A Preliminary Trial of Adherence-Coping-Education (ACE) Therapy for Early Psychosis

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Abstract: A pilot randomized controlled trial was conducted to examine the effectiveness of adherence-coping-education (ACE) therapy. Twenty-four individuals with early psychosis were randomized to receive 14 sessions of either ACE therapy in addition to treatment as usual, or supportive therapy in addition to treatment as usual. Participants were assessed at baseline, midtreatment, and posttreatment on measures of medication attitudes, psychotic and depressive symptoms, and social functioning. ACE therapy was well tolerated and was associated with significant decrease in symptoms, as well as trend-level improvements in attitudes toward treatment. These results lend initial support for the feasibility of ACE Therapy, and suggest that it may have promise in facilitating recovery for individuals recovering from an initial psychotic episode.

Key Words: Schizophrenia, cognitive-behavioral therapy, early psychosis, psychosocial treatments, treatment adherence.

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Medication adherence is critical in facilitating recovery from a first psychotic episode (Robinson et al., 1999). However, psychoeducational interventions have shown little impact on medication adherence in controlled trials (Zygmunt et al., 2002), suggesting the need for interventions that specifically address medication attitudes and adherence behaviors. One such intervention, compliance therapy (CT), has been associated with improvements in treatment attitudes and adherence in a sample of individuals with acute symptoms (Kemp et al., 1996, 1998). The benefits of such an intervention for early psychosis, however, have not yet been explored. Individuals in the initial stages of psychotic illnesses have unique treatment needs as compared to patients with chronic illness. These include developing adaptive coping strategies to deal with the stigma and trauma after an initial hospital admission (Tarrier et al., 2007) and forming beliefs and attitudes about their illness and treatment (often in the face of significant symptom remission). Consequently, an adherence-oriented intervention for early psychosis must take into account these phase-specific needs.

Adherence-coping-education (ACE) therapy (Perkins et al., unpublished manual) is an adaptation of CT aimed at enhancing insight into one's illness and promoting treatment adherence during the initial recovery period after a first psychotic episode. ACE therapy is provided for a longer period than CT (14 sessions vs. 4–6 in CT) in consideration of the long recovery process in early psychosis, as well as limited effects reported in trials of adherence-focused therapies of briefer durations (e.g., Gray et al., 2006; O'Donnell et al., 2003). As compared to CT, ACE therapy devotes additional time to each of the core therapeutic goals (establishing rapport, exploring treatment ambivalence, promoting relapse recognition, etc.), and also adds a "rehabilitation phase," in which clients explore psychosis as a traumatic life experience. This study was a preliminary evaluation of the effectiveness of ACE compared with a control treatment [supportive therapy (ST)]. The primary hypothesis was that individuals receiving ACE would show a greater increase in positive attitudes toward their medication than individuals receiving ST at 3 months (midtreatment) and 6 months (posttreatment). A secondary hypothesis was that individuals in the ACE group would show greater reduction in symptoms at midtreatment and posttreatment than individuals in the ST group.

METHODS

Twenty-four participants recovering from a first psychotic episode were recruited from local inpatient and outpatient clinics. Inpatients who expressed interest in the study were not enrolled or assessed until after hospital discharge and clinical stabilization. Participants needed to be 16 years of age or older, meet DSM-IV (American Psychiatric Association, 2000) diagnostic criteria for schizophrenia, schizoaffective disorder, or schizophreniform disorder, and have been in treatment for a first episode of psychosis for less than 12 months. Eligibility for study participation was determined during a screening visit, at which time a diagnostic screen was conducted and informed consent was obtained. Baseline assessments were conducted and participants were then randomized to treatment.

Participants were randomized to receive either ACE in addition to treatment as usual (TAU) or supportive therapy (ST) in addition to TAU. Both therapy interventions con-

sisted of a total of 14 therapy sessions, each lasting 30–45 minutes, over the course of 6 months (i.e., 6 weekly sessions followed by 8 biweekly sessions). We originally planned on providing 6, one-month booster sessions following the initial 14 sessions. However, given the project's size, budget, and time frame, we decided that booster sessions were not feasible. Thus, we did not offer them to the last half of the sample, which is why we focus on outcomes following mid-treatment and posttreatment. ACE is a manual-based psychotherapy consisting of 4 phases: (1) establishing therapeutic alliance; (2) promoting treatment adherence; (3) developing a plan for maintenance treatment; and (4) rehabilitation. In ACE Therapy, the therapist assumes an active role consistent with traditional cognitive-behavioral therapies, and the therapeutic stance emphasizes empathy for the patient's point of view. ACE Therapy draws upon the Health Belief Model (Becker and Maiman, 1975), a theoretical framework developed in preventative healthcare. This model posits that an individual's decision to adhere to treatment is a dynamic process wherein patients weigh advantages and disadvantages of treatment, and that beliefs about advantages and disadvantages change over time (i.e., in response to education, or as symptom severity or treatment side effects change). Key therapeutic techniques used include motivational interviewing (e.g., linking taking medications or not to the client's ability to reach important goals), inductive questioning, reframing, using normalizing rationales, selective validation of the patient's beliefs and attitudes, and graded analysis of evidence to address beliefs about illness and treatment.

ST was intended to control for the nonspecific aspects of therapy, such as therapeutic relationship and regular contact with a therapist. ST has 2 phases, which are: (1) establishing a therapeutic alliance, and (2) providing emotional support and discussing nonillness issues or topics. ST therapists were instructed not to bring up or discuss issues related to medication or medication adherence. If patients brought up these issues in ST, the therapist was to listen with an empathic therapeutic stance, and advise the patient to discuss these issues with his or her treating physician. Each therapy session was audiotaped and reviewed by D.L.P. for fidelity to the treatment and procedures. A blinded independent assessor listened to a random sampling of 10% of therapy tapes and assigned each tape to either ACE or ST with 96% accuracy.

Assessments were conducted at baseline, midtreatment (3 months), and posttreatment (6 months) by interviewers blind to treatment condition. Medication adherence was assessed by patient report using prompts including; "Over the past month, on how many days did you not take/miss your medication?" (<7, 7–13, 14–20, >20). Additionally a global judgment of medication adherence based on patient report and other available information was made by the study assessor. Medication and treatment attitudes were assessed using 2 composite variables theoretically derived from the Health Belief Model. The "Need for Treatment" and "Benefits of Medication" variables each include items from both the Rating of Medication Influences scale (Weiden et al., 1994) and the Insight and Treatment Attitudes Questionnaire (McEvoy et al., 1989). These composite variables have been shown to

significantly predict likelihood of medication nonadherence for individuals recovering from a first psychotic episode (Perkins et al., 2006). The Need for Treatment and Benefits of Medication scales are calculated as the average of the individual item scores and had a range of 1–3, with higher scores indicating positive beliefs. Symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) and the Calgary Depression Rating Scale (Addington et al., 1993). The Quality of Life Scale (QLS) (Heinrichs et al., 1984) was used to assess social and vocational functioning.

Two-tailed t tests and χ^2 analyses were used to compare the ACE and ST groups on demographic characteristics and baseline measures, and to compare dropouts with the participants who were included in final data analyses. Within-group effect sizes (Cohen's d) were calculated for baseline to posttreatment changes on all outcome measures. These analyses were evaluated according to the recommended conventions (medium $0.2 < d \le 0.50$; and large $d < 0.5$) (Cohen, 1988) and were complemented by traditional significance testing. Additionally, linear mixed-effects regression models were computed using time and treatment group as fixed effects and random intercepts for each participant. F tests were based on Kenward-Roger's adjusted degrees of freedom solution (Kenward and Roger, 1997). Finally, Fisher exact test tests were used to compare the proportion of participants assigned to each intervention who showed clinically significant change (i.e., 25% or 50% reductions in PANSS positive scores) at mid- and posttreatment assessments.

RESULTS

All outcome analyses were completed using a modified intent-to-treat sample ($N = 19$) consisting of individuals who completed both a baseline assessment and at least 1 follow-up assessment, and who had attended at least 1 session of their assigned intervention. Of the 24 participants randomized to receive treatment, 3 participants did not attend any follow-up assessments (i.e., dropped out before midstudy). One additional participant had missing data at baseline, and was therefore excluded from analyses. Finally, 1 participant in the ACE group was excluded from analyses as an age outlier (i.e., the individual's age was more than 3 standard deviations above the randomized sample mean).

Preliminary Analyses

There was no significant difference between proportions of dropouts (i.e., participants failing to attend at least the midtreatment assessment) in the 2 groups (ACE = 15%, ST = 9%; NS), and dropouts did not differ significantly in demographics or symptoms from individuals included in the outcome analyses. A majority of the sample was white (75%), male (60%), and had never married (75%). Participants in the ACE group were significantly older than those in the ST group ($t(17) = 2.43$, $p = 0.03$). Thus, age was included as a covariate in the mixed effects analysis. There were no significant differences between the 2 groups on outcome variables at baseline.

Therapy attendance was high, with 90% of ACE participants attending all 14 sessions. There was no significant difference in attendance between the 2 interventions (ACE mean =

TABLE 1. Means (Standard Deviations) and Effect Sizes for Outcome Variables for Each Treatment Group Before and After Intervention

	Baseline Mean (*SD*)	Mid-tx Mean (*SD*)	Post-tx Mean (*SD*)	Baseline to Post-tx Change	
				t	Effect Size (*d*)
ACE					
Need for treatment	2.32 (0.41)	2.74 (0.35)	2.57 (0.48)	−2.18	0.60
Benefits of medication	2.44 (0.38)	2.70 (0.27)	2.67 (0.33)	−2.55*	0.59
PANSS positive	15.60 (4.97)	9.80 (3.26)	9.67 (2.69)	3.43**	−1.19
PANSS negative	17.70 (7.06)	16.60 (7.47)	14.11 (5.18)	2.21	−0.51
PANSS general	34.00 (9.26)	25.60 (4.27)	24.56 (3.91)	3.22*	−1.02
CDRS	10.50 (3.38)	12.10 (2.81)	9.67 (0.87)	0.69	−0.25
QLS total	62.90 (28.40)	67.11 (19.66)	76.78 (19.94)	−2.89*	0.49
ST					
Need for treatment	2.45 (0.45)	2.41 (0.55)	2.61 (0.45)	−1.52	0.36
Benefits of medication	2.38 (0.39)	2.45 (0.51)	2.60 (0.37)	−1.60	0.55
PANSS positive	13.78 (5.91)	11.78 (5.36)	11.25 (4.03)	1.17	−0.43
PANSS negative	14.33 (5.29)	13.78 (5.54)	15.75 (7.85)	−0.48	0.27
PANSS general	26.33 (8.23)	27.22 (7.48)	26.13 (7.97)	−0.43	−0.02
CDRS	9.78 (0.97)	10.33 (2.40)	11.13 (3.83)	−0.94	1.39
QLS total	73.38 (33.89)	81.63 (24.25)	79.71 (25.91)	−0.80	0.19

*p < 0.05; **p < 0.01.

13.80 sessions, *SD* = 0.63, range = 12–14; ST mean = 13.44 sessions, *SD* = 1.67, range = 9–14), (*t*(17) = 0.63, *p* > 0.05).

On the measure of medication adherence, there was a ceiling effect wherein 100% of participants endorsed the highest level of adherence at both mid- and posttreatment. As assessor impressions of medication adherence were congruent with patient report, these measures were therefore dropped from all subsequent analyses.

Primary Analyses

Significant within-group improvements from baseline to posttreatment were found for ACE participants on Benefits of Medication, PANSS Positive, PANSS General, and QLS scores, with these changes corresponding to large effect sizes (with a slightly lower effect size, *d* = 0.49 for QLS scores) (Table 1). No significant within-group changes were found for the ST group. There was a significant time-by-treatment interaction for PANSS positive symptoms (*F*[2, 31.9] = 3.98, *p* < 0.05), with significantly greater reductions in symptoms for ACE than for ST at midtreatment (*t*[31.7] = 2.26, *p* < 0.05) and posttreatment (*t*[32] = 2.56, *p* < 0.05) (Table 1). A similar interaction was observed for PANSS general symptoms (*F*[2, 31.8] = 4.44, *p* < 0.05), with greater reductions for ACE than ST at midtreatment (*t*[31.3] = 2.50, *p* < 0.05) and posttreatment (*t*[32] = 2.63, *p* < 0.05). However, the groups significantly differed on baseline PANSS general symptoms (*t*[38.7] = −2.33, *p* < 0.05), which may have contributed to this significant interaction (this is in contrast to the statistic obtained using an independent-samples *t* test for baseline differences on PANSS general scores (*t*[17] = 1.90, *p* = 0.075), reported earlier, and reflects greater degrees of freedom in the model). Results for PANSS positive and general scores were unchanged after controlling for age. The time-by-treatment interaction approached statistical signifi-

cance for Need for Treatment (*F*[2, 28.5] = 2.90, *p* = 0.07); greater improvement in treatment attitudes was observed for participants in ACE compared with ST at midtreatment (*t*[30.4] = −2.10, *p* < 0.05). No other statistically significant interactions were obtained.

A greater proportion of individuals demonstrated a 25% reduction in PANSS positive scores in the ACE group than in the ST group, at both midtreatment (80% vs. 33%; Fisher exact test *p* = 0.07) and posttreatment (60% vs. 33%; Fisher exact test *p* = 0.37). Further, 4 of 10 ACE participants achieved a 50% reduction in symptoms by posttreatment, whereas no ST participants met this criterion during the study (Fisher exact test *p* = 0.09).

DISCUSSION

The current study is one of the first to examine the effectiveness of a CBT intervention for early psychosis that is specifically tailored to addressing treatment adherence and attitudes. The findings suggest that ACE therapy is feasible and that it may improve treatment attitudes in individuals recovering from an initial psychotic episode. The large effect sizes for improvements on our 2 indices of treatment attitudes are especially promising in light of evidence that such attitudes have been found to be predictive of future adherence behavior in this clinical population (Perkins et al., 2006). As treatment attitudes for individuals receiving ACE peaked at midstudy (shortly following the phase of therapy focused on promoting treatment adherence), it may be that specific content within the intervention had differential impact on clients' attitudes. The long-term stability of these findings needs to be evaluated to better characterize these attitude changes.

ACE was also associated with a greater decrease in positive symptoms at both mid- and posttreatment as com-

pared to ST. These data are consistent with findings across trials of cognitive-behavioral interventions for psychosis, and support the demonstrated efficacy of such interventions for psychotic symptom reduction (Wykes et al., 2008). Because our measures of treatment adherence were limited by ceiling effects, however, the impact of ACE on actual medication compliance is unknown. Future studies will benefit from supplementing client- and assessor-reported adherence data with multiple sources including objective measures such as electronic monitoring of pill caps. And finally, these findings clearly need to be replicated in a larger randomized controlled trial before confident conclusions can be drawn. These limitations notwithstanding, the findings show promise for the development of psychotherapeutic approaches to addressing treatment nonadherence, and support the role of cognitive-behavioral interventions as effective adjunctive treatment for early psychosis (Penn et al., 2005).

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