ORIGINAL ARTICLE

A Randomized Controlled Study of Cognitive Therapy for Relapse Prevention for Bipolar Affective Disorder

Outcome of the First Year

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Background: Despite the use of mood stabilizers, a significant proportion of patients with bipolar affective disorder experience frequent relapses. A pilot study of cognitive therapy (CT) specifically designed to prevent relapses for bipolar affective disorder showed encouraging results when used in conjunction with mood stabilizers. This article reports the outcome of a randomized controlled study of CT to help prevent relapses and promote social functioning.

Methods: We randomized 103 patients with bipolar 1 disorder according to the *DSM-IV*, who experienced frequent relapses despite the prescription of commonly used mood stabilizers, into a CT group or control group. Both the control and CT groups received mood stabilizers and regular psychiatric follow-up. In addition, the CT group received an average of 14 sessions of CT during the first 6 months and 2 booster sessions in the second 6 months.

Results: During the 12-month period, the CT group had significantly fewer bipolar episodes, days in a bipolar episode, and number of admissions for this type of episode. The CT group also had significantly higher social functioning. During these 12 months, the CT group showed less mood symptoms on the monthly mood questionnaires. Furthermore, there was significantly less fluctuation in manic symptoms in the CT group. The CT group also coped better with manic prodromes at 12 months.

Conclusion: Our findings support the conclusion that CT specifically designed for relapse prevention in bipolar affective disorder is a useful tool in conjunction with mood stabilizers.

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BIPOLAR AFFECTIVE disorder runs a natural course of frequent relapses and recurrences.[1,2] Treatment of the illness has consisted mainly of pharmacotherapy.[3] However, mood stabilizers fail to protect a significant proportion of patients with this disorder from further relapses.[3-6] Psychotherapy specifically designed for bipolar affective disorder has been sparse. A study of family-focused treatment reported significant results for preventing depression.[7] Another study that taught patients to detect relapses early and seek prompt medical help reported significant results for preventing manic episodes.[8]

Recent psychosocial studies have shed further light on the treatment of this illness. Two areas of particular interest are coping with bipolar prodromes and the disruption of social rhythms. One study found that patients with bipolar affective disorder were able to report common prodromes reliably during an 18-month period.[9] Furthermore, patients' ability to cope with manic prodromes predicted their levels of social functioning and relapses 18 months later. Because manic prodromes may precede a full bipolar syndrome by weeks,[10,11] their early detection and intervention are particularly important to keep mild changes in mood states from spiraling into more severe and prolonged conditions.

A recent study reported that in the 8 weeks prior to manic episodes, a significantly greater proportion of patients had social rhythm disruption events than during the 8-week episode-free control period.[12] Patients with bipolar affective disorder are known to relapse after long-distance traveling or jet lag.[13,14] The American Psychiatric Association recommends regular social and sleep routines as part of the treatment guidelines for bipo-

lar illness.[15] If social rhythm disruption events play an important role in the onset of mania, psychotherapy might have a role in helping patients to cope with such life events to prevent its onset. Some patients who have frequent relapses engage in striving behavior to "make up for lost time." Hence, it is important to promote a good routine and target the extreme striving or goal attainment beliefs. The early detection of prodromes and the introduction of useful coping strategies during prodromal phases are also important aspects in the onset of a full-blown episode. Specific psychological therapies for patients with bipolar affective disorder should incorporate these elements.

Both promoting a good daily routine and the detection of and coping with prodromes involve monitoring and regulating. Cognitive therapy (CT) is based on the assumption that thinking, mood, and behavior affect one another. Therapists aim to teach patients techniques to monitor, examine, and change their dysfunctional thinking and behavior associated with undesirable mood states. Thus, CT is well suited to teaching patients with bipolar affective disorder the relevant skills to better cope with their illness. Less frequent relapses and better control of symptoms will improve their level of social functioning. Two CT pilot studies[16,17] have reported tentatively encouraging results. However, the samples in these pilot studies were small, and their findings need to be replicated in major studies. The purpose of this study was to recruit a large sample of patients with bipolar affective disorder who were experiencing frequent relapses despite the use of mood stabilizers as a means to investigate the efficacy of CT in conjunction with common mood stabilizers such as lithium carbonate, carbamazepine, and valproate sodium in the prevention of relapses.

PRIMARY HYPOTHESES

1. The CT group will have fewer bipolar episodes and fewer days in bipolar episodes.
2. The CT group will have higher social functioning.
3. The CT group will have better coping strategies for bipolar prodromes.
4. The CT group will have lower scores in dysfunctional attitudes relating to high goal-attainment.

SECONDARY HYPOTHESES

1. The CT group will have fewer bipolar depressive episodes.
2. The CT group will have fewer manic or hypomanic episodes.
3. The CT group will have lower depression and mania mood scores, less manic mood fluctuations, and less hopelessness.
4. The CT group will show better medication compliance.

METHODS

PROTOCOL

Subjects were patients with bipolar affective disorder who fulfilled the inclusion criteria: (1) bipolar 1 disorder according to the *DSM-IV*[18]; (2) prescribed prophylactic medication at an adequate dose according to the *British National Formulary*[19]; (3) aged 18 to 70 years; (4) at least 2 episodes in the last 2 years or 3 episodes in the last 5 years (to identify a subgroup vulnerable to relapses); (5) currently not fulfilling criteria for a bipolar episode; (6) Beck Depression Inventory[20] (BDI) score lower than 30; and (7) Bech-Rafaelsen Mania Rating Scale[21] (MRS) score lower than 9. Patients in an acute episode or with high residual symptoms were excluded because the focus of this study was relapse prevention and we did not want to use most therapy sessions for the treatment of an acute episode. Patient exclusion criteria were being actively suicidal (BDI suicide item score of 3) and currently fulfilling the criteria for substance use disorders.

PROCEDURE

Patients were either referred by their psychiatrists or contacted directly via a list of patients who had had blood drawn in the last 12 months to evaluate the serum level with mood stabilizers. After the study had been fully explained, written informed consent was obtained. The patients were interviewed using the Structured Clinical Interview for *DSM-IV*[22] and the Medical Research Council Social Performance Schedule.[23] The Mill Hill Vocabulary, 1995 edition,[24] was also administered at recruitment as an estimate of the IQ of the sample.

Patients' ability to cope with bipolar prodromes was assessed using the Coping with Prodromes Interview.[14] Good interrater reliability was obtained (mania prodromes: $\kappa = 0.69$; SE, 0.13; $P < .001$; depression prodromes: $\kappa = 0.79$; SE, 0.03; $P < .001$). Raters blind to the patients' group status and time of the interview rated patients' ability to cope using the rating guidelines.

Independent assessors who were blind to the patients' group status assessed patients at 6-month intervals using the Structured Clinical Interview for *DSM-IV* to determine relapse status. Relapse was defined as any bipolar episode that fulfilled *DSM-IV* criteria for major depression, mania, or hypomania. In addition, patients also completed the BDI, Internal State Scale (ISS),[25] and Beck Hopelessness Scale[26] (BHS) at recruitment and at monthly intervals to monitor fluctuations of mood. The control subscale of the Dysfunctional Attitude Scale (DAS)[27] was used to assess dysfunctional attitudes of extreme striving. Details of medication prescription were assessed through the monthly return of questionnaires. Medication compliance was monitored with monthly questionnaires returned by the patients and every 6 months by key workers from their psychiatric service who had the most contact with the patient. A key relative (the relative who had the most contact with the patient) was also interviewed independently to collect collateral information about patients' levels of social functioning in addition to patients' self-reports.

ASSIGNMENT

Patients who were found suitable for the study were randomly allocated either to the control group or the CT group. The allocation sequence was generated prior to the recruitment of patients by a computer program and concealed in sequentially numbered and sealed opaque envelopes, which were opened when patients were ready for allocation. The control group received minimal psychiatric care, which was defined as mood stabilizers at a recommended level with regular psychiatric follow-up as outpatients. The CT group received CT plus minimal psychiatric care. There were no criteria for the study termination of patients. Hospitalization or acute suicidal tendency was counted as outcome.

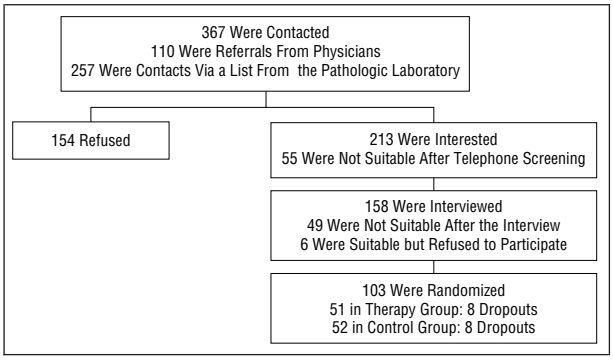

Figure 1. Recruitment flow, randomization assignments, and dropout rate of the study.

PATIENT CHARACTERISTICS

A total of 367 potential patients were contacted. **Figure 1** depicts the recruitment flow, randomization assignments, and dropout rate of the study. Of the 49 patients interviewed but found not to fulfill criteria for the study, the main reasons for noninclusion were as follows: not enough episodes in the last 5 years (16/49), not taking mood stabilizers (11/49), and not fulfilling *DSM-IV* criteria for bipolar 1 disorder (17/49). In the end, 103 patients with *DSM-IV* bipolar 1 disorder who fulfilled all research criteria were recruited for the study.

According to the standard interpretation of the BDI, the distribution of depression levels in the sample recruited into the study was as follows: 44% had no depression (BDI score, 0-9), 31% had a mild to moderate level of depression (BDI score, 10-18), and 25% had moderate depression (BDI score, 19-29). According to the MRS, the distribution of manic symptoms was 11% in the mild or hypomania range (MRS score, 6-9) and 89% in the no mania category (MRS score < 6). **Table 1** summarizes the demographic and clinical features of the CT group (n=51) and control group (n=52).

There were no significant differences between the 2 groups in any of the initial characteristics summarized in Table 1. Patients in the CT group had mean±SD, 13.9±5.5 sessions. Eight patients terminated CT prior to the sixth session (mean±SD number of sessions, 2.6±1.8). These 8 patients were included in the intention-to-treat analysis whenever possible.

INDIVIDUAL CT

Therapy was based on our treatment manual[28] and consisted of 12 to 18 individual sessions within the first 6 months and 2 booster sessions in the second 6 months. In addition to the traditional CT treatment for depression, the following were new elements of our approach:

1. The diathesis-stress model emphasized the need for combined medication and psychological therapies.
2. Cognitive behavioral skills were used to monitor mood, including prodromes, and to modify behavior to prevent prodromal stages from developing into full-blown episodes.
3. The importance of sleep and routine was promoted to avoid sleeplessness triggering an episode.[14,29]
4. Therapists particularly looked out for behavior that compensated for "loss of time" due to previous illness. Attempts were also made to deal with extreme striving attitudes.

The 4 therapists were clinical psychologists (3 men and 1 woman) with a minimum of 5 years of postqualification experience. All therapy sessions were audiotaped for weekly peer supervision, which lasted 1 hour.

Table 1. Initial Characteristics of Groups*

	Cognitive Therapy Group	Control Group
Age, y	46.4 ± 12.1	41.5 ± 10.8
Female sex, No. of patients	28	30
Age at onset, y	28.2 ± 11.4	26.2 ± 9.5
Beck Depression Inventory score	12.8 ± 9.4	14.3 ± 10.7
Hamilton Depression Rating Scale score	5.7 ± 5.4	6.5 ± 6.0
Mania Rating Scale score	2.0 ± 3.2	1.8 ± 2.1
Previous depression episodes	5.8 ± 8.0	5.1 ± 4.2
Previous manic episodes	5.5 ± 6.1	3.9 ± 2.8
Previous hypomanic episodes	1.3 ± 2.7	0.2 ± 0.5
Previous hospitalization	6.3 ± 5.9	5.1 ± 6.3
Proportion of patients taking mood stabilizers, %		
1 Mood stabilizer	80.4	90.4
2 Mood stabilizers	19.6	9.6
Antidepressants	25.5	34.6
Major tranquilizers	51.0	40.4

*Data are presented as mean ± SD unless otherwise indicated.

INSTRUMENTS

Internal State Scale

The ISS consists of 16 self-report, 100-mm visual analog items. The scale has 4 subscales: activation, well-being, perceived conflict, and a depression index; there is also a Global Bipolar scale. The construct validity of the scale was supported by significant relationships between activation scores and physicians' ratings of mania and between the depression index scores and clinical ratings of depression.

Medical Research Council Social Performance Schedule

The Medical Research Council Social Performance Schedule is an observer-rated scale based on a semistructured interview that provides a quantitative assessment of social performance in the last month. The informant is the patient. The interview is directed toward actual behavior and performance in each area and is rated on a 4-point scale. The schedule covers 8 areas of social performance, and an overall score is obtained by totalling the scores. In their original article, the authors reported a better-than-chance interrater agreement. A slightly modified version of the schedule was used to interview patients' key relatives.

The Coping With Prodromes Interview

Patients were asked, based on their experience of past episodes, what the early warnings (prodromes) were that made them think that their moods were either elevating or lowering and what they did when they had these prodromes. Patients' reports of prodromes and the way they coped with prodromes for both depression and mania were recorded verbatim. Using the rating guidelines, patients' ability to cope with prodromes of mania or depression was rated on a 7-point scale (0=poor, 3=adequate, and 6=extremely well). The rating of coping is based on general cognitive behavioral principles.

Medication Compliance Questionnaire

The Medication Compliance Questionnaire[16] is a report of compliance with any prescribed mood stabilizers. Respondents had

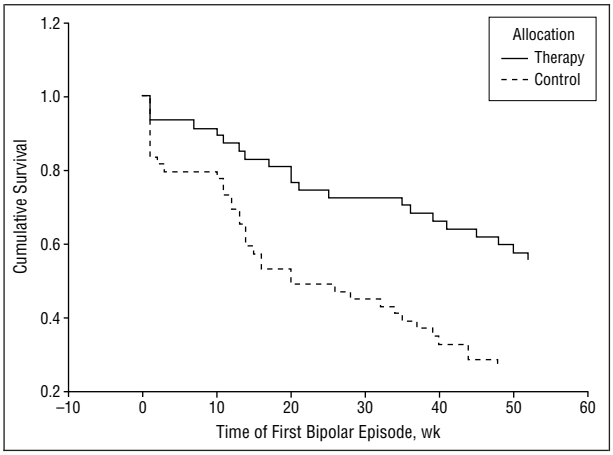

Figure 2. Survival curve from Cox regression intention-to-treat analysis. After controlling for medication compliance, the hazard ratio for relapse was 0.40 (95% confidence interval, 0.21-0.74; *P*=.004).

a choice of noting whether in the past month the patient had either never missed taking the medication, missed taking it once or twice, missed taking it between 3 and 7 times, missed taking it more than 7 times, or stopped taking it altogether. This measure provided more detailed information about whether patients had been taking their medication. The questionnaire was sent out monthly to the patient and at 6 months to the physician or nurse.

Short Version of DAS

The DAS-SV (short version) is a 24-item self-report inventory derived from a factor analytic study of the original DAS form A and form B. The items are rated on a 7-point scale. Three factors were identified: achievement, dependency, and self-control. Of particular interest in this study was the control subscale, which contained some high goal-attainment beliefs; for example, "If I try hard enough, I should be able to excel at anything I attempt" and "I should be happy all the time."

Mania Rating Scale

The MRS consists of 11 items that map into common manic symptoms such as the patient's motor activity, flight of thoughts, voice or noise level, hostility or destructiveness, and sleep. Each item is rated on a 5-point scale. The total scores were interpreted as follows: 0-5=no mania, 6-9=hypomania (mild), 10-14=probable mania, and 15 or more=definite mania. The scale has good interrater reliability and construct validity.

Beck Depression Inventory

The BDI is a well-known 21-item inventory designed to measure the severity of depression in adults and adolescents. It investigates the somatic, cognitive, and behavioral aspects of depression in the last week. Each item is scored on a 4-point scale.

Beck Hopelessness Scale

The BHS is a 20-item true-false inventory. The items consist of statements that reflect different facets of the spectrum of attitudes and expectations about the future. The scale has good internal consistency (coefficient α=.93) and construct validity.

STATISTICAL ANALYSES

Differences between the CT and control groups were assessed using a χ^2 test for dichotomous variables and a Spearman correlation coefficient for ordinal variables and for skew data. Analysis of variance was used for continuous variables. Cox regression was used for survival analysis, with the number of weeks to the first bipolar episode as a dependent variable. Logistic regression was used to compare the proportions of patients who relapsed in the 2 groups. Data from monthly follow-up visits on the mania and depression scales were converted into summary measures: the mean score during the 6 months and the SD of the scores during this period (as a measure of the degree of fluctuation). Where applicable, adjustments for differences in the relevant measures at baseline were carried out using analysis of covariance or logistic regression. The main outcomes of continuous scales at 6 and 12 months of follow-up (social functioning, coping with mania and depression prodromes, MRS, and Hamilton Depression Rating Scale[30]) were tested for group differences using multivariate analysis of covariance (MANCOVA), covarying for the same variable measured at baseline. A significant omnibus test would lead to univariate tests to examine the sources of differences to detect which dependent variable contributed to the significant omnibus test. Unless otherwise stated, all analyses reported in this article were intention-to-treat analyses, and all tests for hypothesized differences were 1-tailed.

RESULTS

EPISODES

Overall, 53% of patients relapsed during the 12 months. **Figure 2** depicts the survival analysis of the 2 groups with the number of weeks prior to the first bipolar episode as the dependent variable. The actuarial cumulative relapse rates for the CT and control groups, respectively, were 28.3% (13/46) and 50% (22/44) at month 6 and 43.8% (21/48) and 75.0% (36/48) at month 12. The hazard ratio for relapse in the CT group relative to the controls was 0.40 (95% confidence interval, 0.21-0.74; *P*=.004) after medication compliance was controlled for.

Table 2 summarizes the proportions of patients who experienced bipolar episodes and who were admitted to the hospital for bipolar episodes during the 12 months. Significantly fewer patients in the CT group experienced depressive, manic, and mixed episodes after the number of previous episodes was controlled for. Similarly, significantly fewer patients in the CT group were admitted for bipolar episodes. When both medication compliance and the previous number of episodes were controlled for, significantly fewer patients in the CT group experienced a bipolar episode during the 12 months than in the control group (Wald χ^2_1=5.89; odds ratio=0.26; *P*=.008).

Table 3 summarizes the mean number of days that patients in the CT and control groups were experiencing episodes. The CT group had fewer days in bipolar episodes as a whole, in depression or mania, after controlling for the number of previous episodes. After medication compliance and the number of previous episodes were controlled for, patients in the CT group still had significantly fewer days in bipolar episodes than the con-

Table 2. Proportion of Patients in the Cognitive Therapy Group and Control Group Who Had Experienced an Episode or Hospital Admission*

	Cognitive Therapy Group Patients With Episode or Admission (n = 48)	Control Group Patients With Episode or Admission (n = 48)	Wald χ^2	Odds Ratio (95% Confidence Interval)	*P* Value (1-tailed)
Bipolar episode	21 (43.8)	36 (75.0)	9.00	0.27 (0.11-0.63)	.001
Major depression	10 (20.8)	25 (52.1)	9.09	0.25 (0.10-0.61)	.001
Manic episode	8 (16.7)	15 (31.3)	6.80	0.15 (0.03-0.62)	.002
Hypomanic episode	8 (16.7)	6 (12.5)	0.39	1.46 (0.03-1.87)	.26
Mixed episode†	0 (0)	2 (4.2)	. . .	. . .	. . .
Bipolar admission	7 (14.6)	16 (33.3)	6.71	0.20 (0.06-0.61)	.003
Depression admission†	0 (0)	6 (12.5)	. . .	. . .	.003
Manic admission‡	7 (14.6)	12 (25.0)	5.40	0.18 (0.04-0.77)	.005
Mixed episodes‡ admission†	0 (0)	2 (4.2)	. . .	. . .	. . .

*Number of previous episodes was controlled for in logistic regression analyses. Data are presented as number (percentage) unless otherwise indicated. Ellipses indicate not applicable.
†Odds ratio cannot be calculated because of 0% in cognitive therapy group.
‡n = 47.

Table 3. Number of Days in Episodes in the Cognitive Therapy Group and Control Group*

	Cognitive Therapy Group	Control Group	SE	*t*	Mean Difference (95% Confidence Interval)	*P* Value (1-tailed)
Days in bipolar episode	26.6 ± 46.0	88.4 ± 108.9	17.5	–3.56	–62.31 (–96.99 to –27.31)	.001
Days in major depression	15.1 ± 35.3	57.8 ± 95.9	15.0	–2.85	–42.76 (–72.56 to –12.96)	.003
Days in manic episode	8.3 ± 22.3	17.3 ± 36.2	5.4	–2.3	–12.47 (–23.22 to –1.72)	.002
Days in hypomanic episode	3.3 ± 11.0	9.2 ± 47.2	7.1	–0.77	–5.50 (–19.65 to –8.66)	.22
Days in mixed episode	0	3.6 ± 17.7	2.6	–1.37	–3.55 (–8.70 to 1.59)	.09

*Number of previous episodes was controlled for in linear regression analyses. Data are presented as mean ± SD unless otherwise indicated.

Table 4. Number of Days Patients in the Cognitive Therapy Group and Control Group Spent in the Hospital for Bipolar Episodes*

	Cognitive Therapy Group	Control Group	Mann-Whitney *U*	*z*	*P* Value
Admission days for bipolar affective disorder	10.3 ± 33.3	17.6 ± 35.9	912.0	–2.18	.02
Admission days for depression	0	6.3 ± 22.4	1081.0	–1.41	.007
Admission days for mania	11.1 ± 33.4	9.4 ± 21.5	1052.0	–1.05	.15
Mixed admission days	0	1.9 ± 10.7	1081.0	–1.41	.16

*Data are presented as mean ± SD unless otherwise indicated.

trol group (SE, 19.6; mean difference, –49.0; $t_{4,64}$=–2.50; *P*=.008).

Table 4 summarizes the mean number of days patients in the CT and control groups spent in the hospital for bipolar episodes. The CT group had significantly fewer days in the hospital for bipolar episodes as a whole and significantly fewer hospital days for depression.

MONTHLY RETURN OF MOOD QUESTIONNAIRES

According to the monthly questionnaires, there was a significant interaction between group and time on the BDI ($F_{1,54}$=4.53; *P*=.02) during the first 6 months when the CT group was receiving therapy. **Figure 3** depicts the monthly return of the BDI for the 2 groups during the first 6 months. The BDI scores of the CT group dropped across time, whereas those of the control group increased with time.

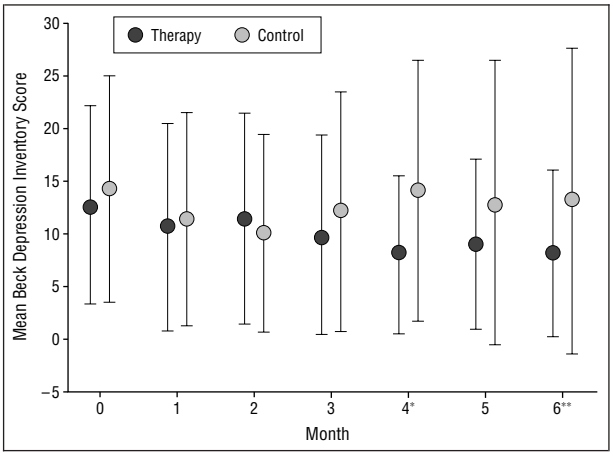

Figure 3. The mean Beck Depression Inventory scores of the cognitive therapy and control groups. Single asterisk indicates groups were significantly different at month 4 (*P*=.02); double asterisk, groups were significantly different at month 6 (*P*=.04).

Table 5. Means and SDs of Dependent Variables and the Results of Univariate Tests Using Multivariate Analysis of Covariance

Dependent Variable	Cognitive Therapy Group	Control Group	$F_{1,43}$	*P* Value
Mania Rating Scale score at mo 6	1.2 ± 1.9	1.2 ± 1.6	0.01	.47
Hamilton Depression Rating Scale score at mo 6	5.4 ± 6.4	6.5 ± 6.4	0.11	.37
Medical Research Council social functioning score at mo 6	0.4 ± 0.5	0.8 ± 0.8	1.68	.10
Coping with mania prodrome at mo 6	1.9 ± 1.7	1.6 ± 1.3	2.75	.05
Coping with depression prodrome at mo 6	1.7 ± 1.6	1.4 ± 1.4	3.51	.04
Dysfunctional Attitude Scale control subscale score at mo 6	29.8 ± 7.1	32.5 ± 8.3	8.21	.003
Mania Rating Scale score at mo 12	1.2 ± 1.8	0.7 ± 1.2	2.47	.06
Hamilton Depression Rating Scale score at mo 12	5.1 ± 5.3	5.8 ± 5.5	0.01	.46
Medical Research Council social functioning score at mo 12	0.4 ± 0.5	0.4 ± 0.6	0.79	.39
Coping with mania prodrome at mo 12	2.2 ± 1.7	1.5 ± 1.1	4.89	.02
Coping with depression prodrome at mo 12	1.7 ± 1.5	1.4 ± 1.2	0.49	.24
Dysfunctional Attitude Scale control subscale score at mo 12	31.0 ± 7.8	33.5 ± 7.8	0.70	.20

There were no significant differences between the 2 groups in the mean total BDI, BHS, and ISS activation scores during the whole year. However, the mean BDI score in the CT group was significantly lower than in the control group at month 4 (CT group: mean±SD, 8.1±7.6; control group: mean±SD, 14.1±12.3; $P<.001$) and month 6 (CT group: mean±SD, 8.2±7.9; control group: mean±SD, 13.2±14.7; $P=.04$). Similarly, the CT group's mean BHS score was significantly lower than that of the control group at month 4 (CT group: mean±SD, 6.6±5.7; control group: mean±SD, 8.2±6.3; $P=05$). In terms of ISS activation, the CT group had a significantly lower mean score compared with the control group at month 3 (CT group: mean±SD, 109.4±86.3; control group: mean±SD, 120.6±114.7; $P=.03$), month 5 (CT group: mean±SD, 93.9±81.2; control group: mean±SD, 142.9±133.0; $P=.03$), and month 11 (CT group: mean±SD, 145.8±126.3; control group: mean±SD, 71.2±75.8; $P=.01$). At no time did the control group have a significantly lower mood score than the CT group.

MOOD FLUCTUATION

During the 12 months, the CT group also had a lower SD of the ISS activation scores (CT group: mean±SD, 61.4±43.1; control group: mean±SD, 78.1±41.1; $P=.03$), BDI scores (CT group: mean±SD, 4.9±3.4; control group: mean±SD, 6.9±4.1; $P=.02$), and BHS scores (CT group: mean±SD, 2.8±2.0; control group: mean±SD, 3.7±2.2; $P=.04$). This indicates a greater degree of mood fluctuation in the control group than the CT group.

MEDICATION COMPLIANCE

Serum levels were available at month 6 for 50.5% (52/103) of patients. When patients were classified into an adequate or inadequate serum level group according to pathologic laboratory guidelines, 93.1% (27/29) of patients in the CT group compared with 78.3% (18/23) of the control group had adequate serum levels. However, the trend failed to reach statistical significance ($\chi^2_1=2.46$; $P=.06$). There was significant agreement between patients' own compliance reports and serum levels: 90.9% (40/44) of patients who reported good compliance (ie, missing their medication <3 times in a month) showed adequate serum levels compared with patients who did not report good compliance (50% [3/6]; $\chi^2_1=7.34$; $P=.004$). At month 6, a significantly greater proportion of patients in the CT group (88.4% [38/43]) than in the control group (66.7% [26/39]) reported good compliance. After covarying for the compliance rating at baseline, this remained significant (Wald $\chi^2_1=4.34$; $P=.02$). There was a significant correlation between key workers' and patients' reports ($r=0.75$; n=64; $P<.001$).

SOCIAL FUNCTIONING, COPING WITH BIPOLAR PRODROMES, DAS, AND CONTROL SUBSCALE

There was a significant correlation between the Medical Research Council Social Performance Schedule scores of the relatives and patients' accounts at month 6 ($r=0.40$; n=45; $P=.006$) and month 12 ($r=0.90$; n=41; $P<.001$). The scores of the MRS, Hamilton Depression Rating Scale, Medical Research Council Social Performance Schedule, coping with mania prodrome, and coping with depression prodrome at both month 6 and month 12 were analyzed using MANCOVA to test for differences between the 2 groups; the scores of these same variables at baseline plus patients' reports of medication compliance were used as covariates. The omnibus test for group differences was significant (Wilks $\lambda=0.65$; $F_{12,43}=1.92$; $P=.03$). **Table 5** summarizes the results of the univariate tests from the MANCOVA.

PSYCHIATRIC OUTPATIENT APPOINTMENTS AND MEDICATION PRESCRIBED

There was no statistically significant difference in mean number of psychiatric appointments during the whole year (CT group: mean±SD, 6.6±12.2; control group: mean±SD, 6.7±6.7). **Table 6** summarizes the proportion of patients prescribed either 2 mood stabilizers, antidepressants, neuroleptics, or no mood stabilizers. There were no significant differences between the 2 groups at any time point.

Table 6. Proportion of Patients Prescribed Either 2 Mood Stabilizers, Antidepressants, Neuroleptics, or No Mood Stabilizers*

	2 Mood Stabilizers		Antidepressants		Neuroleptics		Not Prescribed a Mood Stabilizer	
	Cognitive Therapy Group	Control Group	Cognitive Therapy Group	Control Group	Cognitive Therapy Group	Control Group	Cognitive Therapy Group	Control Group
Baseline	19.6 (10/51)	9.6 (2/52)	25.5 (13/51)	34.6 (18/52)	51.0 (26/51)	40.4 (21/52)	0	0
6 mo	15.9 (7/44)	10.0 (4/40)	22.7 (10/44)	28.2 (11/39)	34.1 (15/44)	35.9 (14/39)	2.3 (1/43)	7.5 (3/40)
12 mo	19.5 (8/41)	11.8 (4/34)	34.1 (14/41)	26.5 (9/34)	31.7 (13/41)	35.3 (12/34)	7.3 (3/41)	9.0 (3/35)

*Data are presented as percentage.

COMMENT

This study targeted patients with bipolar affective disorder who were at high risk for relapse and demonstrated the efficacy of CT in preventing bipolar episodes. When patients were receiving CT, they had significantly fewer bipolar episodes and fewer hospitalizations. The proportion of patients in the control group who relapsed during the year was 75% compared with 44% in the CT group. However, bipolar episodes can vary in length. An important variable was the number of days patients were experiencing bipolar episodes. Our results showed that the control group had more than 3-fold the amount of time in bipolar episodes (mean, 88 days) compared with the CT group (mean, 27 days). In addition, CT reduced the hospitalization rate by half. Compared with 33% in the control group, only 15% of patients in the CT group were admitted to the hospital for bipolar episodes.

Two previous studies reported a robust preventive effect of therapy for bipolar depression[17] and mania.[8] However, the sample in one study was small,[17] and in the other study, patients did not receive CT but were taught to detect early warnings and seek medical help soon.[8] This study provided evidence that CT can be protective for both bipolar depression and mania when patients are taught full CT skills to cope with their illness.

Although subjects were not experiencing an acute episode at recruitment, more than 56% had a mild to moderate level of depression. Cognitive therapy had a significant effect in reducing these residual depression symptoms, as demonstrated by a significant interaction between BDI scores and the group status in the first 6 months of the study. This finding is consistent with a small study that found that CT could be used to deal with moderate levels of depression in bipolar affective disorder.[31] Hence, health care professionals should consider CT in the treatment of residual depression symptoms.

Even though there were no significant differences in mean mood scores between the 2 groups for the whole 12 months, when individual monthly return of questionnaires was analyzed, the CT group had significantly lower mean mood scores than the control group for some of the months. Furthermore, the CT group had significantly less manic symptom fluctuation during the 12 months. Thus, CT appears to lessen mood symptoms and regulate manic mood swings.

Frequent bipolar relapses or being hospitalized for bipolar episodes can be very disruptive to patients' ability to continue their commitments and can consequently reduce patients' social functioning. Low social functioning can act as a vulnerability factor for more frequent relapses.[32] It is important for psychological therapy to aim to increase patients' level of social functioning. In this study, the CT group had significantly higher social functioning according to patients' self-reports and independent reports by close relatives.

The beneficial effects for the CT group could not be attributed to more frequent psychiatric outpatient appointments because there were no significant differences between the 2 groups in terms of mean number of appointments attended. The issue of medication is more complex. There were no significant differences between the 2 groups regarding the proportion of patients prescribed no mood stabilizers, 2 mood stabilizers, an antidepressant, or a major tranquilizer at the 3 time points. In terms of medication compliance, the CT group reported significantly better compliance than the control group. This higher level of compliance was supported by the collateral reports of key physicians. Unfortunately, we managed to obtain serum levels for only half of the sample; however, the serum levels did provide some validity to the self-report questionnaire. Furthermore, the CT group was significantly better in terms of the main outcome variables after medication compliance was controlled for. Nevertheless, the question of whether the CT group's better outcome was simply due to better compliance with their medication has not entirely been resolved in this study.

With regard to coping with bipolar prodromes, patients in the CT group did significantly better than the control group in coping with manic prodromes at both month 6 and month 12. The significant group differences favoring the CT group in coping with depression prodromes at month 6 were lost at month 12. This finding is consistent with the findings of our pilot study.[16] One speculation is that in this study, very few of our patients had significant manic symptoms at baseline. In contrast, most of our sample had significant residual depression symptoms. Perhaps in this context, patients with bipolar affective disorder find it hard to identify when residual symptoms have intensified to become prodromal symptoms. Hence, it is more difficult to teach patients to monitor and cope with depression prodromes than manic prodromes.

Highly driven and extreme goal attainment beliefs were identified as vulnerability factors. Patients with bipolar affective disorder who had these attitudes were as-

sumed to be more likely to engage in extreme goal-pursuing behavior, which would disrupt their sleep and daily routines, leading to more episodes. In this study, therapists targeted these attitudes. At 6 months, the CT group scored significantly lower than the control group regarding such goal-striving attitudes. However, the difference was nonsignificant at month 12. Our experience in working with highly driven patients with bipolar affective disorder was that these attitudes could be highly valued by patients. A vigorous attempt to challenge these beliefs was warranted but not necessarily always successful.

All in all, our study showed that CT was useful in preventing relapses, alleviating symptoms, and promoting social functioning in a group of patients with bipolar affective disorder who had experienced frequent relapses despite the prescription of mood stabilizers. We tested the hypothesis that CT has beneficial effects when used in conjunction with medication. We found that CT can reduce the frequency of relapses and promote social functioning. Cognitive therapy is a worthy addition to pharmcotherapy in the treatment of bipolar affective disorder, particularly for those who experience frequent relapses despite the use of mood stabilizers.

Our study had 3 drawbacks. There was no measure of sleep hygiene or routine. There was also no control for the effect of attention or medication prescribed. However, the aim of the study was to test the beneficial effects of adding CT to commonly used pharmacotherapy for patients with bipolar affective disorder. We specifically targeted a group of patients who did not respond well to medication alone. Medication and other treatment by the clinical team were carefully monitored. The implications for the health care economy will be reported in due course. A long-term follow-up of the sample is also being carried out.

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