HHS Public Access

Author manuscript

J Psychiatr Pract. Author manuscript; available in PMC 2016 September 01.

Published in final edited form as:

J Psychiatr Pract. 2015 September ; 21(5): 320–333. doi:10.1097/PRA.0000000000000092.

Acceptance-based Behavior Therapy for Depression with Psychosis: Results from a Pilot Feasibility Randomized Controlled Trial

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Abstract

Acceptance-based depression and psychosis therapy (ADAPT), a mindfulness/acceptance-based behavioral activation treatment, showed clinically significant effects in the treatment of depression with psychosis in a previous open trial. The goal of the current study was to further test the feasibility of ADAPT to determine the utility of testing it in a future clinical trial, following a stage model of treatment development. Feasibility was determined by randomizing a small number of patients (N = 13) with comorbid depression and psychosis to medication treatment as usual plus enhanced assessment and monitoring (EAM) versus ADAPT for 4 months of outpatient treatment. Both conditions were deemed acceptable by patients. Differences in between-subjects effect sizes favored ADAPT post-treatment and were in the medium to large range for depression, psychosocial functioning, and experiential avoidance (ie, the target mechanism). Thus ADAPT shows promise for improving outcomes compared to medications alone and requires testing in a fully powered randomized trial.

Keywords

acceptance-based depression and psychosis therapy (ADAPT); major depression with psychotic features; schizophrenia; acceptance and commitment therapy; behavioral activation; treatment development

INTRODUCTION

Depression and psychosis frequently co-occur,[1–3], and this pattern of comorbidity is associated with increased illness severity, functional impairment, and treatment resistance

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Conflicts of Interest

The authors declare no conflicts of interest.

compared with either disorder alone.[2,4,5] Traditionally, depression with psychosis has been treated with medications.[6] However, the limitations of psychotropic medications, including inadequate or incomplete response, relapse, and continued functional impairment, are well known.[7,8] Combining medication with evidence-based psychotherapy produces clinically significant improvement over medications alone for severe depression and psychotic disorders.[9,10] However, few studies have specifically focused on addressing both depression and psychosis in psychotherapy.

Two behavioral therapies show promise for treating depression with co-occurring psychosis. Behavioral activation is designated as having strong empirical support for the treatment of depression by the American Psychological Association[11] based on meta-analyses showing evidence of its efficacy.[11,12] The goal of behavioral activation as to increase engagement in functional, goal-directed, and valued activities to improve patient contact with environmental positive reinforcement.[13] Behavioral activation has also recently shown promise for treating the negative symptoms of schizophrenia.[14] Acceptance and commitment therapy is a behavioral therapy that is designed to increase psychological flexibility by fostering cognitive defusion, acceptance, mindfulness, self-as-context, values, and committed action.[15] Acceptance and commitment therapy is recognized by the American Psychological Association as having a modest level of empirical support for the treatment of depression and psychosis.[16,17] It is also listed as an evidence-based practice by the Substance Abuse and Mental Health Services Administration.[18] Several meta-analyses have demonstrated the efficacy of acceptance and commitment therapy for a number of different conditions and its potential advantages compared with other psychological treatments.[19–23] Both behavioral activation and acceptance and commitment therapy share similar philosophical underpinnings, making their techniques more compatible with each other and making it easier to integrate them.

Behavioral activation and acceptance and commitment therapy both posit that experiential avoidance, or the attempt to escape unwanted internal experiences (eg, thoughts and feelings) even when doing so causes impairment, is an important factor in the development and maintenance of psychopathology.[24] Experiential avoidance has been implicated in nonpsychotic depression,[25,26] and recent research also suggests similar associations with psychotic experiences. For example, Shawyer et al reported that experiential avoidance was related to depression and hallucinations in a sample of 43 patients with psychotic disorders.[27] A study by White et al in a sample of 30 patients following a psychotic episode showed that the presence of experiential avoidance predicted depression and anxiety symptoms.[28] Recent work has also shown that experiential avoidance is positively associated with delusional experiences such as paranoia,[29,30] and that it may contribute to cognitive impairments in schizophrenia.[31] Experiential avoidance theoretically underpins the experiences of both psychosis and depression by fostering preoccupation with internal experiences that exacerbate these symptoms.[32] Thus, experiential avoidance may offer an efficient psychosocial treatment target in individuals prone to experiencing both depression and psychosis, and research in this area suggests the importance of changing avoidant-based coping habits.

We initially embarked on a program of research to develop a novel psychosocial treatment for psychosis and depression based partly on the stage model adopted by the National Institutes of Health.[33] In Stage 1, pilot trials are conducted to refine the treatment protocol and examine the feasibility and acceptability of the intervention. Stage 1a entails conducting an open trial. Stage 1b involves a small pilot randomized controlled trial to examine initial efficacy and develop methods and procedures in preparation for future testing. Stage 2 involves conducting a full-scale randomized controlled trial to test the formal efficacy of the intervention, and Stage 3 examines the effectiveness of the intervention in more "real world" settings. However, the stage approach has been criticized in recent years for being too linear and rigid. Emerging treatment development models propose ways of improving this approach, such as increasing clarity of underlying assumptions, links with basic research, and attention to mechanisms of action and dissemination/implementation issues earlier in the process.[34] Recent recommendations also have argued for a reduced focus on formal hypothesis testing (due to unreliability of effects in small samples) in Stage 1b studies, and instead have emphasized the goal of further assessing the feasibility and acceptability of treatments and verifying the appropriateness of the randomization procedures being used.[35]

Recently, White et al. conducted a pilot randomized controlled trial of a treatment based on acceptance and commitment therapy for addressing emotional dysfunction following a psychotic episode ($N = 27$).[28] Compared with treatment as usual, acceptance and commitment therapy produced greater improvements in depression, negative symptoms, and mindfulness, and resulted in fewer crisis contacts. Although White et al focused mainly on patients diagnosed with primary psychotic disorders following a psychotic episode, our work targeted currently symptomatic patients with affective psychosis (eg, major depression with psychotic features). We had earlier conducted an open trial of acceptance-based depression and psychosis therapy (ADAPT), which integrates behavioral activation and acceptance and commitment therapy for psychotic depression.[36] Results of the open trial showed large, clinically significant and sustained treatment effects on depression, psychotic symptoms, and psychosocial functioning, and that the processes targeted by the intervention (eg, experiential avoidance, behavioral activation) were associated with improvement. The open trial provided the initial "proof-of-concept" and suggested the utility of examining ADAPT further in a randomized design.

ADAPT integrates BA and ACT strategies for depressive and psychotic experiences by targeting underlying avoidance behaviors that often take the form of distraction from or excessive struggle or entanglement with these unwanted internal experiences. The focus of the treatment is on helping patients work on gradual behavioral changes week-by-week, slowly building from simple tasks (eg, getting out of bed at a designated time and attending to hygiene) to more complex goals (eg, looking for a job). An acceptance-based rationale for behavioral activation and corresponding supporting strategies are integrated throughout this process to help patients cope with obstacles (eg, psychotic symptoms, rumination, negative cognitions, traumatic memories) that may arise and make it more difficult to move forward and to encourage patients to choose to engage rather than avoid. Based on acceptance and commitment therapy, ADAPT places acceptance and behavior change in the service of important life changes (eg, framed to the patient as increasing willingness to experience

uncomfortable thoughts and feelings in the moment while pursuing valued goals). Thus, the focus of acceptance- and values-based behavioral activation is not on decreasing symptoms per se (as in traditional behavioral activation), but on improving functioning as defined by the person with or without symptoms.

We have found that the strategies in behavioral activation and acceptance and commitment therapy are complementary. A specific and reliable technology has been developed for behavioral activation that addresses depressive symptoms by teaching patients to conduct a functional analysis of behavior to identify habitual patterns of avoidance and then to replace those patterns with more approach-oriented alternative actions that counteract depression. However, behavioral activation in the context of severe depression and psychosis is often particularly challenging for patients due to rumination and intolerance of distress that result in difficulties persisting with goal-directed activities. Acceptance and commitment therapy teaches patients a more diverse set of coping strategies than behavioral activation that also target common co-occurring symptoms. For example, acceptance and commitment therapy teaches patients additional mindfulness and acceptance strategies to counter rumination and patterns of negative thinking that may impede progress toward goals. Acceptance and commitment therapy also reduces distress related to psychotic symptoms (via acceptance), teaches patients how to be less reactive to these experiences (via mindfulness), and includes motivational enhancements to promote commitment to goals (via clarification of values).

Consistent with the description of a contextual behavioral science approach presented by Hayes and colleagues,[37] the study presented here was part of a larger research program designed to develop a principle-driven treatment, based on behavioral activation and acceptance and commitment therapy, targeting a cross-cutting aspect of psychological dysfunction (ie, experiential avoidance) that would have the ability to produce improvements in symptoms as well as functioning. To continue working toward this broader goal, the small pilot randomized controlled trial described here was a feasibility study designed to serve as a logical next step after the open study[36] to further refine treatment conditions and procedures in preparation for future larger clinical trials of ADAPT. We randomized a small number of patients to medication treatment as usual plus ADAPT versus an enhanced assessment and monitoring condition (EAM). Information from the study was collected to help inform a “go/no go” decision concerning the utility of continued testing of ADAPT and expansion of this research program (eg, see Preskorn 2014[38] for a discussion of such proof of concept studies).

METHOD

Participants

Participants were randomly assigned to medication treatment as usual (mTAU) + EAM or to mTAU + ADAPT. Participants were recruited from a psychiatric hospital or the surrounding community and met the following criteria: (a) DSM-IV diagnosis of major depressive disorder, severe with psychotic features, or schizoaffective disorder, depressive type, as determined by the Structured Clinical Interview for DSM-IV (SCID-I)[39]; (b) current major depressive episode based on the SCID; (c) over 18 years of age; (d) ability to speak and read English sufficiently to complete study procedures; and (e) receiving concurrent

pharmacotherapy provided by a clinician in the community. Exclusion criteria were: (a) bipolar disorder or (b) pregnancy due to contraindications for medication use in this population.

Medication Treatment as Usual + Enhanced Assessment and Monitoring

All patients were receiving pharmacotherapy provided by a community treatment provider, which typically involved antidepressant and antipsychotic medications, as well as other medications as appropriate. Pharmacotherapy was unrestricted, and the specific choice of medications and schedule of contacts were determined by the provider and patient. mTAU was chosen because it is currently considered the first-line treatment for depression with psychosis.[40] We were therefore interested in assessing the additional effects of ADAPT as a logical first step in assessing the potential benefits of the therapy.

Given the severity of symptoms in the sample, we enhanced TAU in the comparison condition to minimize differential expectations for improvement between conditions and to ensure ethical care. Research suggests that systematic assessment and feedback to clinicians can improve treatment outcomes.[41] After obtaining patient consent, brief feedback letters were mailed to the medication providers of patients assigned to EAM after each study assessment. Study assessments were conducted at baseline, post-treatment, and at 3 month follow-up, with a total of 3 letters sent to providers as part of EAM. The letters included information on the patient's symptoms and functioning derived from the assessments to aid in treatment planning. If significant suicide risk or clinical deterioration was detected, this information was also provided in the standard letter, and communicated to the clinician immediately by phone if imminent risk was identified. We also provided additional referrals for treatment and community resources as needed to patients at the time of study assessments.

Medication Treatment as Usual + Acceptance-Based Depression and Psychosis Therapy

Patients receiving ADAPT also received mTAU in the form of pharmacotherapy provided by a community treatment provider similar to that received by patients in the comparison condition. Readers are referred to the report of our previous open trial for a more detailed description of ADAPT.[36] The original protocol used in the open trial involved 24 sessions over 6 months, but it was reduced to 16 sessions over 4 months in this study to improve the feasibility of implementation and to test the effects of a shortened protocol. The same overall content was delivered. Phase 1 (2 sessions) was focused on rapport building and included clarification of values and goals. The Valued Living Questionnaire[42] was administered and discrepancies between values and actions were discussed. The therapist helped the patient identify relevant values and develop initial short-term goals to work on during treatment. Phase 2 (6 sessions) introduced behavioral activation skills, including a functional analysis of avoidance behaviors including experiential avoidance, and fostered values-consistent activation strategies (in contrast to the simple scheduling of pleasant events typical of traditional behavioral activation). The commonly used TRAP (trigger-response-avoidance pattern) and TRAC (trigger-response-alternative coping) models from behavioral activation[13] were used to teach patients how to identify avoidance behaviors based on functional analysis and to engage in action-oriented coping strategies instead.

Phase 3 (6 sessions) focused on developing mindfulness and acceptance skills to support values-consistent efforts to achieve change. Strategies included metaphors and experiential exercises that are commonly used in acceptance and commitment therapy[15] to target processes such as cognitive defusion, willingness, present moment awareness, self-as context, and committed action. Phase 4 (2 sessions) focused on relapse prevention and successful treatment termination/transition. In this phase, the focus was on reviewing progress, continuing to clarify important life values, and developing longer term goals to continue to work toward these values posttreatment. Referrals for additional treatment were provided when needed.

Measures

At baseline, the mood and psychotic disorder sections of the SCID-I were administered to generate the patient's Axis I diagnosis or diagnoses. [39] Participants also completed several additional measures. The *Quick Inventory of Depressive Symptomatology-Clinician* (QIDS-C) is a 16-item interviewer-rated scale that is reliable and valid for assessing severity of depression.[43] Severity ranges on the QIDS-C are 0–5 = none, 6–10 = mild, 11–15 = moderate, 16–20 = severe, and 21–27 = very severe. The *Brief Psychiatric Rating Scale* (BPRS)[44] is an interview-rated scale that is a widely used outcome scale that assesses symptom severity. The BPRS Psychosis Subscale (thought disturbance, 4-items) was used in this study. [45] Mueser et al reported a mean total score on the BPRS Psychosis Subscale of 8.4 in a sample of 528 individuals with schizophrenia after stabilization following an acute exacerbation.[46] The brief version of the *World Health Organization Disability Assessment Schedule* (WHODAS-II) [47,48] is a 12-item self-report measure that has evidence of reliability and validity for assessing various aspects of psychosocial and physical disability. A score of 10 or above indicates significant functional impairment. The *Acceptance and Action Questionnaire-II* (AAQ-II) is a 7-item, validated self-report measure of experiential avoidance/psychological inflexibility.[49] The clinical cutoff for the AAQ-II is a score above 28, indicating higher levels of psychopathology. The *Behavioral Activation for Depression Scale* (BADS) is a 25-item validated self-report measure of activation and withdrawal related to depression.[50] The *Credibility and Expectancy Scale* (CES) is a self-report measure of patients' initial expectations for improvement from treatment.[51] The CES was administered after the treatment rationale was explained to participants in each condition. This occurred after the baseline assessment for patients assigned to EAM and after session 1 for patients assigned to ADAPT. The *Client Satisfaction Questionnaire-8* (CSQ-8) is an 8-item self-report measure that reflects respondents' satisfaction with services.[52]

Procedure

Patients were recruited from a local psychiatric hospital or outpatient clinic. Referrals were obtained from the treating clinicians and through the review of electronic medical records after obtaining a HIPAA waiver for this purpose. After obtaining permission from the patient's treating clinician, a research assistant approached the patient on the hospital unit or by phone (if an outpatient) to describe the study. If the patient was potentially interested in participating, the purpose, risks, and benefits of the study were explained and informed consent was obtained using procedures approved by the Institutional Review Board of Butler Hospital. Assessments were conducted at pretreatment, posttreatment (4 months after

the baseline assessment), and follow-up (7 months after baseline). Interviewers were trained to administer measures until acceptable interrater reliability (> 0.80) was achieved. Posttreatment interviewers were kept blind to the patient's condition. Patients were compensated $50 for the baseline assessment and $25 for each follow-up assessment. Patients were randomized to conditions using an urn randomization computer program that balanced for gender and recruitment setting. Urn randomization (also known as an adaptive "biased-coin" design) is a technique that randomly assigns patients of a given subgroup to conditions, but systematically biases the randomization in favor of balance among the different conditions on the selected variables.[53]

Patients were not assigned to therapists randomly but instead based on availability. The lead author (BG) and creator of ADAPT treated 1 patient in the study for treatment development purposes. The remaining participants were treated by 3 study therapists who were initially trained in the treatment manual by the lead author, and whose sessions were recorded and regularly reviewed to ensure treatment integrity. These therapists had doctoral degrees in clinical psychology and previous training in traditional cognitive-behavioral therapy for depression, including behavioral activation. One of the therapists also had some previous training and experience implementing interventions based on acceptance and commitment therapy for nonpsychotic populations. Formal treatment integrity was assessed using a rating instrument developed from the ADAPT treatment manual[54] that assessed consistent (eg, use of acceptance and commitment therapy metaphors and exercises, values-consistent behavioral activation, functional analysis of avoidance behaviors) versus inconsistent (eg, cognitive restructuring, pleasant events scheduling) strategies, as well as the general characteristics of effective psychotherapy (eg, rapport building, therapeutic alliance) based on similarly developed measures (see, for example, Forman et al 2007[55]). Approximately 10% of session recordings of the other study therapists were randomly selected and rated by the lead author. Overall treatment integrity was high, with an average of 93.9% of sessions found to be adherent to the specific components of the protocol and no sessions rated as containing significant amounts of non-ADAPT content. Furthermore, the mean competence rating per session was 5.42 (SD = 0.24), on a scale from 0 = poor to 6 = excellent, suggesting that study therapists were able to reliably and proficiently follow the protocol.

Statistical Analyses

The primary aim of this study was to establish the acceptability and feasibility of testing ADAPT in a subsequent fully powered clinical trial, rather than to power this study for certain *p* values. Given the small sample size, the data being collected were best able to inform issues of feasibility, acceptability, and the potential clinical significance of the effects of ADAPT, which could then be investigated more fully in future studies. We assessed feasibility by examining the available recruitment pool of subjects based on our selection criteria and the ability of therapists to learn and deliver the treatment. Acceptability was assessed through measures of patient satisfaction with treatment, retention rates throughout the study, and completion of study assessments. Baseline differences between conditions were examined in a preliminary manner using nonparametric tests. The potential effects of ADAPT were examined on various measures of symptoms (eg, depression, psychosis), overall psychosocial functioning, and potential mediators of change targeted by

ADAPT (eg, experiential avoidance). Based on the previous open trial, [36] medium to large effects were expected. Given the small sample size, we report Cohen's *d* effect sizes when interpreting outcomes, as well as the Reliable Change Index[56] to supplement analyses with the corresponding odds ratio between groups. We recognize that there is significant variability among these effect sizes and that percentages reported are based on a small sample; thus, these findings should be interpreted cautiously. Results are reported for completers only and for intention-to-treat (ITT) samples (carrying forward the last observation or "worst case" analysis) to examine the consistency of the results.

RESULTS

Sample Characteristics

Of the 38 patients who were initially consented into the study, 20 did not complete baseline assessments because we were unable to contact them following hospital discharge. Eighteen patients completed baseline assessments to determine eligibility, 13 of whom met eligibility criteria and 5 of whom did not (mainly due to incorrect diagnosis or insufficient depression severity at the time of assessment). The 13 eligible patients were randomized to EAM (n = 7) or ADAPT (n = 6).

Demographic and clinical characteristics of the sample are shown in Table 1. Participants had a mean age of 50 years (SD = 17.0) and 14 years (SD = 2.5) of education. A total of 54% (n = 7) were female, 15% were Hispanic (n = 2), 33% were married (n = 4), and 33% (n = 4) had a household income less than $30,000 per year. Regarding psychotic symptoms, 85% (n = 11) had hallucinations and 69% (n = 9) had delusions at baseline. A total of 85% (n = 11) had a diagnosis of major depressive disorder with psychotic features and 15% (n = 2) were diagnosed with schizoaffective disorder, depressive type. One patient (8%) was recruited from an outpatient setting, with the remaining recruited during a psychiatric hospitalization. A total of 62% (n = 8) of the sample reported a past suicide attempt and 69% (n = 9) had a past inpatient hospitalization. The average number of suicide attempts and past hospitalizations was 1.5 (SD = 1.6) and 3.2 (SD = 7.0), respectively. A total of 85% (n = 11) of the sample had a comorbid diagnosis: 62% (n = 8) had an anxiety disorder, 15% (n = 2) had a substance use disorder, 15% (n = 2) had a personality disorder, and 23% (n = 3) had an eating disorder.

Four patients dropped out prior to the posttreatment assessment: 3 (43%) in the group randomized to EAM and 1 (17%) in the group assigned to ADAPT (P = 0.56). The 1 patient who dropped out of ADAPT started treatment, but then withdrew without explanation after a few sessions. One patient dropped out of EAM after reporting that the assessments made him feel worse; the 2 others could not be reached to ascertain their reasons for withdrawal. Two patients who completed the posttreatment assessment failed to complete the follow-up for unknown reasons as they could not be reached: no patients were lost to follow-up in the EAM group versus 2 of the 5 remaining patients (40%) in the ADAPT group (P = 0.44).

Patients assigned to the ADAPT condition completed an average of 11.3 (SD = 5.1) sessions. Although we did not collect detailed information on dosages, all patients (n = 13) were prescribed an antidepressant medication and 92% (n = 12) were prescribed

antipsychotic medication at baseline. Among the treatment completers, at the posttreatment assessment, 100% of patients (n = 9) were prescribed antidepressant medication and 78% (n = 7) were prescribed antipsychotic medication. At the posttreatment assessment, all patients (100%) self-reported good adherence to their primary psychiatric medications (ie, missing no more than 1–2 doses in the previous month).

Treatment Outcomes

Visual examination of baseline scores indicated similar demographic characteristics and severity of symptoms between the two treatment conditions, and no significant differences were identified using nonparametric tests (Table 2). Results from the CES at baseline indicated that the EAM group had a mean of 34.0 (SD = 11.1) and the ADAPT group had a mean of 44.0 (SD = 4.4), representing a large effect size difference (d = 1.18), z = −1.81, P = 0.069. The average total score on the CSQ-8 at post-assessment was 25.5 (SD = 3) for the EAM group versus 29.5 (SD = 2.4) for the ADAPT group, out of a possible total score of 32, which represents a large effect (d = 1.47), z = −1.75, P =0.080. These results indicate that treatment expectations and overall satisfaction were relatively high in both groups, but somewhat better in the group randomized to ADAPT.

Treatment outcomes for the completers and ITT samples are reported in Table 2 for comparison purposes. Between-subjects effect sizes at posttreatment ranged from small to large, but all favored the ADAPT condition. Between group differences were large for depressive symptoms (QIDS-C) and psychosocial functioning (WHODAS-II) and small for psychotic symptoms (BPRS-Psychosis). Differences in experiential avoidance (AAQ-II) were in the medium to large range and changes in behavioral activation (BADS) were in the small range at posttreatment. Figures 1 and 2 show the pre and post results for the QIDS-C (primary outcome) and AAQ-II (potential target mechanism), respectively, with relevant cutoff scores noted for the ITT sample. Given the smaller sample size for the follow-up assessments, we conservatively report only the descriptive statistics in Table 2; although visual inspection suggests maintenance of treatment gains.

Given the small sample size, we also report clinically significant changes from pre- to posttreatment on an individual level. Patients achieving clinical significant improvement were assessed using the Reliable Change Index (RCI), which takes into account the reliability of an instrument to determine if treatment gains exceed the error attributable to measurement.[56] In contrast, reliable clinical deterioration is demonstrated when scores show worsening over time by exceeding the RCI value in the opposite direction. When calculating RCIs, interrater reliability estimates from our own research group were used for the QIDS-C, with intraclass correlation coefficient (ICC) = 0.93, and for the BPRS, with ICC = 0.95, as is appropriate for interviewer-rated measures. Furthermore, internal consistency reliability estimates from the current sample were used when calculating RCI for the self-report measures: WHODAS-II (functioning) α = 0.81, AAQ-II (experiential avoidance) α = 0.87, and BADS α = 0.81 (behavioral activation). Traditionally, test-retest reliabilities are used for calculating RCI when available. However, since such reliabilities were not consistently available for the measures used in this study derived from similar clinical samples, other

estimates such as internal consistency can be substituted where appropriate (eg, see Jacobson et al 1984[58]).

For the QIDS-C, 50% (*n* = 3/6) of those in the ADAPT condition compared with 29% (*n* = 2/7) of those in the EAM condition met criteria for reliable change at post-treatment, odds ratio (OR) = 2.5 (95% confidence interval [CI] = 0.3–24.7). For the BPRS-Psychosis subscale, reliable change at posttreatment was ADAPT = 67% (*n* = 4/6) vs EAM = 43% (*n* = 3/7), OR = 2.7 (95% CI = 0.3–25.6). For the AAQ-II, 50% (*n* = 3/6) met criteria for reliable change in the ADAPT condition compared with 14% (*n* = 1/7) in the EAM condition at post-treatment, OR = 6.0 (95% CI = 0.4–85.3). A total of 33% (*n* = 2/6) met criteria for reliable change on the WHODAS-II in the ADAPT condition versus 14% (*n* = 1/7) in the EAM condition at post-treatment, OR = 3.0 (95% CI = 0.2–45.2). Finally, 33% (*n* = 2/6) met criteria for reliable change on the BADS in the ADAPT condition versus 14% (*n* = 1/7) in the EAM condition at post-treatment, OR = 3.0 (95% CI = 0.2–45.2). Overall, there was very little evidence of clinically significant worsening of symptoms over time in the sample. Reliable worsening based on the RCI was demonstrated in one patient (16%) in the ADAPT condition and one patient (14%) in the EAM condition from pre to post assessment on the AAQ-II only.

DISCUSSION

This randomized controlled pilot trial examined the feasibility, acceptability, and potential efficacy of ADAPT for patients with depression and psychosis. We were able to recruit patients with comorbid depression and psychosis in the study as planned. However, due to the often quick and unexpected discharge from the psychiatric hospital where patients were initially recruited, some participants failed to follow through with the baseline assessment to determine eligibility. Therefore, identifying further ways of streamlining this process and reducing assessment burden might help to improve retention in future trials. Overall, we observed a 31% posttreatment attrition rate among those randomized to treatment, which was within expected margins (eg, see Swift and Greenberg 2012[59]). We were also able to train 3 study therapists in the new therapy protocol and overall treatment integrity was high in the study. Furthermore, ADAPT showed considerable promise in terms of patient-rated credibility and acceptability. The comparison condition (EAM) also appeared to be acceptable and feasible for most patients, although ratings of expectancies for improvement and treatment satisfaction appeared to be greater for ADAPT. Therefore, additional methods of improving engagement in EAM should be considered for future studies, or EAM could be augmented by additional strategies (eg, supportive therapy or psychoeducation).

Moreover, patients demonstrated improvements during ADAPT that were large for depressive symptoms compared with those seen in the EAM group. Previous studies in nonpsychotic depression have also shown greater benefits for combined treatment over medication alone.[9] Similar reductions in the severity of positive psychotic symptoms were seen in both the ADAPT and EAM conditions, which could have resulted from a “floor effect” on this measure. These findings are consistent with previous studies of acceptance and commitment therapy for psychosis. A recent meta-analysis of mindfulness/acceptance interventions for psychosis showed that these treatments are most effective for distress

related to psychosis and negative or affective symptoms.[60,61] It has increasingly been recognized that an individual's relationship or response to a psychotic symptom is more important than its frequency.[62] In accordance with the aim of ADAPT, the improvements observed in psychosocial functioning are particularly promising in this population. Furthermore, the processes targeted by the intervention, especially experiential avoidance, appeared to show changes consistent with those observed in the ADAPT open trial[36] and previous studies of acceptance and commitment therapy for psychosis.[63] Given our ability to identify a "signal" for the efficacy of our intervention on clinical outcomes (eg, depression severity) and to successfully engage our target treatment mechanism (eg, experiential avoidance), results of this pilot study suggest that a full-scale clinical trial of ADAPT is warranted.

Some important differences between this study and the previous open trial of ADAPT[36] should be noted. As discussed earlier, the treatment phase in the open trial was 6 months, whereas it was 4 months in this study, which could have affected the overall magnitude of effects. With regard to other differences, the sample in the previous study was comprised entirely of patients with major depression with psychotic features. In this study, we expanded our selection criteria to include patients with primary psychotic disorders with significant co-occurring depression. Although our sample was small, it should be noted that only 1 patient in each condition was diagnosed with schizoaffective disorder. Age was similar across the samples in the two studies, but a greater percentage of women were included in the open trial than in this pilot randomized controlled trial (86% vs 54%, respectively). In addition, ratings of treatment expectations and treatment satisfaction in this study were similar to those in the previous open trial of ADAPT. Although the severity of psychosis at baseline was similar in the two trials, it should be noted that the severity of depression at baseline was somewhat higher in the sample treated in the previous open trial (eg, QIDS-C mean score = 21.1, *SD* = 3.3).[36] It is difficult to compare effect sizes across studies due to the small sample sizes and the lack of a comparison group in the previous open trial. Although the overall magnitude of changes was similar across studies, effects appeared to be somewhat attenuated on certain measures (eg, BADS) in the trial described here, which may possibly have been related to the changes in the study design and sample composition discussed above. However, only a future large-scale randomized controlled trial will be able to establish the true effects of ADAPT, given the error variance found in effect sizes derived from small samples.

The strengths of this study included the use of a randomized design, high treatment integrity, and blinded assessments. A weakness of this study was the small sample size, which limited our ability to conduct formal statistical testing. Confidence intervals around the effect sizes were large, precluding definitive conclusions about the efficacy of ADAPT; however, it is important to emphasize that this was not the aim of this study. In addition, the EAM comparison group did not fully control for several nonspecific treatment factors, including expectations for improvement, and the greater time and attention provided in the ADAPT condition. Therefore, the specific efficacy of ADAPT is unknown at this point. A number of patients we initially screened for the study were not eligible based on our specified selection criteria. This points to the high degree of patient heterogeneity in our clinical population,

and future research should further explore the need to adapt treatment for perhaps even a broader range of presentations. Compared with outpatient settings, we had the greatest success recruiting patients from psychiatric hospital where more acutely ill individuals with active psychotic and depressive symptoms are likely to be found. Although we collected 3-month follow-up data, and visual examination of means suggested that post-treatment improvements were at least maintained, the reduced sample size was too small to draw definitive conclusions about long-term effects and retention was suboptimal. Finally, medication treatments were unstandardized and could have affected group differences in undetected ways.

CONCLUSION

The results of the study described here are consistent with previous studies showing the benefits of psychotherapy in addition to medications for severe depression and psychotic disorders. The clinical population with comorbid depression and psychosis is challenging and often exhibits multiple problems, including suicidality and severe functional impairment. Thus, it is important for therapists to carefully assess the needs of each patient and tailor the intervention for the various clinical problems that are present. It is also important to pace the intervention appropriately, so that one does not overwhelm the patient or disrupt the therapeutic alliance. Although ADAPT was delivered in a structured fashion based on a treatment manual, flexibility was built into the protocol so that it could be modified based on the specific clinical presentation and needs of the patient. For example, therapists were instructed to select the acceptance and commitment therapy strategies that were most relevant and applicable for the person and they were not restricted to only using certain metaphors or experiential exercises. The therapists also conducted a functional analysis of symptoms based on individual patient factors. Furthermore, behavioral activation strategies were applied to the individualized goals and personal values that were elicited from the patient based on his or her particular clinical presentation and life situation. A detailed discussion of the use of acceptance/mindfulness-based clinical approaches for psychosis is available elsewhere.[64,65]

As with behavioral activation and acceptance and commitment therapy, ADAPT offers an alternative perspective for the treatment of psychosis and depression. This intervention focuses less on symptom reduction and more on living a values-consistent life, with support for re-engaging with activities that improve functioning. The medication treatments that patients receive for depression and psychosis often reduce symptoms to some degree, but they can also produce unintended effects that have a negative impact on functioning.[66–69] Psychosocial treatments have been shown to reduce future relapses in depression[70] and psychosis.[71] Future research should investigate how adjunctive psychosocial interventions such as ADAPT can be used to support longer term recovery in this population.

Acknowledgments

Source of Funding

This work was supported by a grant from the National Institute of Mental Health (K23-MH076937) awarded to Dr. Gaudiano.

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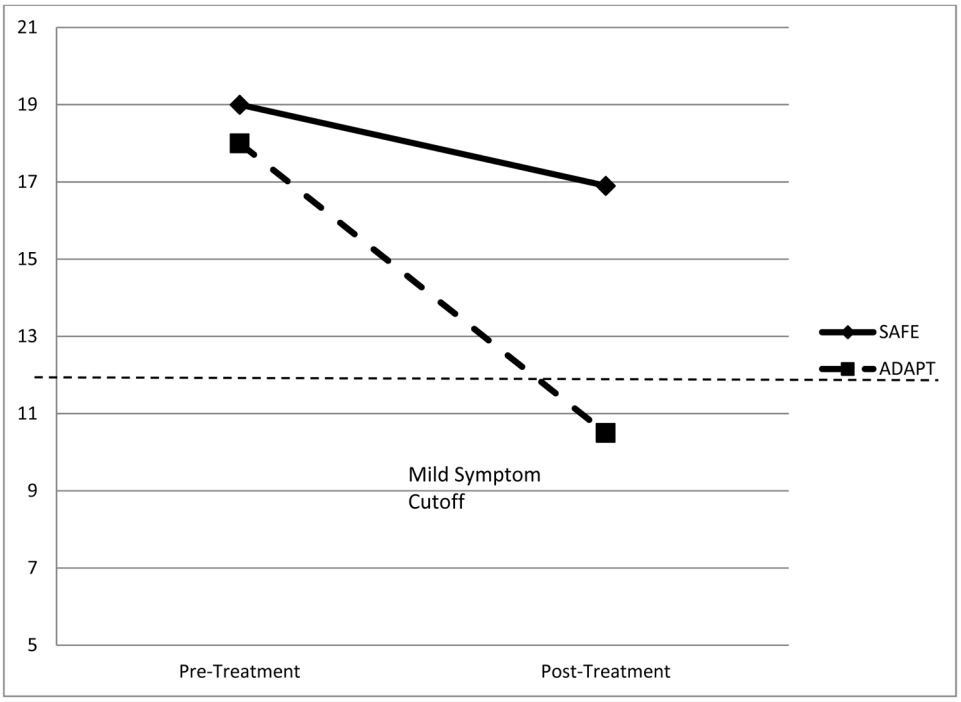

Figure 1.
Changes in depressive symptoms (Quick Inventory of Depressive Symptomatology-Clinician Rating administered by blind evaluators)

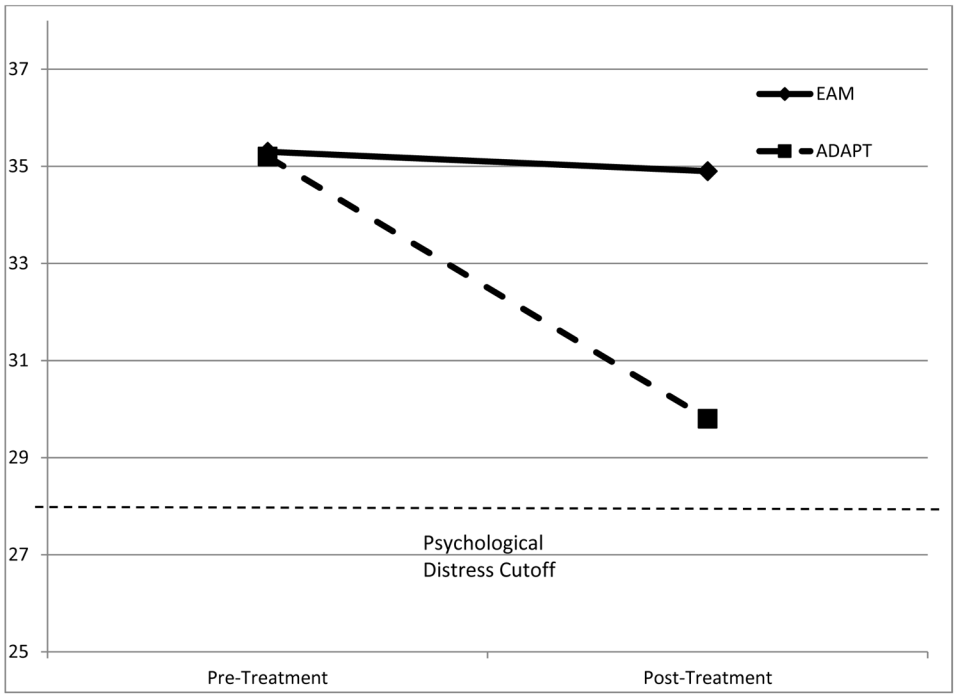

Figure 2.
Changes in experiential avoidance (Acceptance and Action Questionnaire-II)

Table 1

Demographic and Baseline Characteristic of the Patient Sample

Variable	ADAPT *n* = 6 *Mean (SD)*/*n*(%)	EAM *n* = 7* *Mean (SD)*/*n*(%)
Age (yr)	44.8(16.1)	54.6(17.5)
Education (yr)	14.0(2.9)	14.5(2.2)
Gender (female)	4(67)	3(43)
Ethnicity (Hispanic)	2(33)	0(0)
Marital status (married)	1(17)	3(50)
Income (< $30,000)	3(50)	1(14)
Recruitment site (psychiatric hospital)	6(100)	6(86)
Symptoms		
Hallucinations	5(83)	6(86)
Delusions	6(100)	3(43)
Primary SCID-I diagnosis		
Major depressive disorder with psychotic features	5(83)	6(86)
Schizoaffective disorder, depressive type	1(17)	1(14)
Comorbid psychiatric diagnosis	6(100)	5(71)
Psychotropic medications		
Antidepressant	6(100)	7(100)
Antipsychotic	6(100)	6(86)
Past suicide attempt	4(67)	4(57)
Previous inpatient hospitalization	3(50)	6(86)

ADAPT = acceptance-based depression and psychosis therapy; EAM = enhanced assessment and monitoring; SCID-I = Structured Clinical Interview for DSM-IV Axis I disorders

* Data missing for 1 patient for some demographic variables.

Table 2

Outcome Measures

Measure	*Pretreatment M(SD)*	*Posttreatment M(SD)*	*Follow-up M(SD)*	*Between-subjects posttreatment effect size* *
QIDS-C				
Completers				0.81
ADAPT	17.2(6.4)	8.2(8.1)	8.0(1.7)	
EAM	19.3(4.5)	15.8(2.6)	15.0(1.4)	
ITT				0.86
ADAPT	18.0(6.0)	10.5(9.2)	11.8(8.2)	
EAM	19.0(3.3)	16.9(2.3)	16.4(2.1)	
BPRS-Psychosis				
Completers				0.06
ADAPT	13.4(3.3)	8.4(4.1)	6.0(3.5)	
EAM	12.5(4.0)	7.3(2.2)	6.3(1.7)	
ITT				0.29
ADAPT	13.2(3.0)	9.0(3.9)	7.7(3.3)	
EAM	10.0(4.7)	6.9(2.9)	6.3(2.7)	
WHODAS-II				
Completers				1.31
ADAPT	32.2(4.8)	17.3(9.1)	13.3(3.5)	
EAM	32.5(13.0)	27.8(5.2)	26.8(4.5)	
ITT				0.78
ADAPT	31.2(5.0)	19.8(8.1)	19.7(7.4)	
EAM	32.4(9.9)	27.9(5.9)	27.3(5.6)	
AAQ-II				
Completers				1.14
ADAPT	36.2(8.5)	29.5(7.7)	21.0(10.5)	
EAM	32.8(4.5)	31.3(8.2)	26.5(3.9)	
ITT				0.64
ADAPT	35.2(8.0)	29.8(6.0)	27.5(10.5)	
EAM	35.3(8.2)	34.9(9.4)	32.1(9.5)	
BADS				
Completers				0.43
ADAPT	71.5(34.3)	93.5(49.3)	107.0(16.4)	
EAM	68.5(13.5)	81.8(29.6)	86.3(12.9)	
ITT				0.16
ADAPT	69.8(26.9)	83.3(41.3)	78.3(36.2)	
EAM	64.3(14.2)	75.0(27.1)	77.6(20.7)	

ADAPT = acceptance-based depression and psychosis therapy; EAM = enhanced assessment and monitoring; ITT = intent-to-treat sample; QIDS-C = Quick Inventory of Depressive Symptomatology-Clinician; BPRS-Psychosis = Brief Psychiatric Rating Scale–Psychosis Subscale; WHODAS-II = World Health Organization Disability Assessment Scale-II; AAQ-II = Acceptance and Action Questionnaire-II; BADS = Behavioral Activation in Depression Scale.

*Time by treatment between-subjects effect size differences were converted to Cohen's *d* effect sizes, with small = 0.20; medium = 0.50; large = 0.80.[57]