., participants, pharmacotherapists, and evaluators were kept blind to treatment condition). At eight weeks, the blind was broken and PLA participants were offered their choice of treatment at study expense. ADM was administered in a single blind manner for the final eight weeks of the acute phase (i.e., participants and therapists were aware that the medication was active and only evaluators were kept blind as to treatment condition). Paroxetine was selected as the medication because SSRIs are the most widely used and best tolerated antidepressant medications class. Paroxetine, in particular, demonstrates the strongest efficacy among the SSRIs (Hollon et al., 2002).

Both ADM and PLA followed the clinical management protocol developed for the TDCRP, modified for use with a selective serotonin reuptake inhibitor (Fawcett et al., 1987). While formal psychotherapy strategies were proscribed, the pharmacotherapists were encouraged to develop therapeutic relationships characterized by support, reassurance, and optimism about the treatment regimen in order to maximize participant adherence. Toward this end, the pharmacotherapists also were encouraged to provide information, help participants develop reasonable expectations regarding treatment, and give limited advice. The typical session

consisted of the administration of the HRSD by the pharmacotherapist, inquiry about treatment response, side effects, and non-study medication, and further renewal or modification of the participant's pill dosage. Medical evaluation also was conducted as indicated and a pill count was conducted at each visit to determine participants' compliance with the medication protocol. Participants were seen weekly for the first four weeks and biweekly thereafter through week 16 (although PLA participants were terminated at week 8). The first pharmacotherapy session was approximately 30-45 minutes, and subsequent sessions lasted up to 30 minutes. Medications were provided on a flexible schedule designed to bring each participant to a maximally tolerated dose of up to 50 mg per day. All medicated participants were to receive 10 mg/day of paroxetine with the dosage increased to 20 mg in week 2, to 30 mg in week 4, to 40 mg in week 6, and to the maximum dose of 50 mg in week 12. If there were significant side effects at any point, the dose could be reduced temporarily and raised again at a later time. All decisions of this nature were made in consultation with the supervising psychiatrist (DLD).

Measures

Participants completed both standardized clinical interview and self-report measures. All interviewers were trained, certified, and monitored in the assessment techniques by senior project personnel. Interviewers were blind to participants' treatment condition and were supervised weekly to prevent rater drift.

Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1997); Structured Clinical Interview for DSM-IV Axis II Personality Disorders (First, Spitzer, Gibbons, Williams, & Benjamin, 1996). The SCID-I is a semi-structured clinical interview that yields judgments with respect to all five axes of DSM-IV diagnosis. It served as the primary clinical diagnostic instrument in the study. The SCID-II also

was used to assess for the presence of selected personality disorders (i.e., Avoidant, Dependent, Obsessive Compulsive, Depressive, Schizotypal, Borderline, and Antisocial Personality Disorder). Trained clinical evaluators administered both instruments at pre-treatment.

Modified Hamilton Rating Scale for Depression (Hamilton, 1960). The 17-item version of the HRSD is the most commonly used interview-based measure of depressive severity and has documented reliability and validity (Williams, 1988). The HRSD was modified to include atypical sleep, appetite, and weight symptoms and administered by clinical evaluators at pre-treatment, mid-treatment, and post-treatment, and at non-standard assessments as required (e.g., early termination). In addition, the HRSD was administered at each session for the first eight weeks for ADM and PLA participants by the treating pharmacotherapists, analogous to what typically is done in most pharmacotherapy trials.

Beck Depression Inventory, Second Edition (BDI-II; Beck et al., 1996). The BDI-II is a widely employed self-report measure of the severity of depressive symptoms, with excellent psychometric properties (Beck, et al., 1996). The BDI-II was administered at pre-treatment, mid-treatment, post-treatment, and at non-standard assessments as required (e.g., early termination); at each time point, participants were asked to rate their symptoms during the past week.

Measurement of Adherence and Competence. Treatment adherence in the current trial was assessed by a team of five undergraduate raters blind to treatment condition and trained to use a version of the Collaborative Study Psychotherapy Rating Scale (CSPRS; Hollon et al., 1988), modified to accommodate the inclusion of BA. The revised instrument contained a total of 66 items, rated on a 0-6 scale, including at least 15 items presumed to be unique to each of the respective conditions. After establishing reliability, raters completed a total of 90 tapes (n = 36 each for the CT and BA conditions; n = 18 for ADM).

The Cognitive Therapy Scale (CTS) was used to assess the competence with which CT was delivered (Young & Beck, 1980). The CTS is an 11-item instrument designed to measure the quality of treatment delivery for CT therapists, with demonstrated reliability when used by expert raters (Dobson, Shaw, & Vallis, 1985; Vallis, Shaw, & Dobson, 1986). A total score of 40 or greater on the CTS represents the standard threshold of acceptable competence in CT delivery. The off-site CT supervisors (SDH and KSD) rated 36 CT sessions (i.e., 12 per therapist) as part of the ongoing process of quality control and Leslie Sokol, Ph.D., of the Beck Institute also provided expert ratings on a subset of the tapes. Pharmacotherapy tapes were monitored on an ongoing basis by the supervising psychiatrist (DLD), and an external pharmacotherapy expert, Jan Fawcett, M.D, assessed a subset for competence. No comparable measure of competence in BA was available at the time of the study.

Response and Remission Criteria. Response represents significant symptomatic improvement, whereas remission represents improvement to the point of being asymptomatic within normal range. On the HRSD and BDI, response was defined as at least 50% reduction from baseline. Remission was defined as scores ≤ 7 on the HRSD and ≤ 10 on the BDI.

Reliability of Measures. A randomly selected subset of taped clinical interviews was rated by a second group of study clinical evaluators to ascertain interrater reliability. Analyses revealed a high level of rater agreement. For the major depressive disorder diagnostic module of the SCID, the Kappa coefficient was 0.78. For the HRSD, the intraclass correlation was 0.95 for intake interviews and 0.99 for follow-up interviews. Experts at Vanderbilt University also rated a sample of taped HRSD interviews, with a cross-site intraclass correlation of 0.98.

For treatment adherence ratings, after didactic training, raters completed 8 randomly selected audiotaped therapy sessions that were also rated by the treatment integrity supervisor

(JM). Average two-way, mixed ICCs (consistency definition) for the group's ratings across classes of items were .83 for the cognitive items, .94 for the behavioral items, and .97 for the pharmacotherapy items. For competence ratings for CT, the two CT supervisors exhibited strong concordance, with a reliability of .94 for total CTS scores across 12 sessions. Concordance between either of the CT supervisors and the external expert was more modest, with an average ICC of .47 across 36 sessions. However, concordance was suppressed by a single outlier; when this outlier was omitted, concordance was .59.

Statistical Analyses

Tests of baseline differences in demographic and clinical characteristics were investigated using Analysis of Variance (ANOVA) for continuous variables and Chi-square tests of independence for categorical variables. In the presence of small or empty cells in the tests of categorical variables, the Chi-square test was replaced by Fisher's exact test.

Randomization did not achieve equivalence between conditions on only gender. Although gender did not predict response to treatment, it was included as a covariate because the outcomes of BA, which had significantly fewer women, were of primary interest.

Two sets of primary outcome analyses were conducted; the first set sought to determine whether the sample was pharmacologically responsive by comparing change among participants receiving ADM, in contrast to participants receiving PLA, on the HRSD administered at each treatment session over the first half of the acute phase. The second set examined change across the full acute phase and included only the three active treatment conditions. Separate analyses were conducted for each outcome measure within each severity subgroup. Separate analyses for each severity group were implemented due to potential problems with multicollinearity associated with including both the dichotomous severity variable (based on the HRSD) and pre-

treatment severity (the continuous form of the BDI-II or HRSD) as the first outcome measure in the same analysis. Planned contrasts tested for differences between all possible treatment pairs. Given the primary hypotheses of no difference between active treatments, corrections for multiple comparisons were not used.

Hierarchical linear modeling (HLM), controlling for gender, was used as the primary method to investigate treatment differences using the intent-to-treat sample (Raudenbush & Bryk, 2001). The standard HLM model involves two levels: within-subject (Level 1) and between-subject (Level 2). At Level 1, the outcome varies within subjects over time as a function of a person-specific growth curve. At Level 2, the person-specific change parameters are viewed as varying randomly across subjects, as a function of the participant's treatment. The person-specific parameters correspond to a random intercept and random slope per subject. To determine which person-specific parameters were needed, procedures were used in which the log-likelihood between the nested models was compared to determine the number of random effects needed (Verbeke & Molenbergh, 2000). Effect size calculations for the HLM models were derived as specified by Raudenbush and Liu (2001) and Verbeke and Molenbergh (2000).

For the modified intent-to-treat comparisons of ADM and PLA on the in-session HRSD, random effects were included estimating the variability in the intercepts and the variability in the slopes between subjects. For the comparisons of active treatments, a single random effect for the intercept term was used for the HRSD and random effects for the intercept and slope were used for the BDI. Homogeneity of random effects across treatment groups existed in all analyses except the analysis of the BDI Low Severity group.

Treatment differences in categorical rates of response and remission at post-treatment were examined using Cochran-Mantel-Haenszel (CMH) tests, controlling for gender. Categorical

analyses were conducted with the full intent-to-treat sample, using last observation carry forward (LOCF) for participants who failed to complete treatment or were lost to follow-up.

Bioequivalence testing (Rogers, Howard, & Vessey, 1993; Schuirmann, 1987) was used to determine whether treatments were sufficiently close in outcomes to be considered statistically equivalent. We chose this margin of non-inferiority to correspond to the effect size for the ADM to PLA comparison during the active phase of treatment based on the HRSD ratings conducted at each pharmacotherapy session, derived as specified by Raudenbush and Liu (2001) and Verbeke and Molenbergh (2000). Currently, the FDA standard for bioequivalence is Schuirmann's 2 one-sided t-tests (Schuirmann, 1987); this determines if the difference between ADM and BA lies completely within the non-inferiority margin, which considers the two to be negligibly different.

To assess whether missing data had a substantive influence on results, the pattern-mixture approach was used (Hedeker & Gibbons, 1997). To determine if the differential trends over time were dependent on completion status, a three-way interaction of completion status, time, and treatment group was included in the HLM analysis. A significant finding for this three-way interaction would suggest that the slope estimates and treatment group comparisons were dependent on completion status; a non-significant finding would indicate that the slope estimates and treatment group comparisons were not biased by completion status.

All analyses were conducted using SPSS Version 11.5 and SAS Version 9.1.

Results

Participant Enrollment

Of the 388 participants who completed a comprehensive intake assessment, 250 were eligible for randomization (of whom nine declined participation), resulting in 241 participants randomized to treatment (CT = 45; BA = 43; ADM = 100; PLA = 53). Of the 138 excluded

participants, the majority were screened out due to sub-threshold major depression or low severity as measured by the BDI or HRSD (n = 89); the remainder were screened out due to medical complications (n = 16), diagnostic considerations (n = 19), substance abuse or dependence (n = 8), acute suicidality (n = 3), or other reasons (n = 3). Figure 1 presents the flow of participants over the course of the study.

Baseline Characteristics

Table 1 presents sample baseline demographic and clinical characteristics. Treatment groups did not differ, with the exception of gender. In the full sample, there was a significant difference between treatments in gender, χ^2 (3, N = 241) = 9.30, p = .026, with fewer women assigned to BA (47%; n = 20) as compared to CT (73%; n = 33), ADM (68%; n = 68), and PLA (72%; n = 38). This difference was driven by the low severity subgroup, χ^2 (3, N = 103) = 9.18, p = .027, in which fewer women were assigned to BA (28%; n = 5) as compared to CT (75%; n = 15), ADM (61%; n = 26), and PLA (59%; n = 13).

Treatment Integrity

Adherence. Therapists in the various conditions were strongly adherent to the respective treatments. The cognitive items on the adherence scale received the greatest ratings in the CT condition sessions (M = 6.07) while receiving negligible endorsement in the BA and ADM sessions (M = 0.58 and 0.06, respectively). The behavioral items received the greatest endorsement for the BA condition (M = 8.65), a lesser though substantive degree of endorsement for CT (M = 5.01), and negligible endorsement for ADM (M = 0.22). The pharmacotherapy items received the greatest endorsement in ADM sessions (M = 8.06), while receiving negligible endorsement in the BA and CT conditions (M = 0.57 and 0.06, respectively).

CT Competence. Study supervisors (SDH and KSD) rated CT therapists as delivering the treatment competently (M = 46.86, SD = 4.05). External ratings from the Beck Institute suggested a more modest level of competence (M = 40.33, SD = 4.17) and were significantly lower than those of study supervisors (t (35) = 8.08, p < .001).

ADM Dosage. Mean dosage did not differ as a function of severity and is therefore presented for the full sample of ADM participants. The mean (± *SD*) paroxetine dose during the first week of treatment was 10.0 ± .00 mg/day. The mean (± *SD*) daily dose was increased to 19.26 ± 2.64 mg in the second week, to 24.52 ± 6.25 in the fourth week, 30.00 ± 8.74 in the sixth week, and 31.67 ± 11.45 in the eighth week. By the 12th week, the mean dosage had been increased to 35.17 ± 13.08, which was maintained through the end of the acute phase.

Attrition

Overall rates of attrition were generally low, with the exception of the ADM condition. Rates of attrition did not differ as a function of severity and are therefore presented only for the full sample. Over the full acute phase, there were significant differences between active treatments in rates of attrition, χ^2 (2, N = 188) = 19.02, p < .001. The rate of attrition for ADM (44%; n = 44) was significantly higher than for either CT (13.3%; n = 6), χ^2 (1, N = 145) = 12.92, p < .001, or BA (16.3%; n = 7), χ^2 (1, N = 143) = 10.07, p = .002.

With respect to the timing of attrition, there were significant differences in the rates of refusal of randomization between patients assigned to pharmacotherapy in contrast to CT or BA, χ^2 (2, N = 241) = 0.08, p = .04 (Fisher's exact test); 14% of the patients assigned to pharmacotherapy (n = 22) failed to attend a single session in contrast to 2% in CT (n = 1) and 7% in BA (n = 3). Overall, there were significant differences in attrition rates during the first eight weeks, χ^2 (3, N = 241) = 17.30, p = .001, with 36% of participants in ADM (n = 36)

dropping out in contrast to 11% in CT (n = 5), 9% in BA (n = 4), and 23% in PLA (n = 12). Pair-wise comparisons between treatments indicated a significantly higher rate of attrition between ADM versus CT, χ^2 (1, N = 145) = 9.48, p = .002, and ADM versus BA, χ^2 (1, N = 143) = 10.64, p = .001; there was a trend toward higher attrition in ADM than PLA, χ^2 (1, N = 153) = 2.87, p = .090. The rates of attrition between the active treatments were not significantly different during the second half of the acute phase, χ^2 (2, N = 143) = 3.24, p = .20 (Fisher's exact test).

Reasons for the high level of attrition in ADM were diverse. In addition to being significantly more likely not to start treatment if assigned to one of the pill conditions, 9% (n = 9) of the ADM participants dropped out due to side effects, 5% (n = 5) were withdrawn due to non-adherence to study protocol, 6% (n = 6) experienced lack of efficacy or worsening of symptoms (including one participant who died by suicide), 3% (n = 3) dropped out due to dissatisfaction with study treatment, 1% (n = 1) relocated, 1% (n = 1) dropped out due to feeling improved, and 5% (n = 5) were lost for reasons unknown. Of PLA participants who dropped out after starting treatment, 2% (n = 1) dropped out due to side effects, 2% (n = 1) dropped out due to concerns about confidentiality, 2% (n = 1) relocated, and 2% (n = 1) were lost for reasons unknown. Of CT participants, 2% (n = 1) dropped out due to dissatisfaction with study treatment, 2% (n = 1) experienced lack of efficacy or worsening of symptoms, 2% (n = 1) found the research burdensome, and 4% (n = 2) were lost for reasons unknown. Of BA participants, 2% (n = 1) dropped out due to dissatisfaction with study treatment, 2% (n = 1) experienced lack of efficacy or worsening of symptoms, 2% (n = 1) found the research burdensome, and 2% (n = 1) relocated.

Side Effects

Side effects were recorded based on pharmacotherapist inquiry and participant report. Overall, side effects reported by participants receiving medication were consistent with the known profile for paroxetine**.** Results are presented for the full sample, as differences were few as a function of initial severity (high severity participants reported more nausea and less diarrhea than low severity participants). Relative to placebo participants, participants receiving paroxetine reported more sexual side effects [anorgasmia, 17% versus 0%, χ^2 (1, N = 153) = 10.14, p = .001; and decreased libidio, 15% versus 0%, χ^2 (1, N = 153) = 8.81, p = .003]; gastrointestinal distress [nausea, 19% versus 6%, χ^2 (1, N = 153) = 5.01, p = .025], sleep-related difficulties [insomnia, 25% versus 9%, χ^2 (1, N = 153) = 5.33, p = .021; somnolence, 38% versus 6%, χ^2 (1, N = 153) = 18.47, p < .001; yawning, 12% versus 0%, χ^2 (1, N = 153) = 6.90, p = .008 (Fisher's exact test)]; dry mouth, 17% versus 6%, χ^2 (1, N = 153) = 3.92, p = .048; and excessive sweating, 13% versus 0%, χ^2 (1, N = 153) = 7.53, p = .004 (Fisher's exact test). Side effects were not assessed in BA and CT, but were assumed to parallel those reported by placebo participants.

Pharmacological Responsiveness of Sample

For the high severity subgroup, there was evidence of differential improvement over time by treatment on the HRSD as conducted in-session by the pharmacotherapists, F (1,64) = 5.87, p = 0.018. High severity participants receiving ADM improved significantly more per treatment week than did participants receiving PLA; in contrast, for the low severity subgroup, there was no evidence of differential improvement over time by treatment on the HRSD, F (1, 49) = 0.98, p = 0.33. Slope estimates (± standard errors) for the high severity subgroup were -1.22 (± 0.16) for ADM and -0.57 (± 0.22) for PLA. Slope estimates (± standard errors) for the low severity subgroup were – 1.05 (± 0.16) for ADM and -0.77 (± 0.23) for PLA. Associated effect sizes were 0.65 and 0.31 for the high and low severity subgroups, respectively.

Analysis of Active Treatment Outcomes

Table 2 provides descriptive statistics on the primary outcome measures as a function of severity. In the high severity subgroup, there was significant overall improvement by time for all groups on the BDI, F (1, 83) = 219.86, $p < .0001$, and on the evaluator-rated HRSD, F(1, 190) = 443.85, p<0.0001. In addition, as shown in Figure 2, significant differences in slopes were found among the treatments on both the BDI, F (2, 81) = 4.15, $p = .019$, and on the HRSD, F (2, 188) = 3.12, p = .0.047.Participants in BA improved significantly more per treatment week than did participants in CT on both the BDI, t (81) = 2.23, p = .0.029, and on the HRSD, t (188) = 2.09, p = .038. Similarly, participants in ADM improved significantly more per treatment week than did participants in CT on both the BDI, t (81) = 2.76, $p = .007$, and on the HRSD, t (188) = 2.31, p = .0.022 There were no significant differences in the rates of improvement comparing participants in BA and ADM on the BDI, t (81) = 0.245, p = .80, or on the HRSD, t (188) = 0.04, p = 0.97. BDI slope estimates (±standard errors) are -1.12 (±0.20) for CT, -1.76 (± 0.20) for BA, and -1.82 (± 0.15) for ADM. HRSD slope estimates (with standard errors) are -0.74 (±0.09) for CT, -0.99 (± 0.08) for BA, and -0.99 (± 0.063) for ADM. Associated effect sizes for BA relative to CT were 0.87 (BDI) and 0.59 (HRSD); for ADM relative to CT, effect sizes were 0.96 (BDI) and 0.51 (HRSD); and for ADM relative to BA, effect sizes were 0.09 (BDI) and 0.01 (HRSD).

Bioequivalence testing (Rogers, Howard, & Vessey, 1993; Schuirmann, 1987) was used to determine whether ADM and BA were sufficiently similar to each other to be considered statistically equivalent. Using both the BDI and HRSD, ADM and BA lie within the margin of non-inferiority with a probability larger than 99.9%.

As shown in Figure 2, in the low severity subgroup, there was significant overall improvement by time for all groups on the BDI, F (1, 62) = 166.10, $p < .0001$, and on the HRSD,

F (1, 146) = 193.02, p <. 0001. However, there was no evidence of differential improvement over time by treatment on the BDI, F (2, 60) = 0.47, p = 0.63 or the HRSD, F (2, 144) = 0.05, p = 0.95. Specific pair-wise comparisons between treatments also failed to indicate significant differences in slopes, and associated effect sizes were also small.

Categorical rates of response and remission at post-treatment also were calculated for the high and low severity subgroups, using LOCF for participants who dropped out of treatment or failed to provide post-treatment data. Because our primary hypotheses concern the high severity subgroup, categorical outcomes for this group are presented in Figures 3 and 4, respectively.

Among the more severely depressed participants, overall combined rates of response and remission based on the BDI were 48% (n = 12) in CT, 76% (n = 19) in BA, and 49% (n = 28) in ADM. Based on the HRSD, overall rates were 56% (n = 14) in CT, 60% (n = 15) in BA, and 40% (n = 23) in ADM. Results indicated a non-significant trend on the BDI, χ^2 (2, N = 107) =5.64, p = 0.06, and no significant differences between treatments on the HRSD, χ^2 (2, N = 107) = 3.62, p = 0.16. The direction of the differences on the BDI were driven by the superior performance of BA, in which a significantly greater percentage of BA participants met BDI response criteria as compared both to participants receiving CT, χ^2 (1, N = 50) = 3.92, p = .048, or ADM, χ^2 (1, N = 82) = 4.91, p = .027. Rates of remission for the high severity subgroup based on the BDI were 40% (n = 10) in CT, 52% (n = 13) in BA, and 42% (n = 24) in ADM. Based on the HRSD, overall rates of remission were 36% (n = 9) in CT, 56% (n = 14) in BA, and 23% (n = 13) in ADM. There were no significant differences between treatments on the BDI, χ^2 (2, N = 107) = .99, p = .61. Results indicated significant differences between treatments on the HRSD, χ^2 (2, N = 107) = 8.88, p = .012, with a significantly greater percentage of BA participants reaching remission as compared to ADM participants, χ^2 (1, N = 82) = 9.82, p = .002.

The poor performance of CT relative to BA and ADM on the continuous measures was in part a consequence of a subset of extreme non-responders based on observed post-treatment outcomes. Specifically, considering all high severity patients, 28% (n = 7) of CT participants endorsed post-treatment scores of greater than 30 on the BDI, in contrast to only 2% (n = 1) of ADM and 0% (n = 0) of BA participants. On the HRSD, 12% (n = 3) of CT participants endorsed post-treatment scores of greater than 20, in contrast to only 5% (n = 3) of ADM and 4% (n = 1) of BA participants.

Among the less severely depressed participants, overall rates of response based on the BDI were 65% (n = 13) in CT, 50% (n = 9) in BA, and 56% (n = 24) in ADM. Based on the HRSD, overall response rates were 60% (n = 12) in CT, 39% (n = 7) in BA, and 47% (n = 20) in ADM. Results indicated no significant differences between treatments on the BDI, χ^2 (2, N = 81) = 0.25, p = .88, or on the HRSD, χ^2 (2, N = 81) = 1.02, p = .60. Rates of remission based on the BDI were 55% (n = 11) in CT, 44% (n = 8) in BA, and 42% (n = 18) in ADM. Based on the HRSD, overall rates of remission were 50% (n = 10) in CT, 39% (n = 7) in BA, and 33% (n = 14) in ADM. The CMH test, adjusting for gender, was used to test differences in rates of remission. Results indicated no significant differences between treatments on the BDI, χ^2 (2, N = 81) = 0.77, p = .68, or on the HRSD, χ^2 (2, N = 81) = 1.59, p = .45.

Analysis of Missing Data

To determine if the differential trends over time were dependent on completion status, a three-way interaction of completion status, time, and treatment group was included in the HLM analysis to assess the impact of missing data. On the BDI, results indicated a non-significant effect for completion status by time by treatment group interaction for the high severity subgroup, F (2,64) = 0.23, p = 0.80., and low severity subgroup, F (1, 52) = 2.79, p = 0.10.

Similarly, on the HRSD, results indicated a non-significant effect for the completer status by time by treatment group interaction for the high severity subgroup, F (2, 256) = 0.16, p = 0.86, and low severity subgroup, F (1, 142) = 1.18, p = .28. These results suggest that the parameter estimates generated by the original HLM models are valid and are not biased by missing data. Additionally, two-way ANOVA models were also used to test for differences in baseline HRSD and BDI by completion status and treatment condition for the high and low severity subgroups. For the BDI, all p-values were greater than .35; for the HRSD, all p-values for the two-way interaction of completion status and treatment condition were greater than .28.

Discussion

The results of this study indicate that behavioral activation is comparable in efficacy to antidepressant medication, the current standard, and more efficacious than cognitive therapy, one of the best supported psychotherapies, among more severely depressed participants. The results also provide further confirmation of the importance of initial severity in the analysis of treatment outcome; differential treatment effects were observed only among those patients who were more severely depressed.

In any comparison between psychotherapy and medication, it is important to examine whether the sample was responsive to medications and that pharmacotherapy was adequately implemented. Among more severely depressed participants in this trial, antidepressant medication significantly outperformed placebo through eight weeks of treatment. There were no significant differences in outcome between antidepressant medication and placebo for the less severely depressed participants, consistent with findings from numerous other studies (Hollon et al., 2002). In the absence of a “true” drug effect for such patients, there may be little justification

for prescribing psychoactive medications when there are comparably effective psychosocial alternatives free of side effects.

Across the full acute phase, for the more severely depressed participants, behavioral activation and antidepressant medication were comparable on both self-report and clinical ratings; moreover, behavioral activation brought a significantly greater percentage of participants to remission and retained a greater percentage of participants in treatment. The performance of behavioral activation with respect to antidepressant medication challenges current treatment guidelines, which state that moderately and severely depressed participants require medication (American Psychiatric Association, 2000). The availability of viable alternatives to antidepressant medication is particularly important given that not all participants want to take medication, particularly given typical side effect profiles (Hollon et al., 2002).

The findings of this study with respect to cognitive therapy are at odds with other recent studies in which cognitive therapy was comparable to antidepressant medication (DeRubeis et al., 2005). However, this pattern of findings is consistent with the TDCRP (Elkin et al., 1989), in which cognitive therapy was not significantly different from placebo and was significantly outperformed by antidepressant medication. Although the quality of cognitive therapy in the TDCRP has been criticized, it is not clear that these same concerns apply in the present trial. Moreover, the outcomes of cognitive therapy in this study were comparable to other recent trials; specifically, the remission rate of 36% among cognitive therapy patients in this study compares favorably to the 40% remission rate recently reported by DeRubeis et al. (2005). Thus, the current results suggest that the superiority of behavioral activation was not due to poorly implemented cognitive therapy, but rather to the greater efficacy of behavioral activation.

The results of this study build on earlier behavioral approaches to depression (Ferster, 1973; Lewinsohn, 1974) and replicate and extend the findings of our earlier component analysis study (Jacobson et al., 1996). Sustained use of simple behavioral strategies, such as goal setting, self monitoring, activity scheduling, problem solving, and graded task assignment, was highly efficacious. Although the long prevention effects of this approach relative to cognitive therapy are still to be determined, the short-term outcomes in this study are consistent with more recent activation oriented interventions for depression (e.g., Blumenthal et al., 1999; Hopko, Lejuez, LePage, Hopko, & McNeil, 2003) and with the findings of studies across multiple diagnostic categories suggesting that the cognitive components of cognitive therapy may add little incremental benefit over purely behavioral interventions (e.g., Borkovec, Newman, Pincus, & Lytle, 2002; Foa, Rothbaum, & Furr, 2003; Gloaguen, Cottraux, Cucherat, & Blackburn, 1998).

This growing body of research raises questions about the necessity of directly targeting participants' negative thinking to achieve treatment response. In this regard, it is important to note that Beck and colleagues have long suggested that therapists focus on behavioral strategies early in treatment when patients are more depressed and return to that emphasis later if patients start to worsen (Beck et al., 1979). Although the current data do not specifically address whether change in cognition is a mediator of symptom change, they provide strong evidence that behavioral methods are sufficient to produce symptom change, irrespective of whether improvement is mediated by cognitive change or not (cf., Bandura, 1977). Future analyses will more directly address the underlying mechanisms of change.

Additionally, the results of this trial also suggest that the expanded behavioral activation model may have unique advantages over the behavioral strategies tested in the component analysis study (Jacobson et al., 1996). Although further research is necessary to identify specific

processes of change, the added elements of the expanded behavioral activation model may account for its stronger relative performance vis-à-vis cognitive therapy in the current trial. In particular, targeting avoidance behaviors may be an important innovation. Although addressing avoidance is standard in treatments for anxiety, recent models propose that avoidance may be a fundamental element underlying multiple psychopathologies and that blocking avoidance may be a critical element of treatment (Barlow, Allen, & Choate, 2004). However, with the exception of the use of "opposite action" for sadness within Dialectical Behavior Therapy (Linehan, 1993), treatments for depression have heretofore not specifically emphasized targeting avoidance.

Avoidance minimizes immediate distress, but at the cost of both diminishing opportunities for reinforcement and allowing exacerbation of ongoing stressors. BA explicitly targets the reduction of avoidance behaviors related to both intrapersonal and interpersonal difficulties. For example, a client responded to interpersonal conflict with a co-worker by avoiding work for multiple days. Although this avoidance minimized aversive interactions with her co-worker, the client also missed the experience of accomplishing tasks at work, which had served an antidepressant function for her in the past. Staying home also created new problems, such as earning less money and engendering frustration on the part of her supervisor, while doing nothing to address the original problem with the co-worker. To interrupt this cycle, the BA model uses focused activation strategies to explicitly target such avoidance patterns and associated functional consequences. In essence, in BA, clients learn to identify patterns of avoidance and to respond with activation; this basic principle is applied repeatedly across multiple situations in therapy.

Moreover, the behavioral activation model utilizes a fundamentally different approach to negative and ruminative thinking than used in cognitive therapy. First, behavioral interventions

address the function of negative or ruminative thinking, in contrast to cognitive therapy's emphasis on thought content. Behavioral activation encourages attention to the consequences of ruminating (avoidance and withdrawal) and the use of activation strategies as alternatives. In this regard, behavioral activation shares important elements with other contemporary behavioral therapies that emphasize function rather than topography of behavior (e.g., Hayes, Strosahl, & Wilson, 1999; Jacobson & Christensen, 1996; Linehan, 1993). In this regard, behavioral activation strategies are not unlike the use of questions in cognitive therapy that address the "utility" of thoughts (as opposed to the "validity" of thoughts); it is possible that an emphasis on the utility or function of thinking has a particularly important role in the treatment of depression. Second, behavioral activation specifies "attention to experience" interventions to counter ruminative thinking by attending to direct sensations. Similar to recent mindfulness-based treatments (e.g., Segal, Williams, & Teasdale, 2002), these interventions provide a method for addressing rumination that is fundamentally distinct from engaging the content of thoughts. Clients are encouraged to notice when they are ruminating and to move their attention away from the content of ruminative thoughts toward direct and immediate experience; for instance, a client may be asked to experiment with attending to the sights or smells around her when she notices that she is ruminating.

A number of limitations should be noted. First, given that the expanded behavioral activation model was developed at the University of Washington and cognitive therapy supervisors were offsite, allegiance effects may have influenced the findings. These concerns were mitigated, however, because investigators with allegiance to their respective treatments were responsible for overseeing those treatments and supervision by these experts was provided throughout the trial. Future trials are essential in which behavioral activation is implemented in

other venues and comparison treatments have the benefit of on-site expertise. Moreover, such tests of the generalizability of findings are additionally important given the study exclusion criteria and particular sample characteristics (e.g., differences in gender between conditions).

Second, the lack of competency ratings for our behavioral activation therapists is a limitation. Despite the positive outcomes of behavioral activation in this study, the development and validation of independent competency assessments of behavioral activation remains an important issue for future research.

Third, the rate of attrition in antidepressant medication was higher than that reported in other trials using paroxetine (e.g., DeRubeis et al., 2005). We cannot rule out the possibility that patients in our trial were unrepresentative in their unwillingness to accept or inability to tolerate medication or that the treatment implementation contributed to the high rate of attrition. For example, antidepressant medication may have demonstrated better retention had the protocol allowed for a more aggressive dosage schedule and greater flexibility in treatment delivery (e.g., augmenting or switching medications). Moreover, the greater attrition in antidepressant medication complicated interpretation of the results. There was no evidence that attrition biased the findings based on HLM analyses; these analyses, which took attrition into account, indicated that antidepressant medication was as efficacious as behavioral activation and superior to cognitive therapy among more severely depressed patients. At the same time, categorical analyses, which considered only whether patients actually met criteria for response or remission, indicated that antidepressant medication was no better than cognitive therapy and less efficacious than behavioral activation. The difference is that the HLM analyses essentially estimated what likely would have happened if the medication dropouts had remained in treatment (they should have done as well as patients in behavioral activation), not how they actually did (fewer of them

actually benefited from treatment). This distinction should not be overlooked when evaluating the relative advantages of the respective interventions.

In summary, behavioral activation did particularly well in this study. It was at least as efficacious as antidepressant medication, even among more severely depressed participants, and retained a greater proportion of patients long enough for them to benefit from treatment. This suggests that behavioral activation may be a viable alternative to antidepressant medication, challenging current treatment guidelines. Behavioral activation also was more efficacious than cognitive therapy among more severely depressed participants, challenging the assumption that directly addressing negative beliefs is essential for change and raising the possibility that elements of the expanded behavioral activation model may be more robust interventions for depression than cognitive interventions. Finally, interest in behavioral activation was based in part of the notion that it would be a more exportable treatment that was easier to implement and train than cognitive therapy or other more complex interventions. If this is the case, the public health advantages could be significant. Such questions await future study.

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Table 1. *Baseline Characteristics of Participants*

	Full Sample (N = 241)	High Severity (n = 138)	Low Severity (n = 103)
Sex: *n* (% female)	159 (66.0)	100 (72.5)	59 (57.3)
Race: *n* (% White)	197 (81.7)	118 (85.5)	79 (76.7)
Age: *M* (*SD*)	39.90 (10.97)	39.86 (11.50)	39.95 (10.28)
Currently married or cohabiting: *n* (%)	94 (39.0)	53 (38.4)	41 (39.8)
College graduate: *n* (%)	121 (58.7)	65 (55.1)	56 (63.6)
Employed outside home: *n* (%)	171 (71.0)	92 (66.7)	79 (76.7)
BDI: *M* (*SD*)	32.01 (7.48)	35.30 (6.97)	27.60 (5.67)
HRSD: *M* (*SD*)	20.74 (4.12)	23.60 (2.89)	16.90 (1.67)
Severity			
Low (HRSD 14-19): *n* (%)	103 (42.7)	--	103 (100.0)
High (HRSD $\geq$20): *n* (%)	138 (57.3)	138 (100.0)	--
Current episode length (months): *Mdn* (*SD*)	12.00 (71.30)	12.0 (68.77)	11.0 (74.89)
No. of prior episodes: *Mdn* (*SD*)	1.00 (1.44)	1.00 (1.56)	0.00 (1.23)
Depressive Subtype			
Melancholic: *n* (%)	73 (30.3)	46 (33.3)	27 (26.2)
Atypical: *n* (%)	42 (17.4)	22 (15.9)	20 (19.4)

Recurrent Depression: *n* (%)	139 (57.7)	88 (63.8)	51 (49.5)
Chronic Depression (> 2 yrs.): *n* (%)	83 (34.4)	47 (34.1)	36 (35.0)
Age of onset of 1st episode: *M* (*SD*)	27.65 (13.27)	26.22 (13.14)	29.55 (13.27)
Previous psych hospitalization: *n* (%)	23 (9.5)	18 (13.0)	5 (4.9)
Any current Axis I Dx: *n* (%)	68 (28.2)	50 (36.2)	18 (17.5)
Any lifetime Axis I Dx: *n* (%)	121 (50.2)	79 (57.2)	42 (40.8)
Avoidant, Dependent, Obsessive Compulsive, or Depressive PD: *n* (%)	49 (20.3)	32 (23.2)	17 (16.5)
Any current anxiety Dx: *n* (%)	57 (23.7)	43 (31.2)	14 (13.6)
Any lifetime sub. abuse/dep.: *n* (%)	102 (42.3)	63 (45.7)	39 (37.9)

Note. Statistics summarized in each cell of the table are given after the variable name.

Table 2. *BDI and HRSD Mean, Standard Deviation, and Ns by Condition Over Time*

	Intake			8 week			16 Week		
	Mean	SD	N	Mean	SD	N	Mean	SD	N
Low Severity									
BDI									
CT	27.30	6.89	20	12.94	10.29	17	9.76	8.15	17
BA	28.72	4.59	18	15.33	10.03	15	11.00	10.08	13
ADM	27.79	5.67	43	13.89	8.61	28	7.91	6.29	22
PLA	26.59	5.43	22	14.68	7.81	19	--	--	--
HRSD									
CT	16.65	1.84	20	10.41	4.05	17	7.19	4.09	16
BA	17.28	1.45	18	12.40	6.58	15	7.92	7.68	13
ADM	16.98	1.60	43	11.57	5.32	28	8.45	5.26	22
PLA	16.68	1.86	22	12.05	5.54	19	--	--	--
High Severity									
BDI									
CT	34.12	5.67	25	21.00	14.64	21	17.44	15.57	18
BA	36.68	5.91	25	16.82	8.56	22	8.75	7.96	16
ADM	35.61	7.13	57	14.39	11.00	38	7.78	9.61	27
PLA	34.55	8.36	31	22.50	12.97	22	--	--	--
HRSD									

CT	22.72	2.61	25	12.67	6.96	21	10.33	7.62	18
BA	23.16	2.53	25	12.86	6.93	22	7.56	6.94	16
ADM	23.79	2.60	57	13.13	7.74	38	8.63	7.19	27
PLA	24.32	3.69	31	16.09	7.60	22	--	--	--

Note. BDI = Beck Depression Inventory; HRSD = Hamilton Rating Scale for Depression; CT = Cognitive Therapy; BA = Behavioral Activation; ADM = Anti-Depressant Medication; PLA = Pill-placebo

Note. The data on PLA are presented for illustrative purposes. The analyses related to pharmacological responsiveness are based on weekly ratings on the HRSD and are not included in this table

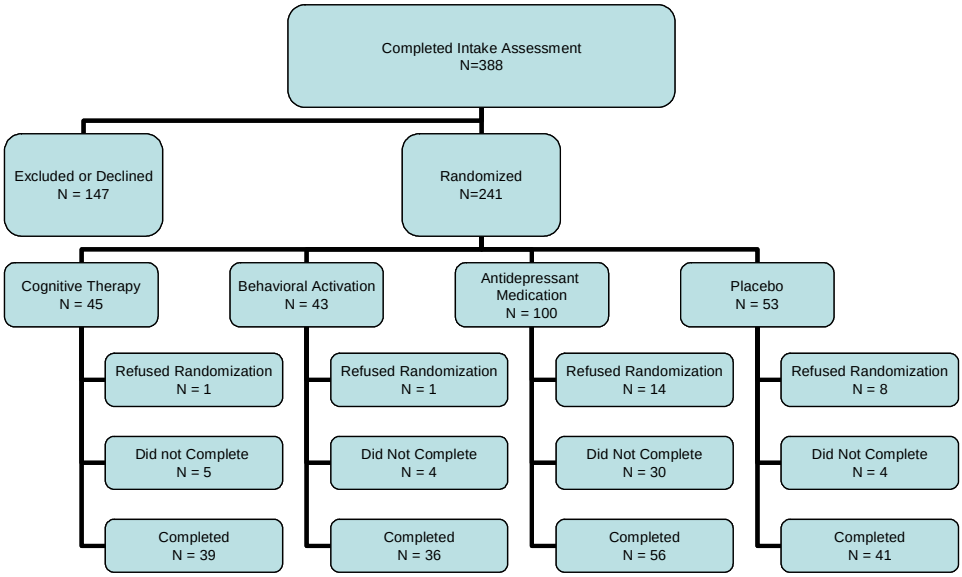
Figure Captions

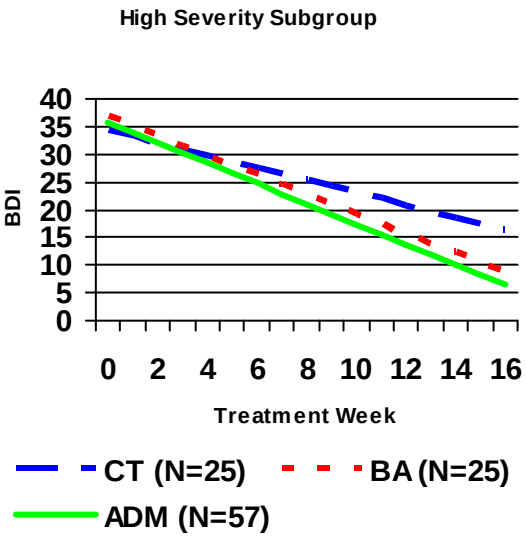
Figure 1. *Participant flow*

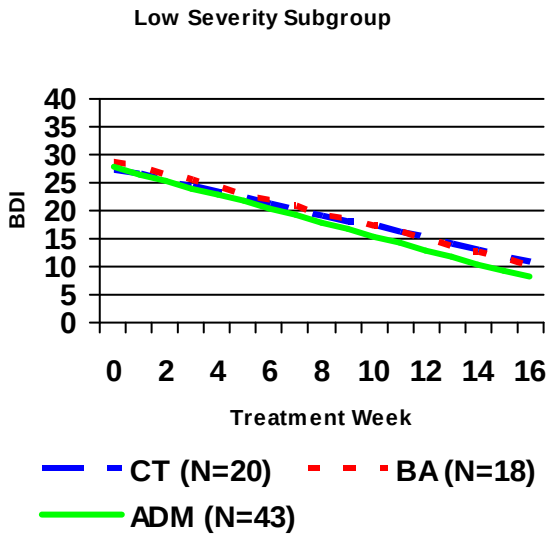
Figure 2. *BDI and HRSD slope trajectories for all active treatments during the full acute phase*

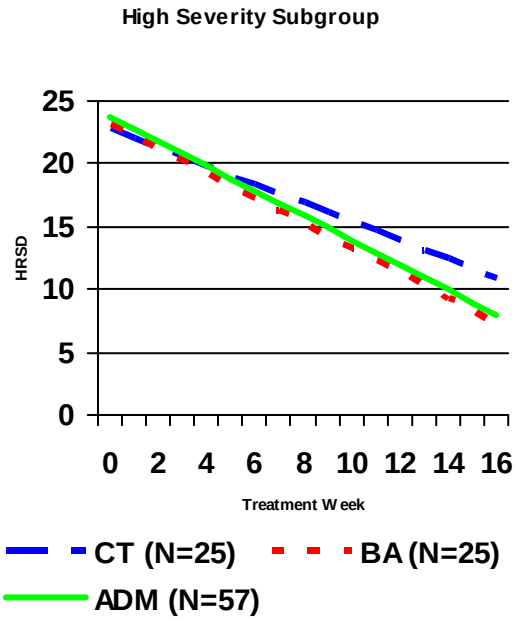
Figure 3. *Response and remission rates at post-treatment based on the BDI for the high severity subgroup*

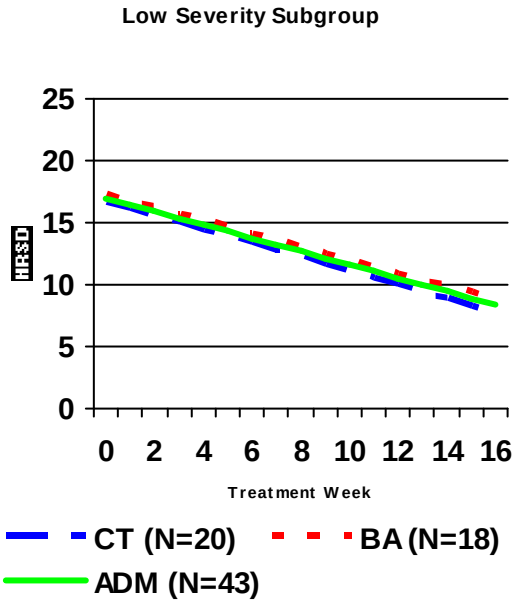
Figure 4. *Response and remission rates at post-treatment based on the HRSD for the high severity subgroup*

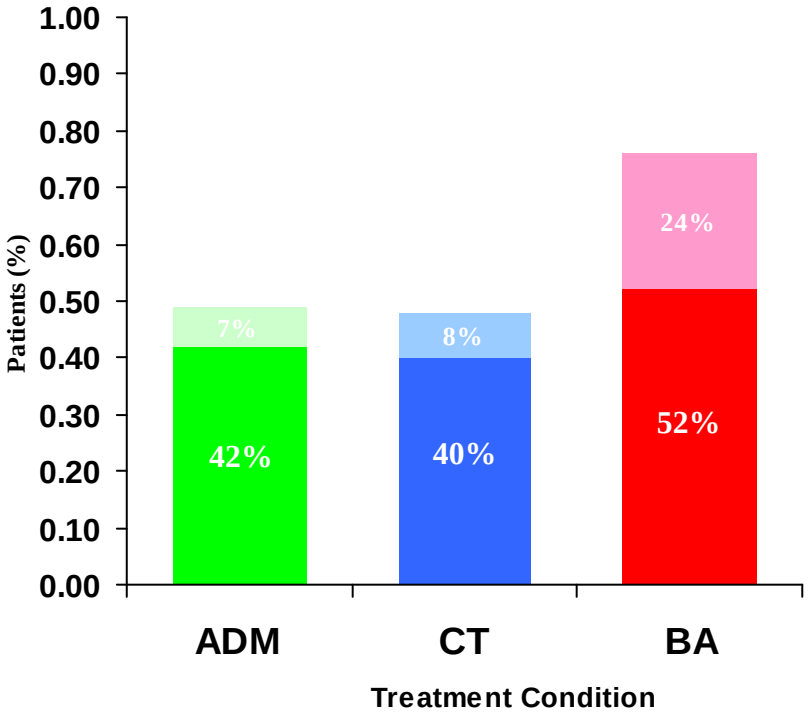

Completed Intake Assessment
N=388
Excluded or Declined
N = 147
Randomized
N=241
Cognitive Therapy
N = 45
Behavioral Activation
N = 43
Antidepressant Medication
N = 100
Placebo
N = 53
Refused Randomization
N = 1
Did not Complete
N = 5
Completed
N = 39
Refused Randomization
N = 1
Did Not Complete
N = 4
Completed
N = 36
Refused Randomization
N = 14
Did Not Complete
N = 30
Completed
N = 56
Refused Randomization
N = 8
Did Not Complete
N = 4
Completed
N = 41


High Severity Subgroup
BDI
40
35
30
25
20
15
10
5
0
0 2 4 6 8 10 12 14 16
Treatment Week
CT (N=25)
BA (N=25)
ADM (N=57)

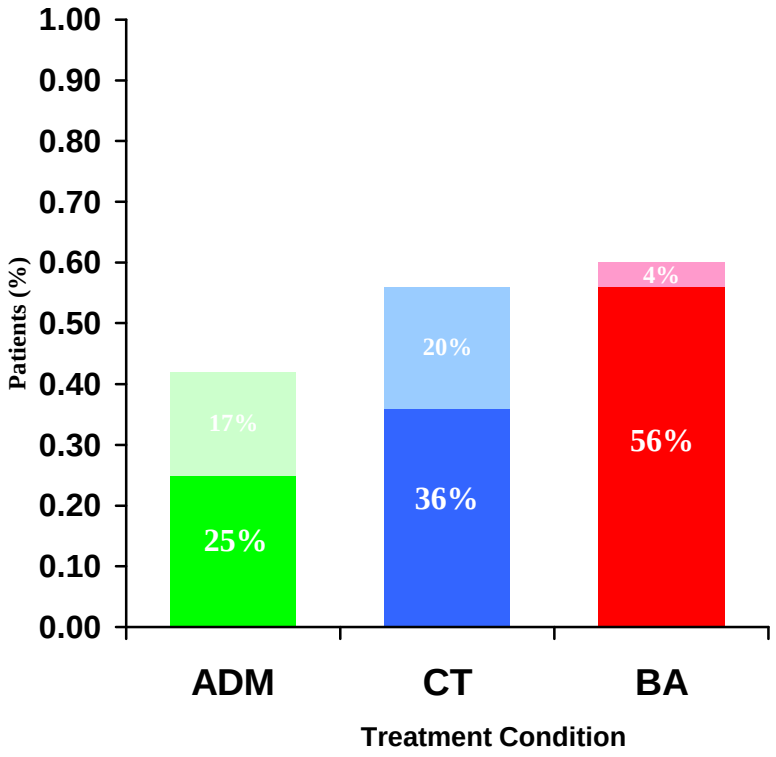

Low Severity Subgroup
BDI
40
35
30
25
20
15
10
5
0
0 2 4 6 8 10 12 14 16
Treatment Week
CT (N=20)
BA (N=18)
ADM (N=43)


High Severity Subgroup
HRSD
25
20
15
10
5
0
0 2 4 6 8 10 12 14 16
Treatment Week
CT (N=25)
BA (N=25)
ADM (N=57)


Low Severity Subgroup
HRSD
25
20
15
10
5
0
0 2 4 6 8 10 12 14 16
Treatment Week
CT (N=20)
BA (N=18)
ADM (N=43)



Note: Total bar represents BDI response; lower bar represents remission



Note: Total bar represents HRSD response; lower bar represents remission

Acknowledgements

We dedicate this study and manuscript to the late Neil S. Jacobson, Ph.D. Dr. Jacobson was the originator of this study and shaped every aspect of its inception and implementation. His untimely death in 1999 left an irreplaceable gap, but his ideas about behavior therapy and his commitment to empirical inquiry have continued to serve as an inspiration and guide.

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Footnotes

[1]IRB approval inadvertently lapsed for approximately six weeks at the time of the original principal investigator's death; approval for use and publication of data collected during that time was subsequently granted by the IRB.