An Update on the Role of Psychotherapy in the Management of Bipolar Disorder

David J. Miklowitz, PhD

Corresponding author
David J. Miklowitz, PhD
Department of Psychology, Muenzinger Building, University of Colorado, Boulder, CO 80309-0345, USA.
E-mail: miklowitz@colorado.edu

Current Psychiatry Reports 2006, **8:**498–503
Current Science Inc. ISSN 1523-3812
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Recent studies have examined the value of combining structured forms of psychotherapy with medication maintenance for patients with bipolar disorder. These studies have been influenced by the growing body of literature on stress in the elicitation of manic and depressive episodes. Randomized trials published within the past 5 years indicate positive benefits of cognitive-behavioral therapy, interpersonal and social rhythm therapy, family-focused therapy, and group psychoeducation as adjuncts to mood stabilizers in delaying recurrences, stabilizing symptoms, and improving medication adherence. Open trials of family interventions for pediatric-onset bipolar patients also have yielded promising results. Questions remain about the relative advantages of one psychosocial approach over the others, whether there are subgroups of patients who respond to each type of intervention, the impact of psychotherapy on role functioning, mediators of treatment effects, and the potential utility of early intervention as a means of delaying the onset and/or severity of the disorder.

Introduction

Bipolar disorder is an illness with strong genetic and biological underpinnings, and pharmacotherapy is the cornerstone of the acute and maintenance treatment of the illness. However, psychiatrists are increasingly recognizing that the illness cannot be fully controlled with pharmacotherapy alone. A naturalistic study from the Systematic Treatment Enhancement Program for Bipolar Disorder [1] of 1469 symptomatic bipolar patients revealed that only 58% recovered within 1 year; of these, 49% had recurrences within 2 years. Rates of depressive recurrence were more than twice as high (35%) as rates of manic recurrence (14%), suggesting that pharmacotherapy may be more effective in preventing manic than depressive recurrences [2]. Residual symptoms of mania and depression were strong predictors of recurrence. In a 13-year prospective study of bipolar I and II patients, subsyndromal symptoms—notably depression—were present during approximately one half of the weeks of follow-up [3]. Patients stabilize more slowly from episodes of depression than mania, even when medications are optimized [4].

Can combining pharmacotherapy with psychotherapy improve upon these outcomes? Is adjunctive psychotherapy useful as an acute or maintenance agent, and if so, what kind? This article will review the randomized controlled trials of psychotherapy as an adjunct to pharmacotherapy, with emphasis on studies published within the past 5 years.

Historical Perspective

At least three trends influenced the current renewed interest in psychotherapy for bipolar illness. Prior to the advent of lithium, psychotherapy was the only treatment available for bipolar disorder other than hospitalization. Psychological theories of mania and depression abounded, and case studies were published on the use of intensive psychoanalysis [5]. With the introduction of lithium and the anticonvulsants, along with substantial data on the etiological role of genetic vulnerability, psychotherapy was all but forgotten. In the 1980s, the focus of psychotherapy shifted to helping patients adjust to the illness and accept the need for medications instead of uncovering the psychological origins of the disorder [6]. Notably, during this interval, a single randomized trial of cognitive-behavioral therapy (CBT) as adjunct to lithium found beneficial effects on risk for hospitalization and adherence to medications [7].

A second trend that influenced the development of current psychotherapies for bipolar disorder was the emerging literature on psychotherapy for schizophrenia. During the 1970s and 1980s, a number of "psychoeducational" studies showed that combining neuroleptic medication with behavioral family therapy or individual social skills training reduced rates of psychotic relapse and improved functioning over 1- to 2-year periods,

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although not necessarily through the avenue of improving medication adherence [8]. Investigators began to apply some of the same methods that had been used successfully with schizophrenic patients to bipolar patients, with appropriate adjustments of the content and process of the psychoeducational sessions [9].

A third trend concerned the role of psychosocial stress in the recurrences of bipolar disorder. For example, Ellicott et al. [10] found that patients with bipolar disorder who had high life stress scores were at a 4.5 times greater risk for relapse over 2 years than patients with medium or low levels of life stress. In a prospective study of manic patients, Miklowitz et al. [11] found that patients who were discharged from the hospital to families in which caregiving relatives were rated high on expressed emotion (criticism, hostility, or emotional overinvolvement) or families characterized by high levels of affective negativity in day-to-day interactions were highly likely to relapse within a 9-month follow-up interval.

Johnson and Miller [12] found that negative life events were associated with slow recovery from bipolar depressive episodes. However, life events that were positive and involved goal attainment (eg, getting promoted) were associated with an increase in manic symptoms [13]. A retrospective study found that bipolar patients often experienced events that disrupted their sleep/wake rhythms in the months preceding manic onset, although not prior to depressive onset [14,15]. These studies underlined the role of stress in mediating the relations between biological vulnerability and relapse and paved the way for studies of psychosocial treatment as adjunctive to medication.

CBT

The assumption behind CBT approaches is that bipolar patients, like unipolar patients, have distorted cognitions and assumptions that lead to negative mood states. Unlike traditional CBT for depression [16], CBT for bipolar disorder also addresses distorted cognitions during the manic state, also called hyperpositive thinking [17]. Although several models of CBT exist, the commonalities include the following: educating patients about the symptoms, course, and treatment of bipolar disorder; scheduling pleasurable events to alleviate inactivity; teaching the skill of cognitive restructuring, in which patients learn to identify maladaptive thoughts, challenge them on logical or experiential grounds, and replace them with balanced or adaptive thinking; problem-solving; and developing relapse prevention plans.

A comprehensive study of CBT was performed by Lam et al. [18,19••], who compared a 6-month CBT intervention (12 to 18 sessions plus two booster sessions) with pharmacotherapy versus treatment as usual with pharmacotherapy (*n* = 103). The patients had had at least three illness episodes in the previous 5 years but had been in remission for at least 6 months. In the first study year, patients in CBT had lower rates of relapse than those in treatment as usual (44% vs 75%) and spent less time ill. In the 12 to 30 months following CBT, no differences in relapse were found between the CBT and usual treatment groups, although CBT continued to positively influence mood ratings and days spent in episodes.

CBT was evaluated in a five-site UK multicenter "effectiveness" trial of 253 bipolar patients treated at community mental health centers [20••]. As in the Lam et al. [18,19••] study, this study compared CBT (22 sessions) and medications with usual care and medications, but unlike the prior study, patients could enter in any clinical state (recovered, subsyndromal, or syndromal). There were no differential effects of CBT and pharmacotherapy on time to recurrence over an 18-month follow-up. Patients with fewer than 12 prior illness episodes had fewer recurrences in CBT than in treatment as usual, but patients with 12 or more episodes had fewer recurrences in treatment as usual than in CBT. Possibly, CBT is most appropriate for patients in the early stages of their disorder or those who are less recurrent.

Interpersonal and social rhythm therapy (IPSRT)

IPSRT [21••], like its forerunner, the interpersonal psychotherapy of depression [22], focuses on the interpersonal context of episodes of depression and mania. Initially, clinicians conduct an illness history and identify a recent problem area on which to focus (ie, grief, role disputes, role transitions, or interpersonal deficits). In the IPSRT of bipolar disorder, there is an additional focus on regulating and stabilizing sleep/wake rhythms, along with patterns of social routine and stimulation. Patients fill out the Social Rhythm Metric [23], a self-report instrument for tracking and quantifying daily and nightly routines, along with ratings of mood. As treatment ensues, clinicians assist patients in keeping regular routines (eg, bedtimes, wake times, exercise) and minimizing the impact of events that could disrupt their moods and daily/nightly stability. The interpersonal focus concerns the resolution of the patient's current problems (eg, how to communicate better with one's spouse) and the development of strategies for preventing the same problems from recurring in the future.

Frank et al. [21••] tested IPSRT in a large-scale maintenance trial at the University of Pittsburgh, in which bipolar I patients (*n* = 175) were randomly assigned following a mood disorder episode (acute treatment) to IPSRT plus protocol pharmacotherapy or an active comparison treatment, intensive clinical management plus protocol pharmacotherapy. Patients again were randomly assigned, once they had recovered from their index study episode, to IPSRT or intensive clinical management (maintenance treatment). The results were complex but supported the efficacy of IPSRT as a maintenance treatment. Although patients who received IPSRT during the acute treatment phase stabilized at the same rate as patients in intensive clinical management, those in IPSRT had longer survival

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times (without recurrence) during the maintenance phase of the study, regardless of whether they received IPSRT during the maintenance period. Moreover, patients who showed an ability to regulate their social routines and sleep/wake cycles during the acute phase—which was more likely to occur in IPSRT than in intensive clinical management—were less likely to have recurrences during maintenance treatment. Thus, IPSRT was an effective preventative agent and, consistent with its hypothesized mechanisms, appeared to operate through the stabilization of social rhythms.

An open trial with an "historical comparison" group [24] examined the effects of IPSRT in combination with family-focused treatment (FFT; mean 29 individual and family sessions over 1 year) for bipolar I and II patients (n = 30). All patients began in an acute illness episode and received standard medication management by study-affiliated psychiatrists. The involvement of family members was hypothesized to have a positive impact on patients' willingness and ability to regulate their social routines and sleep/wake rhythms. Patients in the combined treatment were compared with 70 bipolar I and II patients who had received medication, two sessions of family education, and crisis management in the context of an earlier study. Over 1 year, patients in the integrated family and individual therapy had longer delays prior to relapse and experienced less severe depressive symptoms than patients in the historical comparison group. The effects were not attributable to differences in medication regimens or compliance.

Thus, IPSRT is a promising individual approach to treatment of bipolar patients following an acute episode. The mechanisms of action of IPSRT appear to include social rhythm stabilization, but it is not clear whether other mechanisms (eg, interpersonal problem resolution, enhancing medication adherence) operate as well.

Family intervention

Family therapy approaches to bipolar disorder have a long history. Fitzgerald [25] discussed family therapy as a way of augmenting response to lithium, and Davenport et al. [26] described the benefits of a psychoanalytic couples' group. Only recently have approaches to family intervention become empirical. Two studies conducted in the late-1980s demonstrated the utility of psychoeducation for couples and families coping with bipolar disorder, either done on an inpatient or an outpatient basis [27,28].

Miklowitz and Goldstein [9,29] developed a manual-based, 21-session intervention called FFT, which is used in patients who are stabilizing from an acute episode. The treatment consists of four components: 1) an initial assessment phase; 2) psychoeducation about the nature, course, and treatment of bipolar disorder, including the importance of medication consistency, identifying early warning signs of relapse, and implementing relapse prevention strategies; 3) communication enhancement skills, notably role-playing and rehearsal of tools for active listening and expressing positive or negative feelings; and 4) problem-solving skills. In two recently completed randomized trials, FFT and pharmacotherapy were found to delay recurrences above and beyond pharmacotherapy alone or pharmacotherapy with individual therapy.

In the first trial, 101 patients were randomly assigned to FFT and pharmacotherapy or an active crisis management comparison treatment consisting of two sessions of family education, crisis intervention sessions as needed, and pharmacotherapy [30••]. Patients in FFT were more likely to survive the 2-year follow-up without relapsing (52%) than patients in active crisis management (17%). Patients in FFT also had less severe depressive and manic symptoms over the 2-year study. Posthoc analyses uncovered two mediators of these effects: greater consistency of medication adherence and improvements in the emotional tone of patient/relative verbal interactions [30••,31].

A second trial [32••] examined the relative effectiveness of FFT and pharmacotherapy versus a comparably intensive 21-session individual therapy and pharmacotherapy combination. The individual therapy had many of the same components as the FFT (psychoeducation, monitoring of moods, and encouragement of medication adherence), but family members were not involved. Patients in the two groups did not differ in relapse rates during the first year of treatment, but during a 2-year post-treatment follow-up, patients in FFT had fewer rehospitalizations (12%) and relapses (28%) than patients in individual therapy (60% and 60%, respectively). Moreover, patients in FFT were less likely to require hospitalization when they did relapse than patients in individual therapy. Possibly, relatives learned to identify patients' relapses before they escalated and thus were able to implement early intervention plans (eg, calling physicians to arrange emergency medication adjustments) before hospitalization was necessary.

A research group in Barcelona, Spain, examined the effects of family intervention on caregivers [33]. Relatives of 45 bipolar patients were randomized to a psychoeducational and coping skills group (12 sessions) or a no-treatment control group. All patients were euthymic and received medications throughout the study. Those relatives receiving psychoeducation reported greater reductions in emotional distress associated with the patients' illness and greater knowledge of how to cope with bipolar illness than those in the comparison group. Family interventions may prove to be cost effective if they have a positive impact on the emotional stability of caregivers as well as patients.

There is one negative trial of family intervention. Miller et al. [34] randomly assigned 92 bipolar patients to pharmacotherapy with individualized family therapy, multifamily psychoeducation groups, or pharmacotherapy alone. Unlike the previous trials, the primary outcome variable was time to recovery from the acute illness

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episode at intake; the impact of these interventions on time to recurrence or symptom severity over time was not reported. The groups did not differ in the proportion recovered or time to recovery, suggesting that certain types of family intervention may be less effective for acute stabilization than for maintenance of stability over longer intervals.

Family approaches to juvenile-onset bipolar disorder

Three groups have independently designed family psychoeducational approaches to childhood-onset bipolar disorder. Youths with bipolar disorder typically have multiple comorbid disorders and recalcitrant courses of illness that require complex combinations of medications [35].

Miklowitz et al. [36,37] adapted FFT for teenage bipolar patients and found positive effects on depression, mania, and parent-rated behavior problems in a small (n = 20), 2-year open trial. A large-scale randomized trial of this modality is now underway. Pavuluri et al. [38] examined the combination of FFT, CBT, and pharmacotherapy for school-aged (mean 11 years) children (n = 34) and observed reductions from pre- to post-treatment in mania, aggression, psychosis, and depression scores.

Fristad et al. [39] randomly assigned 35 children (aged 8 to 11) with unipolar disorder and bipolar disorder to multifamily groups or a waiting list. Over 6 months, parents assigned to the multifamily groups reported a greater understanding of mood disorder, more positive family interactions, increased parental support (as reported by children), and increased use of appropriate services relative to parents on the waiting list.

Group psychoeducational approaches

Given the expense of manual-based psychotherapy approaches in real world settings, several investigators have undertaken group-based models that involve treating several patients at once. A randomized trial from the Barcelona group found that patients in a 21-week structured psychoeducation group had longer intervals prior to recurrences than patients in an unstructured support group [40••]. During the 2-year study, relapses occurred earlier and more often among patients in the unstructured group (92%) than in the structured groups (67%). Patients in the structured group had higher and more stable lithium levels as well [41]. However, the structured groups had a higher dropout rate (27%) than the unstructured groups (12%).

In the largest psychotherapy study to date (n = 441), Simon et al. [42,43••] evaluated group psychoeducation in the context of a multicomponent intervention delivered within a managed care network. They randomly assigned bipolar patients to pharmacotherapy alone or a care management program consisting of pharmacotherapy, structured group psychoeducation (following the model of Bauer and McBride [44]), interdisciplinary care planning, facilitation of follow-up care, and crisis intervention. Over 2 years, patients in the care management program had lower levels of manic symptoms and less time in manic episodes. No effects were found on depressive symptoms. Importantly, the program could be implemented with only modest increases in the costs of care.

Conclusions and Recommendations for Future Research

Adjunctive psychotherapy has long been recommended for the treatment of bipolar disorder but has only recently received serious research interest. The major modalities with empirical support appear to be individual cognitive and interpersonal therapy, FFT and other forms of family psychoeducation, and structured group psychoeducation. The majority of the benefits have been observed during maintenance treatment, although the acute impact of these interventions deserves further study.

These interventions have many commonalities, as discussed by Scott and Gutierrez [45]: They all include psychoeducation about bipolar disorder, encouragement of medication adherence, relapse prevention strategies, mood monitoring, and illness management skills. It is not clear whether the theoretical or practical differences in the approaches translate into better effects for one approach versus another; this question is being addressed in the Systematic Treatment Enhancement Program [46]. Even more importantly, it is not clear whether there are “hidden moderators” of these treatment effects. Each study has identified subgroups of patients who responded best to the approach. For example, Lam et al. [17] found that CBT was less effective among patients who had a “sense of hyperpositive self” marked by dynamism, persuasiveness, and productiveness. As mentioned, Scott et al. [20••] found that patients only responded to CBT if they had had fewer than 12 previous episodes. The University of Pittsburgh trial [21••] found that IPSRT was less effective among patients with medical comorbidities. The large-scale study of group psychoeducation and care management [43••] only observed effects among patients who entered with clinically significant mood symptoms. Finally, Miklowitz et al. [47] and Kim and Miklowitz [48] found differential effects of FFT as a function of whether families were initially high or low in expressed emotion. Examination of moderators within studies that directly compare the various approaches is warranted, although these studies will need to be powered with adequate sample sizes.

Few studies have examined the impact of psychotherapy on life functioning. Functioning clearly is impaired in bipolar disorder [49] and not fully normalized by pharmacotherapy. Future studies should consider the effects of adjunctive psychotherapy on work functioning, family and social functioning, and quality of life.

The role of mediators in the pathways from psychosocial treatment to clinical outcomes has received scant attention. Mediational analyses have increased in sophistication [50,51] and could be usefully applied to this area. We do not know how psychotherapy works,

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only that it does work. Does psychotherapy improve medication adherence or reduce the need for complex pharmacotherapy regimens? Alternatively, are changes in biopsychosocial factors hypothesized to be important in these treatment models (eg, negative or hyperpositive cognitions, family expressed emotion, responses to life events, sleep/wake regularity) necessary before we can observe treatment benefits?

Finally, the role of psychotherapy in the early onset of the disorder deserves study. There is beginning evidence that early intervention with pharmacotherapy alters the course of childhood-onset bipolar disorder [52•]. Introducing a structured, psychoeducational, coping-oriented intervention for children with a bipolar parent may have similar preventive effects. It is not clear whether all children who are genetically at risk would benefit from such an intervention, or only those who show the early subsyndromal signs of the illness and functional impairment. Treatment development studies to address these questions are essential.

Acknowledgments

Preparation of this manuscript was supported by National Institute of Mental Health grants MH073871 and MH62555, a Distinguished Investigator Award from the National Alliance for Research on Schizophrenia and Depression, and a Faculty Fellowship from the University of Colorado.

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