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Adjunctive Behavioral Activation for the Treatment of Bipolar Depression: A Proof of Concept Trial

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Abstract

Background—Grounded in a model focused on exposure to response-contingent positive reinforcement, and with evidence supporting its acute treatment effects for unipolar depression, an adjunctive behavioral activation (BA) intervention may be especially well suited to the treatment of bipolar depression. The goal of this study was to modify BA for the adjunctive treatment of bipolar depression and to pilot it in a proof of concept trial to assess its preliminary feasibility and acceptability for this population.

Methods—Twelve adults with bipolar depression were recruited from hospital settings and enrolled in a 20-week open trial of the modified BA, delivered in 16 outpatient sessions, as an adjunct to community pharmacotherapy for bipolar disorder. Symptom severity was assessed at pre- and post-treatment by an independent evaluator. Patient satisfaction was also assessed post-treatment.

Results—Feasibility and acceptability were high, with 10 of 12 patients completing treatment, an average of 14.8 (*SD* = 5.2) of 16 sessions attended, and high levels of self-reported treatment satisfaction. Patients exhibited statistically significant improvement from pre- to post-treatment on measures of depressive symptoms, manic symptoms, and severity of suicidal ideation.

Conclusions—Although preliminary and requiring replication in a larger sample, these study data suggest that a modified BA intervention may offer promise as an adjunctive approach for the acute treatment of bipolar depression. Future studies that employ more rigorous randomized controlled designs and that directly assess potential mechanisms of action are recommended.

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Conflicts of Interest
The authors declare no conflicts of interest.

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Keywords

bipolar disorder; depression; behavioral activation; treatment; psychotherapy

Identified by the World Health Organization as one of the top 10 causes of disease burden worldwide,[1,2] bipolar disorder (BD) is a serious, disabling, and highly recurrent illness that is marked by significant functional impairment.[3,4] Although a diagnosis of BD is primarily dependent on a history of manic or hypomanic episodes, data from several large-scale, prospective studies have revealed the overwhelming burden of bipolar depression over time. Compared with mania, depressive episodes in BD are more frequent, considerably longer, and less likely to remit, with individuals spending roughly one-third to one-half of their lives suffering from depressive symptoms.[5–8] Bipolar depression, in turn, is associated with substantial functional impairment[9] and marked risk for suicide.[10,11]

Despite the severe and chronic nature of bipolar depression, knowledge concerning effective treatment is limited. Relatively few randomized controlled trials are available to guide pharmacologic treatment decisions,[12,13] and available data suggest that mood stabilizing medications are significantly less effective in treating depressive versus manic symptoms.[14] The use of adjunctive antidepressant medication remains controversial given mixed efficacy data[15] and the potential risk of treatment-emergent mania.[16] Moreover, patients may have difficulty tolerating pharmacologic treatments due to adverse effects, frequently resulting in poor rates of medication adherence.[17] Numerous psychosocial interventions have been developed and investigated as adjuncts to pharmacotherapy for BD, yet the large majority of psychosocial treatment studies have been limited to samples who were euthymic[18–23] or presented with mixed polarity.[24–30] Remarkably, the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)[31] remains the only randomized controlled trial of adjunctive psychotherapy for acute bipolar depression to date. Results from the STEP-BD trial supported the comparative efficacy of adjunctive family-focused therapy (FFT), cognitive-behavioral therapy (CBT), and interpersonal and social rhythm therapy (IPSRT) for the reduction of bipolar depression symptoms, with no differences between the active intervention groups in overall outcome, but significant differences in time to recovery and in 12-month recovery rate when compared to a collaborative care control condition.

When considering existing treatments, it is worth noting how well they match established mechanisms of illness. For example, FFT targets the family discord[32] and high expressed emotion (EE)[33,34] that have been shown to predict a poor course of illness in BD. CBT targets dysfunctional beliefs associated with the risk for and severity of mood symptoms (depression, in particular),[23,35] and IPSRT targets the social and circadian rhythm disruption that may precede and result from bipolar mood episodes.[36] Yet with the exception of Johnson and Fulford's[37] GOALS intervention, which is focused on secondary prevention of mania in euthymic individuals, no established psychosocial interventions for BD directly intervene on the level of the reward dysregulation that is also implicated in the underlying pathology of BD. Indeed, consistent with the positive emotion persistence (PEP)[38] and behavioral activation system (BAS) hypersensitivity[39,40] models of BD, there is evidence for unique patterns of heightened affective reactivity, reward drive, and sensitivity to goal

attainment in BD that appear to be associated with a lifetime history of and risk for mania. Data from our research group and others further suggest that these patterns of reward sensitivity may extend to periods when individuals with BD are depressed,[41] and that, when depressed, individuals with BD concurrently display heightened sensitivity of the behavioral inhibition system (BIS),[41–43] which guides withdrawal and avoidance motivations in response to aversive stimuli.

Given this sensitivity to both reward and punishment, an adjunctive behavioral activation (BA) intervention may be especially well suited for the treatment of bipolar depression. Initially designed as a treatment for unipolar depression,[44–46] BA directly targets the avoidance behaviors that patients may use to temporarily alleviate distress or to escape unpleasant feelings. Such mood-dependent behaviors are likely to negatively reinforce depression, thus resulting in a vicious cycle of avoidance and depression. Therefore, the aim of BA is to break this cycle of avoidance and depression by emphasizing action according to a personalized goal or plan, rather than a feeling or mood. That is, the patient is encouraged to work from the “outside-in” and to commit to behavior change despite internal mood states such as low motivation or lethargy.[44] Within this framework, the therapist and patient work together to undermine avoidance by increasing meaningful behaviors that will maximize exposure to natural reinforcements.[45,47,48]

Consistent with a model focused on increasing exposure to response-contingent positive reinforcement, there is some evidence from samples with unipolar depression that response to BA is associated with neural changes in brain regions (eg, the orbitofrontal cortex)[49,50] implicated in reward responsiveness, which have also been implicated in underlying BD pathophysiology.[51,52] BA further benefits from a sound evidence base for the reduction of depressive symptoms in unipolar samples,[53,54] and there is some evidence that BA may be more effective than a full CBT intervention for the treatment of severe depression,[55] which is frequently encountered in BD.[56] Additional potential benefits of BA for bipolar depression include a focus on regulation of sleep and activity levels, which may be especially important for mood stabilization in BD,[57] and a focus on the avoidance and withdrawal that result from the atypical symptoms (eg, hypersomnia, leaden paralysis)[58] that are common to bipolar depression.[59] Finally, BA is a relatively streamlined, pragmatic intervention, which lends itself well to dissemination in community settings.[60,61]

Although BA is theoretically and clinically well matched to the treatment of bipolar depression, it is important to address potential modifications that may be required when considering an adjunctive BA intervention. Most notably, it is critical that providers be aware of the sensitivity to goal attainment and the risk for mania in BD[39,40] when developing personalized goals and task assignments in BA. Whereas the aim of BA for unipolar depression is to decrease avoidance and increase activation, a BA intervention for bipolar depression may need to be adjusted to strike a careful balance between these two targets, so as not to indiscriminately activate or increase goal-directed activity, but rather to facilitate a return to role functioning through a process of behavioral *regulation*. In addition, there are some important key components of psychosocial interventions that are shared across existing treatments for BD that are considered to be the standard of care (eg, psychoeducation, attention to medication adherence, relapse prevention)[34] that may also be

important to incorporate into a BA model of treatment. To date, no research on BA for the treatment of bipolar depression has been published. Given the many potential benefits of BA, the primary goal of this study was to develop a modified BA for the adjunctive treatment of bipolar depression and to pilot it in an open proof of concept trial in order to evaluate its preliminary feasibility, acceptability, and efficacy.

METHOD

Participants

Participants were 12 individuals with bipolar depression who were recruited through hospital inpatient ($n = 8$) and outpatient ($n = 4$) sources. Criteria for inclusion were: a) diagnosis of bipolar I or II disorder, most recent episode depressed, as assessed using the Structured Clinical Interview for DSM-IV-TR Axis I disorders (SCID-I),[62] b) score ≥ 30 on the Inventory of Depressive Symptoms–Clinician rating (IDS-C),[63] c) ongoing medication management for bipolar disorder with a community provider, d) 18 years of age or older, and e) ability to speak, read, and understand English sufficiently well to complete study procedures. Exclusion criteria were: a) current bipolar mixed episode, b) evidence of rapid cycling within the past 12 months, c) schizophrenia or schizoaffective disorder, d) current hazardous alcohol or substance use, as evidenced by a score > 10 on the Alcohol Use Disorders Identification Test (AUDIT)[64] or ≥ 2 (for females) or ≥ 6 (for males) on the Drug Use Disorders Identification Test (DUDIT),[65] e) presence of borderline or antisocial personality disorder as assessed by the Structured Clinical Interview for DSM-IV Axis II disorders (SCID-II),[66] f) pregnancy, lactation, or a medical indication that contraindicates the use of psychotropic medications, and g) sufficient cognitive impairment to interfere with study participation (Mini Mental State Examination (MMSE)[67] < 23). Demographic and clinical characteristics of study participants are presented in Table 1.

Assessments

Diagnosis—To assess for the presence of bipolar disorder, the mood disorders and psychosis screener modules of the SCID-I[62] were administered at baseline by trained bachelor's level research assistants. The borderline and antisocial personality disorders modules of the SCID-II[66] were also administered at baseline to determine participant eligibility. Training on the SCID interviews consisted of a formal didactic workshop followed by several weeks of: a) trainee review and practice scoring of gold standard assessment recordings, b) supervised role plays, c) trainee observation of assessments in real time, and d) supervisor review of trainee-conducted assessments in real time. All raters were required to achieve kappa = 0.80 with expert faculty ratings before conducting independent diagnostic assessments. Final diagnostic decisions were based upon consensus, following a review of the SCID-I and SCID-II between the raters and the clinical team.

Symptom severity—Severity of depressive symptoms was assessed using the 30-item IDS-C,[63] on which scores range from 0 to 84, with the following severity ranges: none (0–11), mild (12–23), moderate (24–36), severe (37–46), and very severe (47–84). The IDS-C has demonstrated strong psychometric performance in several large-scale clinical trials.[63] Severity of manic symptoms was assessed using the 15-item Clinician-Administered Rating

Scale for Mania (CARS-M).[68] In addition to its established reliability and validity as an interview-based measure,[68] an additional benefit of the CARS-M is that it does not conflate mania and psychosis, but instead measures them on separate subscales. Only the mania subscale scores, ranging from 0 to 50, are included in this report. Severity of suicidal ideation was assessed using Modified Scale for Suicidal Ideation (MSSI).[69] This 18-item interview-based scale has demonstrated high levels of interrater reliability and convergent validity[69] and has been used in several clinical trials.[70] MSSI scores range from 0 to 54.

All symptom severity ratings were conducted by bachelor's level research assistants who underwent training similar to that described for the SCID interviews, with a requirement that they achieve an intraclass correlation coefficient (ICC) = 0.80 with expert faculty ratings before conducting independent assessments. In this study, agreement between expert faculty and research assistant ratings for the IDS-C (ICC = 0.98), CARS-M (ICC = 0.89), and MSSI (ICC = 0.99) was high.

Treatment satisfaction—Overall treatment satisfaction was assessed post-treatment using the Client Satisfaction Questionnaire-8 (CSQ-8).[71] This brief questionnaire contains 8 Likert-type items, with total scores ranging from 1 to 32. Higher scores reflect greater satisfaction with treatment received. The CSQ-8 has been used extensively in psychosocial treatment research, and data from previous studies support its reliability and validity.[72,73] In this study, internal consistency of the CSQ-8 was high (Cronbach's alpha = 0.96).

Procedure

All study procedures were approved by the Brown University and Butler Hospital Institutional Review Boards. Hospital charts from newly admitted patients were screened on the basis of the study's inclusion and exclusion criteria using a Protected Health Information waiver. After obtaining permission from the treating psychiatrist, patients who appeared to meet study criteria were approached, given a brief verbal overview of the study, including the nature, purpose, risks, and benefits, and invited to participate. Participants were also recruited through direct referral from outpatient mental health providers. Prior to the baseline assessment, all participants provided written informed consent to participate. The SCID-I, SCID-II, AUDIT, DUDIT, and MMSE were administered at baseline to determine eligibility. The IDS-C, CARS-M, and MSSI were administered at pre- and post-treatment and used as outcome measures for the study. All post-treatment assessments were conducted by research assistants who were blind to study aims and procedures. The study treatment was delivered by the study's first author (LMW), supervised by the study's coauthor (IWM) on a weekly basis, and consisted of 16 outpatient sessions of BA over the course of 20 weeks (weekly for the first 12 weeks and biweekly for the last 8 weeks). If clinically indicated, participants could receive up to 4 additional scheduled sessions in the final 8 weeks. Along with post-treatment outcome measures, the CSQ-8 was administered immediately after treatment. Supplemental open-ended questions were included with the CSQ-8, asking participants to share their experiences and overall satisfaction with the treatment program. Assessment and treatment were conducted in an outpatient research clinic located in an academically affiliated private psychiatric hospital. Participants were compensated for completion of study assessments.

Treatment

On the basis of the BA intervention developed by Martell and colleagues,[47,48] we provided 16 sessions of individual BA as an adjunct to community pharmacotherapy in an open pilot trial format. As specified in the manual, treatment targeted (a) *psychoeducation and behavioral monitoring*, (b) *avoidance modification and activity scheduling*, and (c) *behavioral maintenance and relapse prevention*. Although BA as manualized was already compatible with treatment of BD, we further focused the content of the intervention to directly address some of the unique concerns associated with the treatment of BD. Such modifications included incorporating specific psychoeducation about BD; in particular, the therapist addressed the heightened goal striving frequently encountered in BD,[40,74,75] which has the potential to result in plans for behavior change that may be overly stimulating and/or ambitious. Consistent with this concern, the standard BA activity chart was modified to include regular monitoring of mood at set points throughout the day (on a visual analogue scale from 0="most depressed I've ever been" to 100="most manic I've ever been") to identify and monitor any prodromal hypomanic/manic symptoms, as well as to monitor diurnal variation in mood. Assessment of medication non-adherence as an avoidance behavior was also incorporated into the standard functional analysis of behavior typically used in BA,[47,48] and BA activity scheduling was focused on identifying alternatives to avoidance that would not be overly stimulating. Finally, given the high risk for suicide in this population,[10] participants were routinely monitored for suicidal ideation, and elements of safety planning (eg, means restriction)[76] were also incorporated throughout the intervention.

RESULTS

Of the 12 participants, 10 completed the study intervention. Of the 2 who did not complete the trial, 1 participant was lost to follow-up with no additional contact after 3 treatment sessions. After completing 4 treatment sessions, the other participant was rehospitalized for an extended (4+ weeks) period and was thus unable to continue participation in the outpatient treatment protocol. However, this participant completed the post-treatment assessment. Consistent with an intent-to-treat approach, these data are included in all outcome analyses. For all 12 study participants, average session attendance was 14.8 (SD = 5.2) of the 16 sessions offered.

Depression Outcomes

Means and standard deviations for all study variables are presented in Table 2. IDS-C scores revealed that, on average, participants fell into the severe category of depressive symptoms at study entry and the moderate category at study completion. Results from paired samples t tests indicated a statistically significant decrease in depressive symptoms, $t(10) = 5.4$, $P = 0.001$, from pre- to post-treatment, with a large effect size, Cohen's $d = 1.3$. Following study completion, 6 of the 11 (55%) participants for whom data were available met criteria for treatment response, as defined by at least a 50% reduction in depressive symptoms from pre- to post-treatment. Given the high average depression severity at study entry in the study sample, additional analyses focused on the clinical significance of the study findings, using Jacobson and Truax's reliable change index (RCI).[77] Participants were determined to have met criteria for clinically significant improvement in depressive symptoms if their RCI was

< −1.96 from pre- to post-treatment, which was calculated using psychometric data from the IDS-C. Using this threshold, 10 of the 11 (91%) participants demonstrated clinically significant improvement in depressive symptoms (RCIs ranging from −9.38 to −2.32) from pre- to post-treatment.

Other Symptom Outcomes

Consistent with the study design, the average CARS-M score revealed only mild elevations in manic symptoms at baseline. Over the course of treatment, there was nevertheless a statistically significant decrease in manic symptoms, $t(10) = 2.6$, $P = 0.025$, with average post-treatment scores in the low severity range for the sample. Average MSSI scores were in the moderate range for severity of suicidal ideation at study entry, and significantly improved over the course of treatment, $t(10) = 3.6$, $P = 0.005$, with average post-treatment scores in the low severity range. Cohen's d estimates revealed that reductions in manic symptom severity (Cohen's $d = 1.0$) and severity of suicidal ideation (Cohen's $d = 1.0$) both fell within the range for a large effect size.

Treatment Acceptability

Overall, participants reported high levels of satisfaction with the treatment, as assessed by the CSQ-8 (mean = 30.5, $SD = 2.1$). When asked what they found to be helpful about the study treatment, participants wrote,: "being educated," "insight into bipolar [disorder]," "activity charts and discussions," "topics discussed, especially the idea of mood-dependent behavior," "behavior exercises," "helped me become aware of behaviors and form strategies and habits to manage episodes," "homework assignments and exercises," "the fact that [the treatment] was tailored to my situation," "the structure of appointments," and "the opportunity to review, discuss, and plan." When asked what we could do to improve the treatment, the majority of respondents wrote, "nothing" or left this section blank. One participant suggested that the worksheets "could be further refined to be more user friendly," and another reported having "a difficult time managing the logging and writing, although I did get the benefit of what I did do."

DISCUSSION

Although this study represents an early stage of treatment development and future research using larger samples will be necessary, results from this pilot study provide some encouraging, preliminary support for the initial feasibility and acceptability of an adjunctive BA intervention modified for the acute treatment of bipolar depression. In general, participants engaged in and regularly attended the BA therapy sessions, were accepting of the treatment rationale, and reported high levels of satisfaction with the treatment. Consistent with the theoretical rationale for the treatment, participants identified several direct targets of BA (eg, psychoeducation, functional analysis of behavior, alternatives to mood-dependent behavior, behavioral exercises) as elements of the treatment that they found to be particularly helpful.

With the caveat that data derived from small pilot trials should be interpreted with caution,[78] the data from this study provide some preliminary support for further evaluation of BA as an

adjunctive treatment for bipolar depression. On average, there was a significant reduction in depressive symptoms from pre- to post-treatment, with 91% evidencing clinically significant improvement and 55% of the participants reporting a 50% or greater reduction in depressive symptoms. Although it is difficult to directly compare depression response in this trial to other psychotherapy trials for BD, given that the majority of studies have not focused on the acute treatment of depression, and that the primary outcomes in the STEP-BD were time to recovery and recovery rate at 12-month follow-up,[31] study outcomes are generally comparable to those reported for BA in samples of patients with unipolar depression.[53] For example, in the largest trial of BA for unipolar depression to date, Dimidjian et al.[55] reported a 60% response rate in the subset of participants identified as “high severity” at study entry.

Consistent with moderately strong severity of suicidal ideation among participants at study entry, it became clear in our treatment development efforts that a BA intervention for bipolar depression should routinely address the high risk for suicide encountered in BD.[10] Consistent with this clinical stance, data from this study revealed significant reductions in the severity of suicidal ideation from pre- to post-treatment, with average MSSI scores falling into the near-absent range at study completion. Although there has been some psychosocial treatment development directly targeting suicide risk in samples of youth with BD,[79,80] to date there have been comparatively fewer parallel efforts in adult samples. Although the data from this study are preliminary and require replication in larger samples, they add to an emerging literature on non-pharmacologic suicide risk reduction interventions for adults with BD.

Another question about BA for bipolar depression was whether it could be applied in such a way as to limit potential risks associated with “activation” and recurrence of manic symptoms. In this pilot study, the level of manic symptoms remained low throughout the study period, and in fact significantly decreased from pre- to post-treatment. Given the study inclusion/exclusion criteria, this finding likely reflects reductions in some of the overlapping symptoms of mania and depression (eg, irritability, agitation) rather than features that are more unique to mania (eg, elated mood). Nevertheless, given concerns about activation and the potential risk for mania, this finding also reflects the preliminary safety of BA as an adjunctive intervention for bipolar depression, especially when modified to emphasize *regulation* of behaviors.

Despite the significant clinical improvements noted across the study period, participants did, on average, remain symptomatic at study completion. Given the average high severity of depression at study entry, it is possible that a longer duration of BA may be required for this population, which is consistent with the 30 to 40 week duration that has typically been used in delivering other adjunctive psychotherapies for BD.[31] In addition, being an adjunctive intervention, BA was evaluated in the context of routine outpatient pharmacotherapy for BD, which was unrestricted in this study. Thus it is possible that the heterogeneity of medication regimens across the study sample may have influenced study outcomes. For example, the side effect profile of certain medications that are critical for mania prophylaxis (eg, atypical antipsychotics) may mimic certain symptoms of depression (eg, hypersomnia, weight gain, lethargy)[81] and thus may inadvertently contribute to a potential floor effect for change in depression over time among patients treated with such agents. Although this question could

not be more thoroughly evaluated in this study, given its limited size and scope, it may be important to take this issue into consideration in future studies of BA and other adjunctive interventions for bipolar depression.

The study described here was designed as a pragmatic proof of concept trial to assess feasibility and acceptability of adjunctive BA for bipolar depression, and future research will need to address several additional limitations of this research. Studies using larger samples, a randomized controlled design, and post-treatment follow-up will be imperative to properly evaluate the efficacy of BA for bipolar depression. It will also be imperative for future studies to include more racially and ethnically diverse samples as well as individuals with both bipolar I and II depression. Our study was further limited by the use of only one therapist, so that future research should incorporate formal evaluations of therapist fidelity to the treatment manual. Finally, given the pilot nature of this research, it is important to interpret outcomes with caution, as effect sizes derived from small samples may be unstable.[78] As recommended in the literature,[82] indices of clinical significance were provided to complement more traditional inferential statistical methods to partly address this limitation associated with pilot trials.

CONCLUSION

Given the continued challenges clinicians face in the clinical management of bipolar depression, identification of additional interventions that can be included in the larger armamentarium of treatment options remains an area of high priority. Grounded in a model focused on exposure to response-contingent positive reinforcement, which may be particularly salient to the underlying pathology of BD,[38–40] and as a treatment with established efficacy for the reduction of unipolar depression,[53–55] data from this pilot trial provide some preliminary support for BA as potentially feasible, acceptable, and efficacious treatment for bipolar depression. Future research that incorporates measurement and evaluation of purported mechanisms of action of BA (eg, change in approach and avoidance-related behaviors) will be critical in advancing this line of research in BD. Future research will also be necessary to replicate study findings and to more carefully evaluate BA for bipolar depression using more rigorous, randomized controlled designs.

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References

1. Murray, C.; Lopez, A. The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Cambridge, MA: Harvard University Press; 1996.
2. Chisholm D, van Ommeren M, Ayuso-Mateos JL, et al. Cost-effectiveness of clinical interventions for reducing the global burden of bipolar disorder. Br J Psychiatry. 2005; 187:559–567. [PubMed: 16319409]
3. Solomon DA, Keitner GI, Miller IW, et al. Course of illness and maintenance treatments for patients with bipolar disorder. J Clin Psychiatry. 1995; 56:5–13. [PubMed: 7836345]

4. Chang CK, Hayes RD, Perera G, et al. Life expectancy at birth for people with serious mental illness and other major disorders from a secondary mental health care case register in London. PLoS ONE. 2011; 6:e19590. [PubMed: 21611123]
5. Judd LL, Akiskal HS, Schettler PJ, et al. A prospective investigation of the natural history of the long-term weekly symptomatic status of bipolar II disorder. Arch Gen Psychiatry. 2003; 60:261–269. [PubMed: 12622659]
6. Judd LL, Akiskal HS, Schettler PJ, et al. The long-term natural history of the weekly symptomatic status of bipolar I disorder. Arch Gen Psychiatry. 2002; 59:530–537. [PubMed: 12044195]
7. Judd LL, Schettler PJ, Akiskal HS, et al. Long-term symptomatic status of bipolar I vs. bipolar II disorders. Int J Neuropsychopharmacol. 2003; 6:127–137. [PubMed: 12890306]
8. Post RM, Denicoff KD, Leverich GS, et al. Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH life chart method. J Clin Psychiatry. 2003; 64:680–690. [PubMed: 12823083]
9. Calabrese JR, Hirschfeld RM, Reed M, et al. Impact of bipolar disorder on a U.S. community sample. J Clin Psychiatry. 2003; 64:425–432. [PubMed: 12716245]
10. Wedig, MM.; Weinstock, LM. Suicide and bipolar disorder: the state of the evidence. In: Plunkett, JM., editor. Bipolar Disorder: Causes, Diagnosis, and Treatment. New York: Nova Science Publishers; 2012. p. 293-312.
11. Tondo L, Isacsson G, Baldessarini R. Suicidal behaviour in bipolar disorder: risk and prevention. CNS Drugs. 2003; 17:491–511. [PubMed: 12751919]
12. Thase ME. Bipolar depression: diagnostic and treatment considerations. Dev Psychopathol. 2006; 18:1213–1230. [PubMed: 17064435]
13. Yatham LN, Kennedy SH, O'Donovan C, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) guidelines for the management of patients with bipolar disorder: consensus and controversies. Bipolar Disord. 2005; 7(Suppl 3):5–69. [PubMed: 15952957]
14. Suppes T, Kelly DI, Perla JM. Challenges in the management of bipolar depression. J Clin Psychiatry. 2005; 66(Suppl 5):11–16. [PubMed: 16038597]
15. Sachs GS, Nierenberg AA, Calabrese JR, et al. Effectiveness of adjunctive antidepressant treatment for bipolar depression. N Engl J Med. 2007; 356:1711–1722. [PubMed: 17392295]
16. Pacchiarotti I, Bond DJ, Baldessarini RJ, et al. The International Society for Bipolar Disorders (ISBD) Task Force report on antidepressant use in bipolar disorders. Am J Psychiatry. 2013; 170:1249–1262. [PubMed: 24030475]
17. Sajatovic M, Biswas K, Kilbourne AK, et al. Factors associated with prospective long-term treatment adherence among individuals with bipolar disorder. Psychiatr Serv. 2008; 59:753–759. [PubMed: 18586992]
18. Ball JR, Mitchell PB, Corry JC, et al. A randomized controlled trial of cognitive therapy for bipolar disorder: focus on long-term change. J Clin Psychiatry. 2006; 67:277–286. [PubMed: 16566624]
19. Colom F, Vieta E, Martinez-Aran A, et al. A randomized trial on the efficacy of group psychoeducation in the prophylaxis of recurrences in bipolar patients whose disease is in remission. Arch Gen Psychiatry. 2003; 60:402–407. [PubMed: 12695318]
20. Lam DH, Watkins ER, Hayward P, et al. A randomized controlled study of cognitive therapy for relapse prevention for bipolar affective disorder: outcome of the first year. Arch Gen Psychiatry. 2003; 60:145–152. [PubMed: 12578431]
21. Perry A, Tarrier N, Morriss R, et al. Randomised controlled trial of efficacy of teaching patients with bipolar disorder to identify early symptoms of relapse and obtain treatment. BMJ. 1999; 318:149–153. [PubMed: 9888904]
22. Reinares M, Colom F, Sanchez-Moreno J, et al. Impact of caregiver group psychoeducation on the course and outcome of bipolar patients in remission: a randomized controlled trial. Bipolar Disord. 2008; 10:511–519. [PubMed: 18452447]
23. Zaretsky A, Lancee W, Miller C, et al. Is cognitive-behavioural therapy more effective than psychoeducation in bipolar disorder? Can J Psychiatry. 2008; 53:441–448. [PubMed: 18674402]
24. Bauer MS, McBride L, Williford WO, et al. Collaborative care for bipolar disorder: Part II. Impact on clinical outcome, function, and costs. Psychiatr Serv. 2006; 57:937–945. [PubMed: 16816277]

25. Frank E, Kupfer DJ, Thase ME, et al. Two-year outcomes for interpersonal and social rhythm therapy in individuals with bipolar I disorder. Arch Gen Psychiatry. 2005; 62:996–1004. [PubMed: 16143731]
26. Miklowitz DJ, George EL, Richards JA, et al. A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. Arch Gen Psychiatry. 2003; 60:904–912. [PubMed: 12963672]
27. Miller IW, Solomon DA, Ryan CE, et al. Does adjunctive family therapy enhance recovery from bipolar I mood episodes? J Affect Disord. 2004; 82:431–436. [PubMed: 15555694]
28. Simon GE, Ludman EJ, Bauer MS, et al. Long-term effectiveness and cost of a systematic care program for bipolar disorder. Arch Gen Psychiatry. 2006; 63:500–508. [PubMed: 16651507]
29. Weiss RD, Griffin ML, Kolodziej ME, et al. A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. Am J Psychiatry. 2007; 164:100–107. [PubMed: 17202550]
30. Scott J, Paykel E, Morriss R, et al. Cognitive-behavioural therapy for severe and recurrent bipolar disorders: randomised controlled trial. Br J Psychiatry. 2006; 188:313–320. [PubMed: 16582056]
31. Miklowitz DJ, Otto MW, Frank E, et al. Psychosocial treatments for bipolar depression: A 1-year randomized trial from the Systematic Treatment Enhancement Program. Arch Gen Psychiatry. 2007; 64:419–426. [PubMed: 17404119]
32. Weinstock LM, Keitner GI, Ryan CE, et al. Family functioning and mood disorders: a comparison between patients with major depressive disorder and bipolar I disorder. J Consult Clin Psychol. 2006; 74:1192–1202. [PubMed: 17154748]
33. Kim EY, Miklowitz DJ. Expressed emotion as a predictor of outcome among bipolar patients undergoing family therapy. J Affect Disord. 2004; 82:343–352. [PubMed: 15555685]
34. Miklowitz DJ, Scott J. Psychosocial treatments for bipolar disorder: cost-effectiveness, mediating mechanisms, and future directions. Bipolar Disord. 2009; 11(Suppl 2):110–122. [PubMed: 19538690]
35. Parikh SV, Zaretsky A, Beaulieu S, et al. A randomized controlled trial of psychoeducation or cognitive-behavioral therapy in bipolar disorder: a Canadian Network for Mood and Anxiety Treatments (CANMAT) study. J Clin Psychiatry. 2012; 73:803–810. [PubMed: 22795205]
36. Frank E. Interpersonal and social rhythm therapy: a means of improving depression and preventing relapse in bipolar disorder. J Clin Psychol. 2007; 63:463–473. [PubMed: 17417811]
37. Johnson SL, Fulford D. Preventing mania: a preliminary examination of the GOALS Program. Behav Ther. 2009; 40:103–113. [PubMed: 19433142]
38. Gruber J. Rethinking positive emotion disturbance: positive emotion persistence (PEP) in bipolar disorder. Bipolar Disord. 2011; 13:51–52.
39. Alloy LB, Bender RE, Whitehouse WG, et al. High behavioral approach system (BAS) sensitivity, reward responsiveness, and goal-striving predict first onset of bipolar spectrum disorders: a prospective behavioral high-risk design. J Abnorm Psychol. 2012; 121:339–351. [PubMed: 22004113]
40. Johnson SL. Mania and dysregulation in goal pursuit: a review. Clin Psychol Rev. 2005; 25:241–262. [PubMed: 15642648]
41. Weinstock, LM.; Gruber, J.; Miller, IW. A tale of two depressions? Reward sensitivity and emotion regulation differentiate bipolar and unipolar depression. Poster presented at the annual meeting of the Society for Research in Psychopathology; Oakland, CA. September, 2013;
42. Alloy LB, Abramson LY, Walshaw PD, et al. Behavioral approach system and behavioral inhibition system sensitivities and bipolar spectrum disorders: prospective prediction of bipolar mood episodes. Bipolar Disord. 2008; 10:310–322. [PubMed: 18271911]
43. Meyer B, Johnson SL, Winters R. Responsiveness to threat and incentive in bipolar disorder: relations of the BIS/BAS scales with symptoms. J Psychopathol Behav. 2001; 23:133–143.
44. Jacobson NS, Martell CR, Dimidjian S. Behavioral activation treatment for depression: returning to contextual roots. Clin Psychol. 2001; 8:255–270.
45. Lejuez CW, Hopko DR, Acierno R, et al. Ten year revision of the brief behavioral activation treatment for depression: revised treatment manual. Behav Modif. 2011; 35:111–161. [PubMed: 21324944]

46. Lejuez CW, Hopko DR, Hopko SD. A brief behavioral activation treatment for depression: treatment manual. Behav Modif. 2001; 25:255–286. [PubMed: 11317637]
47. Martell, CR.; Addis, ME.; Jacobson, NS. Depression in Context: Strategies for Guided Action. New York: W. W. Norton & Co; 2001.
48. Martell, CR.; Dimidjian, S.; Herman-Dunn, R. Behavioral Activation for Depression: A Clinician's Guide. New York: Guilford; 2013.
49. Dichter GS, Felder JN, Petty C, et al. The effects of psychotherapy on neural responses to rewards in major depression. Biol Psychiatry. 2009; 66:886–897. [PubMed: 19726030]
50. Dichter GS, Felder JN, Smoski MJ. The effects of brief behavioral activation therapy for depression on cognitive control in affective contexts: an fMRI investigation. J Affect Disord. 2010; 126:236–244. [PubMed: 20421135]
51. Nery FG, Chen HH, Hatch JP, et al. Orbitofrontal cortex gray matter volumes in bipolar disorder patients: a region-of-interest MRI study. Bipolar Disord. 2009; 11:145–153. [PubMed: 19267697]
52. Nusslock R, Almeida JR, Forbes EE, et al. Waiting to win: elevated striatal and orbitofrontal cortical activity during reward anticipation in euthymic bipolar disorder adults. Bipolar Disord. 2012; 14:249–260. [PubMed: 22548898]
53. Mazzucchelli T, Kane R, Rees C. Behavioral activation treatments for depression in adults: a meta-analysis and review. Clin Psychol. 2009; 16:383–411.
54. Mazzucchelli TG, Kane RT, Rees CS. Behavioral activation interventions for well-being: a meta-analysis. J Posit Psychol. 2010; 5:105–121. [PubMed: 20539837]
55. Dimidjian S, Hollon SD, Dobson KS, et al. Randomized trial of behavioral activation, cognitive therapy, and antidepressant medication in the acute treatment of adults with major depression. J Consult Clin Psychol. 2006; 74:658–670. [PubMed: 16881773]
56. Weinstock LM, Strong D, Uebelacker LA, et al. Differences in depression symptom endorsement between bipolar disorder and major depressive disorder: lessons learned from the National Epidemiologic Survey on Alcohol and Related Conditions. Bipolar Disord. 2013; 15:110–111. [PubMed: 23231053]
57. Frank E, Hlastala S, Ritenour A, et al. Inducing lifestyle regularity in recovering bipolar disorder patients: results from the maintenance therapies in bipolar disorder protocol. Biol Psychiatry. 1997; 41:1165–1173. [PubMed: 9171907]
58. Weinstock LM, Munroe MK, Miller IW. Behavioral activation for the treatment of atypical depression: a pilot open trial. Behav Modif. 2011; 35:403–424. [PubMed: 21507998]
59. Bowden CL. A different depression: clinical distinctions between bipolar and unipolar depression. J Affect Disord. 2005; 84:117–125. [PubMed: 15708408]
60. Hubley S, Woodcock EA, Dimeff LA, et al. Disseminating behavioural activation for depression via online training: preliminary steps. Behav Cogn Psychother. 2015; 43:224–238. [PubMed: 24382130]
61. Puspitasari A, Kanter JW, Murphy J, et al. Developing an online, modular, active learning training program for behavioral activation. Psychotherapy. 2013; 50:256–265. [PubMed: 23398030]
62. First, M.; Spitzer, R.; Gibbon, M., et al. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P). New York: Biometrics Research, New York State Psychiatric Institute; 2002.
63. Trivedi MH, Rush AJ, Ibrahim HM, et al. The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: a psychometric evaluation. Psychol Med. 2004; 34:73–82. [PubMed: 14971628]
64. Babor, TF.; Higgins-Biddle, JC.; Saunders, JB., et al. The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care. Geneva, Switzerland: World Health Organization; 2001.
65. Berman, AH.; Bergman, H.; Palmstierna, T., et al. The Drug Use Disorders Identification Test Manual. Stockholm, Sweden: Karolinska Institute; 2003.
66. First, MB.; Gibbon, M.; Spitzer, RL., et al. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II). Washington, DC: American Psychiatric Press; 1997.

67. Folstein, MF.; Folstein, SE. Mini-Mental State Examination: Clinical Guide. Lutz FL: Psychological Assessment Resources; 1975.

68. Altman EG, Hedeker DR, Janicak PG, et al. The Clinician-Administered Rating Scale for Mania (CARS-M): development, reliability, and validity. Biol Psychiatry. 1994; 36:124–134. [PubMed: 7948445]

69. Miller IW, Norman WH, Bishop SB, et al. The Modified Scale for Suicidal Ideation: reliability and validity. J Consult Clin Psychol. 1986; 54:724–725. [PubMed: 3771893]

70. Mukhopadhyay, P. Suicide: Its assessment and prediction. In: Kumar, U.; Mandal, MK., editors. Suicidal Behaviour: Assessment of People-at-Risk. New Delhi, India: SAGE Publications; 2010.

71. Attkisson CC, Zwick R. The Client Satisfaction Questionnaire: Psychometric properties and correlations with service utilization and psychotherapy outcome. Eval Program Plann. 1982; 5:233–237. [PubMed: 10259963]

72. Larsen DL, Attkisson C, Hargreaves WA, et al. Assessment of client/patient satisfaction: development of a general scale. Eval Program Plann. 1979; 2:197–207. [PubMed: 10245370]

73. Nguyen TD, Attkisson CC, Stegner BL. Assessment of patient satisfaction: development and refinement of a Service Evaluation Questionnaire. Eval Program Plann. 1983; 6:299–313. [PubMed: 10267258]

74. Johnson SL, Carver CS. Extreme goal setting and vulnerability to mania among undiagnosed young adults. Cognitive Ther Res. 2006; 30:377–395.

75. Johnson SL, Sandrow D, Meyer B, et al. Increases in manic symptoms after life events involving goal attainment. J Aborm Psychol. 2000; 109:721–727.

76. Stanley B, Brown GK. Safety planning intervention: a brief intervention to mitigate suicide risk. Cogn Behav Pract. 2012; 19:256–264.

77. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol. 1991; 59:12–19. [PubMed: 2002127]

78. Kraemer HC, Mintz J, Noda A, et al. Caution regarding the use of pilot studies to guide power calculations for study proposals. Arch Gen Psychiatry. 2006; 63:484–489. [PubMed: 16651505]

79. Goldstein TR, Fersch-Podrat RK, Rivera M, et al. Dialectical behavior therapy (DBT) for adolescents with bipolar disorder: results from a pilot randomized trial. J Child Adolesc Psychopharmacol. 2015; 25:140–149. [PubMed: 25010702]

80. Goldstein TR, Axelson DA, Birmaher B, et al. Dialectical behavior therapy for adolescents with bipolar disorder: a 1-year open trial. J Am Acad Child Adolesc Psychiatry. 2007; 46:820–830. [PubMed: 17581446]

81. Masand PS. Atypical antipsychotics in the treatment of affective symptoms: a review. Ann Clin Psychiatry. 2004; 16:3–13. [PubMed: 15147108]

82. Kraemer HC, Kupfer DJ. Size of treatment effects and their importance to clinical research and practice. Biol Psychiatry. 2006; 59:990–996. [PubMed: 16368078]

Table 1

Demographic and clinical characteristics of study participants (N = 12)

	Mean (SD)	n (%)
Age (y)	47.3 (12.9)	
Sex (female)		6 (50)
Race (white)		12 (100)
Ethnicity (non-Hispanic)		12 (100)
BD subtype (bipolar I)		12 (100)
Age of BD onset (y)	21.7 (13.6)	
Total psychotropic medications	2.8 (1.2)	
Class of psychotropic medication		
Lithium		4 (33)
Atypical antipsychotic		5 (42)
Anticonvulsant		7 (58)
Antidepressant		7 (58)
Benzodiazepine		6 (50)
Stimulant		2 (17)
Hypnotic		1 (8)
Marital status		
Married/cohabiting		4 (33)
Divorced		4 (33)
Single, never married		4 (33)
Household income		
<US$20,000		5 (42)
US$20,000–$39,999		2 (17)
US$40,000–$59,999		2 (17)
US$60,000 and more		3 (25)
Employment status		
Employed, full time		1 (8)
Employed, part time		2 (17)
Retired		1 (8)
Unemployed		5 (42)
Disability		3 (25)

BD indicates bipolar disorder.

Table 2

Means, Standard Deviations, and Differences from Pre- to Post-Treatment for Study Outcomes

	Pre-Treatment	Post-Treatment			
Outcome	***Mean (SD)***	***Mean (SD)***	***t*(10)**	***P***	***d***
IDS-C	44.2 (7.9)	24.9 (12.5)	5.4	0.001	1.3
CARS-M	6.7 (4.3)	2.6 (2.5)	2.6	0.025	1.0
MSSI	15.2 (13.4)	3.0 (7.5)	3.6	0.005	1.0
CSQ-8		30.5 (2.1)			

IDS-C = Inventory of Depressive Symptoms–Clinician Rated; CARS-M = Clinician-Administered Rating Scale for Mania; MSSI = Modified Scale for Suicidal Ideation; CSQ-8 = Client Satisfaction Questionnaire-8