

# Family-Focused Treatment for Children and Adolescents with Bipolar Disorder

David J. Miklowitz, PhD

*Division of Child and Adolescent Psychiatry, University of California, Los Angeles Semel Institute for Neuroscience and Behavior, California, U.S.A.*

## ABSTRACT

The course of bipolar disorder in children and adolescents is highly recurrent and impairing. This article describes the adaptation of family-focused treatment (FFT) for children and adolescents with bipolar disorder. FFT is given in 21 sessions over 9 months, and is usually initiated during the recovery period following an acute episode of depression or (hypo)mania. The treatment consists of an engagement phase followed by psychoeducation, communication enhancement training, and problem-solving skills training. Results of randomized trials in adults and adolescents find that patients with bipolar disorder who receive FFT and pharmacotherapy recover from episodes more quickly and have longer periods of sustained remission than patients who receive briefer forms of therapy and pharmacotherapy. The application of FFT to youth who are genetically at risk for bipolar disorder is described. Problems in disseminating empirically supported family interventions in community settings are discussed.

## INTRODUCTION

Between 50%–66% of adults with bipolar disorder (BD) report disease onset prior to age 18, and 15%–28% before age 13 (1). BD I and II appear to affect about 2% of youth under age 18, although there is variability across cultures (2). Among offspring of parents with BD I or II, subthreshold or “high-risk” forms of the disorder, which affect between 3%–9% of clinically referred youth, can be detected as much as 10 years prior to the onset of full BD (3–5).

Significant controversies exist about the definition, ascertainment, and boundaries of early-onset BD (4, 6–8). Nonetheless, agreement is substantial that BD spectrum disorders and their high risk antecedents have a significant impact on functionality and quality of life (6, 9). Youth who meet DSM-IV definitions of BD I or II or BD, not otherwise specified (BD-NOS), the latter characterized by brief, recurrent subthreshold (hypo) manic and depressive periods, have high rates of affective morbidity, impairment, suicidal ideation, comorbidity and service use (10, 11).

Without early intervention, the social, intellectual, and emotional development of youth with BD may be seriously compromised. Delays to first treatment of BD spectrum disorders in childhood are associated with greater depressive morbidity and less time euthymic in adulthood (12). Accordingly, well-tolerated interventions early in the course of the illness that reduce affective morbidity, enhance functioning, and teach emotion regulation skills could have a dramatically favorable impact on individual suffering. Early interventions in a developing population may allow for the normative acquisition of skills such as personal autonomy, academics, and peer relationships before the more debilitating cycles of patterns of relapses and remissions begin. Currently, youth with BD spectrum disorders are treated with a wide variety of medications and therapies, with little evidence-based practice (10).

Increasingly, family psychoeducational interventions are being used as adjuncts to somatic therapies in the treatment of major psychiatric disorders and medical conditions (13). Substantial progress has been made in the development and application of family interventions to BD. The purpose of this article is to review the current state of knowledge regarding one form of family intervention – family-focused treatment (FFT) – for youth with BD or at risk for BD (see the accompanying articles

**Address for Correspondence:** ✉ Dr. David J. Miklowitz, Division of Child and Adolescent Psychiatry, UCLA Semel Institute for Neuroscience and Behavior, David Geffen School of Medicine at UCLA, 760 Westwood Plaza Rm 58-217, Los Angeles, CA 90024-1759, U.S.A. ✉ dmiklowitz@mednet.ucla.edu

by Nadkarni and Fristad, and West and Weinstein for other approaches. for other approaches to treating families). The article begins by explaining the basis of the FFT approach in expressed emotion (EE) research. The second section describes the clinical methods of FFT for youth with BD. A brief case study is offered. Third, evidence for the effectiveness of FFT in clinical trials of adults and adolescents is reviewed, including recent work in youths at high genetic risk for bipolar disorder. Finally, recommendations for future research and community dissemination efforts are offered.

---

### RESEARCH ON EXPRESSED EMOTION

EE, a construct well-known in the schizophrenia literature, refers to the expression of certain emotional stances or attitudes among caregivers of patients with a psychiatric disorder: criticism, hostility, or emotional over-involvement (over-protectiveness, inordinate self-sacrifice) (14). Families are classified as “high-EE” if one or more caregivers (i.e., parent, spouse, sibling) expresses 6 or more critical comments or shows high levels of hostility or over-involvement during a 1-hour interview regarding the patient’s illness history. The significance of EE is a prognostic one: patients who are discharged from the hospital to families rated high in EE are at 2-3 times greater risk of relapse in the next year than patients who recover in low-EE (less critical or protective) households. This longitudinal association has been observed in numerous studies of patients with schizophrenia, major depression, and other psychiatric and medical disorders (15).

Several studies of EE have been conducted in families of patients with BD, and all indicate that patients whose relatives express high EE attitudes have higher rates of relapse and more severe mood symptoms over 9 month – 2 year periods than patients whose relatives express low-EE attitudes (16-20). One small-scale study found that adolescents with BD with high-EE parents had higher levels of depressive and manic symptoms over 2 years than BD adolescents with low-EE parents, despite ongoing psychosocial and pharmacological treatment (21).

The dynamics of families with high and low-EE relatives offer clues as to why the EE construct – a simple behavioral measure of critical or hostile comments – has such strong prognostic validity. High-EE parents or spouses of patients with schizophrenia or mood disorders are more likely to attribute the negative behaviors of patients to internal, controllable, and personal factors, whereas low-EE parents/spouses are more prone to attri-

bute negative patient behaviors to external, uncontrollable, or universal factors (15, 22). High-EE caregivers of patients with schizophrenia are more likely than low-EE caregivers to use “avoidance coping” (i.e., escapism) when dealing with their offspring’s symptoms (23). Families with high-EE are often locked into negatively escalating cycles of communication, in which criticism from one family member reliably elicits counter-criticism from another, such that conflicts become lengthy and difficult to resolve (24). One study found a link between criticism from parents, odd or grandiose thinking in patients, and later relapse of BD among adult patients (25).

For patients with BD, the implications of EE research are several-fold: 1) modifying the emotionally-charged environment of the family during a post-episode period may hasten the patient’s recovery and delay recurrences; 2) caregivers may benefit from psychoeducation oriented toward distinguishing what behaviors of the patient are controllable (i.e., purposeful) and not controllable (i.e., illness-driven); and 3) families of patients with BD may benefit from learning communication and problem-solving skills to resolve stressful conflicts during the post-episode period. These implications are addressed in one model of integrated treatment for BD: family-focused treatment (FFT).

---

### FAMILY-FOCUSED TREATMENT

Based in large part on our findings regarding EE in bipolar adults, we developed FFT in simultaneous trials at the University of California, Los Angeles (UCLA; 26, 27) and the University of Colorado, Boulder (17, 28). Our most recent work has concerned FFT in adolescents with BD, the focus of this article. FFT involves the patient and his or her parent(s) (or, in the case of some adults, a spouse) or extended relatives, depending on who the patient lives with and who has caregiving responsibilities. It is initiated after a patient has had an acute episode of mania, hypomania, depression, or mixed disorder from which he or she is in the process of recovering. Typically, patients are still symptomatic during this period and at high risk for relapse.

FFT is conducted by a clinical psychologist, social worker or family therapist who works in tandem with a psychiatrist responsible for pharmacotherapy. It consists of four stages: an *engagement* phase, where the therapeutic goal is to connect with the patient and relatives and relay information about the treatment’s structure and expectations; a *psychoeducational* phase, in which thera-

pists lead the family in discussions of the nature, causes, and management of BD; *communication enhancement training*, in which patients and parents rehearse effective speaking and listening skills (e.g., how to give praise and constructive criticism; how to listen actively); and *problem-solving skills training*, in which patients and parents define specific problems, generate and evaluate solutions, and implement solutions to problems in the family's or the individual patient's life. The treatment is ordinarily given in 21 sessions (12 weekly, 6 biweekly, 3 monthly) over 9 months. When practiced in the community, clinicians and families sometimes opt for shorter versions or longer intervals between sessions.

The techniques of FFT for adults with BD can be found in the clinician's manual (29). In the sections that follow, we describe the FFT in relation to the treatment of adolescents with BD. The treatment objectives are listed in Table 1.

**Table 1.** Objectives of Family-Focused Treatment (FFT) for Bipolar Disorder

<p>To assist the patient and parents to:</p> <ul style="list-style-type: none"> <li>• make sense of their experiences with manic and depressive episodes</li> <li>• develop plans to arrest future mood escalations or deteriorations</li> <li>• accept the need for mood-stabilizing medications for ongoing symptom control</li> <li>• distinguish between personality or temperament and bipolar disorder</li> <li>• cope with stressful life events that trigger mood swings</li> <li>• establish a family context that facilitates long-term recovery</li> </ul>
---

## PSYCHOEDUCATION

Psychoeducation, conducted in the first 7-8 sessions of FFT, offers teens and parents didactic information about the symptoms, differential diagnosis, comorbidity, prognosis, treatment, and self-management of BD. Handouts and self-guided homework (e.g., keeping a daily mood and sleep chart) accompany these topics. First, the clinician asks the teen and family to discuss the youth's recent symptoms of BD and helps them distinguish mood symptoms from symptoms of anxiety disorder, substance abuse, schizophrenia, or disruptive behavior disorders. The clinician explains the interactive roles of genetic and biological vulnerability, stress, and coping in the disorder's onset; the role of risk factors (e.g., disruptions in sleep/wake rhythms, substance misuse, escalating family conflicts) and protective factors (e.g., appropriate medication management, consistency with treatment visits, stable sleep/wake patterns, structured family routines). The impact of the disorder on day-to-day fam-

ily functioning is discussed. Care is taken to avoid any implication of blame of parents or the teen. Clinicians explain that many of the patient's behaviors are driven by a biologically- and genetically-based mood illness (rather than willful intention), and that negative reactions of parents often reflect frustration in their attempts to cope with highly stressful family circumstances.

A key component of psychoeducation is the mood management plan, or the planning during periods of mood stability for emergency intervention when the adolescent's moods start to change or when he/she becomes suicidal. With the aid of a flip chart, clinicians pose three questions: What makes your mood worse (or, more elevated/irritable/depressed)? How would we know if your mood had changed? What strategies improve your mood? Families recall previous periods of the teen's mood instability and identify sequences consisting of triggers, early warning signs of mood exacerbation, and preventative measures. A management plan is developed which for mania symptoms usually includes clarifying the conditions under which the treating psychiatrist should be notified, strategies for reducing stress at home and at school, and working towards greater regulation in sleep/wake rhythms. Special emphasis is placed on regulating family routines (e.g., mealtimes, bed times); often, the teen's chaotic sleep/wake schedules may be traced to the lack of structure in the family's life. Plans for managing depressive symptoms may include no suicide/no harm contracts, behavioral activation exercises (i.e., scheduling pleasant events), mindfulness meditation, or constructive self-talk. For some teens, the plan may include management of psychotic symptoms (for example, relaxation or distraction techniques).

## COMMUNICATION ENHANCEMENT TRAINING

CET (sessions 10-15) is designed to reduce aversive interactions among family members and teens and to improve the quality of exchanges. During role-play/skills training exercises and between-session practice, participants learn to (a) down-regulate impulsive expressions of negative affect through pausing and putting difficult feelings into words, (b) communicate in a manner that does not trigger emotional dysregulation in others, and (c) shift attention from destructive emotions to more conciliatory states. Adolescents and family members learn four skills: expressing positive feelings, active listening, making positive requests for

changes in each others' behaviors, and constructive negative feedback. The clinician offers handouts listing the components of each skill (e.g., for active listening: making eye contact, paraphrasing each others' statements), and demonstrates each for the family. Then, participants practice the skills with each other, with coaching and shaping by the clinician. Communication training is done less formally with adolescents than adults, capitalizing on the family's spontaneous interactions. Homework assignments, in which the participants record their efforts to use each skill, enhance generalization to other settings.

---

### PROBLEM SOLVING

In the problem solving module (sessions 16-21), families are taught to identify areas of disagreement, break down large problems (e.g., "we don't get along") into smaller ones ("we need to use lower tones of voice"), generate and evaluate pros/cons of solutions, and choose solutions to implement (e.g., alert each other to aggressive voice tones). Because it requires enhanced executive planning, problem-solving may augment functional capacity.

Participants list their most pressing problems and define each one (e.g., an adolescent does not get homework done, his mother becomes highly anxious, and conflict ensues). Then, family members generate 2-3 solution choices and evaluate the pros and cons of each. Next, the teen and family members conjointly choose a best option or set of options and develop an implementation plan. Families practice problem solving between sessions using a self-guided homework sheet and report on their attempts in the next session. As treatment sessions are tapered in frequency to once per month, more emphasis is placed on between-session practice.

---

### CASE EXAMPLE

Marissa was a 17-year-old with bipolar I disorder and comorbid attention deficit hyperactivity disorder, who lived with her mother, father, grandmother, and two brothers, one 19 and one 16. She was being treated with lithium 1200 mg and quetiapine 200 mg. She had had several instances of self-injurious behaviors (e.g., cutting). Her parents described the household as a "war zone" due to her frequent outbursts of rage. All family members agreed that Marissa's rages created huge problems for the family, but they disagreed on the causes

of these episodes. Her mother described them as being "manic-like," with rapid speech, excessive movements, and flight of ideas. She was particularly worried about how Marissa would cope when she went off to college the following year; would she curse at her professors and alienate her roommates? Marissa claimed that her "attacks" were largely triggered by the highly critical, hostile, and insulting interactions she had with her brothers, who, she said, regularly called her "fat and stupid." When asked, her brothers used more colorful words to describe her behavior.

In the early sessions of FFT, the clinician encouraged Marissa, her parents, and her brothers to identify the triggers, early warning signs, and potential preventative strategies for her rage reactions. Her reactions were often precipitated by family arguments (e.g., certain looks from her brothers) or multiple requests from her parents that confused her. The clinician assisted her in developing a *stress thermometer*, which clarified the stages of her angry escalations. Marissa and her family members were then encouraged to use a set of emotional self-regulation techniques when her mood escalations began, including: disclosing to one another that "something isn't feeling right"; using calming self-talk "when we feel the heat rising"; mindful breathing; exiting the situation (e.g., going outside to cool down), or attempting to separate the warring members of the family.

With repeated practice, Marissa found that she could better control her outbursts with her parents, but was still repeatedly provoked by her brothers. When their interactions degenerated into back and forth yelling matches, she was especially likely to start self-cutting. The communication enhancement module focused on her relationships with her brothers and encouraging each of them to practice active listening (paraphrasing, asking clarifying questions, nodding one's head to show acknowledgment). The use of these skills was helpful to Marissa and her brothers in slowing down their volatile interactions. Being able to limit negative interchanges to a maximum of three "volleys" also helped to reverse these predictable sequences.

In the final segment of FFT, Marissa and her parents worked on problem solving to maximize her chances of making a successful adjustment to college. The sessions included how to manage her medications (i.e., filling her medication prescriptions and taking her pills without reminders), getting herself out of bed in the morning without continual intervention by her parents, and completing household tasks. They also involved emo-

tional self-regulation techniques to use when she felt herself becoming angry with others (e.g., deep breathing, distraction).

By the end of treatment, Marissa still had impulsive, angry reactions brought on by negative interactions with her brothers. However, both Marissa and her parents reported that these episodes were becoming fewer and further between, did not last as long, and were not as destructive. She reported fewer suicidal thoughts and better overall mood states. Her brothers, although still angry with her, acknowledged that they had not understood the nature of her mood disorder, had on many occasions deliberately provoked her. She acknowledged, in turn, that they were becoming more patient with her. At termination, she continued with her ongoing pharmacotherapy appointments but did not seek additional therapy.

**EMPIRICAL STUDIES OF FFT**

The results of 11 trials of FFT in BD are described in Table 2. There have been five published randomized controlled trials (RCTs), one of which concerned bipolar adolescents, and four open trials, two involving children or adolescents. Two other RCTs, one of adolescent BD patients (N = 144) and one of youth at risk for BD (N = 40) are nearing completion (Table 2).

In an RCT at the University of Colorado, 101 adult BD I patients, 82 of whom had been newly discharged from the hospital were randomly assigned to FFT and pharmacotherapy or to crisis management (CM) and pharmacotherapy (28). FFT was given in 21 sessions over 9 months. Patients in CM received 2 sessions of psychoeducation, and crisis intervention sessions over 9 months. The overall 2-year study completion rate was

**Table 2. Results of Trials of Family - Focused Treatment and Pharmacotherapy in Bipolar Disorder**

Study	Sample	Type of Trial	Clinical State	Comparison Group	Key Findings
Miklowitz & Goldstein (26)	32 adults	Open with historical controls (9 mos)	Manic episode in prior 3 mos	Treatment as usual	FFT, 11% relapse rate Comparison, 61%
Miklowitz et al. (28)	101 adults	RCT (2 yrs.)	Depressed or manic episode in prior 3 mos	Crisis management (2 family psychoeducation sessions)	54% survival rate in FFT versus 17% in crisis management
Rea et al. (27)	53 adults	RCT (2-3 yrs.)	Manic episode in prior 3 mos	Individual therapy	36% rehospitalization rate in FFT, 60% in individual therapy
Miklowitz et al. (50)	100 adults	Open with historical controls (1 yr)	Depressed or manic episode in prior 3 mos	Crisis management	FFTplus interpersonal therapy associated with longer delays to relapse and less severe depression than crisis mgmt.
Miklowitz et al. (30, 31)	293 adults	RCT	Acute episode of bipolar depression	Collaborative care (3 education sessions) (RCT)	77% recovered in FFT in 1 year; 65% in IPT; 60% in CBT; 52% in Collaborative care; better social functioning in FFT and IPT
Miklowitz et al. (21)	20 adolescents	Open	Various states	None	Adolescents showed significant improvement over 2 years in depression, mania, and problem behaviors
Miklowitz et al. (33)	58 adolescents	RCT (2 yrs)	Acutely or subsyndromally ill	3 education sessions	Adolescents in FFT recovered from depression 7 weeks faster than adolescents in brief psychoeducation
Miklowitz et al. (44)	13 children (ages 9-17)	Open (1 yr)	Depression or subthreshold manic or hypomanic symptoms	None	Youth in FFT showed significant improvements in depression, mania, and global functioning scores
Perlick et al. (51)	Caregivers of 46 BD I adults, 1 yr	RCT (4.7 months)	Various states	8-12 session health program	Caregivers and patients in FFT had decreases in depressive symptoms
Miklowitz et al. (52)	144 teens w/BD I or II	RCT	Acutely or subsyndromally ill	3 sessions of psychoeducation	In progress; treatment completion and follow-up rates 78%-91%
Miklowitz & Chang (53)	40 children (ages 9-17)	RCT (1 year)	Depression or subthreshold manic or hypomanic symptoms	Enhanced care (1 session of family education)	In progress; completion rates 78%-85%



71% in FFT and 61% in CM, a nonsignificant difference. In a 2-year follow-up, patients in FFT were three times more likely to survive without relapsing (52% versus 17%) and had longer periods of remission without relapse (73.5 weeks versus 53.2 weeks) than patients in CM. FFT was also associated with greater remission of depression and mania symptoms over 2 years.

An RCT at UCLA examined FFT and pharmacotherapy when compared to an equally intensive individual therapy and pharmacotherapy (27) in 53 patients who had just been discharged following a manic episode. Patients in the individual therapy received 21 sessions of psychoeducation, medication adherence monitoring, and relapse prevention planning over 9 months. Patients in the two groups did not differ in rates of relapse or rehospitalization during the first year of treatment. However, in a 1-2 year post-treatment follow-up, patients in FFT showed lower rates of rehospitalization (12%) and symptomatic relapse (28%) than patients in individual therapy (60% and 60%, respectively).

A large-scale comparative effectiveness trial examined FFT in comparison with similarly intensive forms of therapy for adult bipolar patients recovering from a depressive episode (30, 31). In the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), conducted across 15 U.S. sites, 293 acutely depressed BD I and II patients were assigned randomly to a medication algorithm and one of four psychosocial treatments: up to 30 sessions of FFT, interpersonal and social rhythm therapy (IPSRT), cognitive-behavioral therapy (CBT), or a 3-session individual treatment called collaborative care (CC). All three of the intensive therapies were associated with higher 1-year recovery rates (105/163, or 64.4%) than CC (67/130, or 51.5%). Adding intensive psychotherapy to medication management speeded recovery by an average of 110 days during the study year. The rate of recovery for FFT was 77% over 1 year; for IPSRT, 65%; CBT, 60%; and CC, 51.5%. Patients in intensive therapy also had greater improvements in relationship functioning and life satisfaction than patients in CC (31).

The STEP-BD study suggests that patients with BD who enter treatment in states of depression benefit from intensive psychotherapy in combination with optimal medication management. There was no clear evidence that one of these treatments was more effective than the other, although the study was not statistically powered to address this question. Possibly, the common ingredients of intensive therapies for BD – teaching strategies

to monitor and stabilize mood and sleep, intervening early with prodromal symptoms, enhancing consistency with mood stabilizing medications, and working toward resolution of key interpersonal or family problems – contributed to patients' more rapid recoveries.

#### **APPLICATION OF FFT TO ADOLESCENTS WITH BD**

In the trials of FFT for BD adolescents (Table 2), we have recruited patients from both inpatient settings and outpatient referrals. We have included patients recovering from both depressive and manic or hypomanic episodes, as well as patients with or without psychotic symptoms. We have excluded patients with active substance or alcohol abuse, although an adaptation of FFT for adolescents with BD and substance abuse has been developed (32).

In an open trial (21), 20 adolescents (mean age 15 yrs) received 21 sessions of FFT and pharmacotherapy over 9 months. At 2-year follow-up, adolescents showed significant improvements in depression, mania, and total problem behavior scores. In a 2-site RCT, 58 adolescents with BD (75% with BD I or II) were allocated to FFT and pharmacotherapy or 3 sessions of family education and pharmacotherapy (33). Of the 58, 48 (83%) completed 1 year of treatment and follow-up. Over 2 years, patients in FFT had shorter times to recovery from their initial depressive episodes, less time in states of depression, and more time in remission than patients in the briefer treatment. They also had less severe depressive symptoms over time. FFT was particularly effective in stabilizing mania and depressive symptoms among adolescents in high-EE families, even though adolescents in high- and low-EE families did not differ in pretreatment symptom severity (34).

#### **APPLICATION OF FFT TO CHILDREN AT RISK FOR BD**

The effectiveness of FFT in studies of teens and adults with BD raised the question of whether a modified version of FFT could prove effective as an early intervention for youth at risk for BD. Prior research has identified at least three behavioral phenotypes that, when present in a child with a parent with BD I or II, may signal an increased risk for developing the disease over time. The Course and Outcome in Bipolar Youth study, a 4-5 year naturalistic follow-up of children with BD I, II, or NOS (defined as one DSM-IV symptom less than full criteria for a (hypo)manic episode, a clear change in functioning, and a minimum of 4 lifetime episodes each lasting  $\geq 1$  day), were at substantial risk for converting to BD I or II in 4 years (35). In the most recent (5 year)

report from this study, the risk of conversion was 58% among BD NOS youth with familial BD I or II, and 36% in BD NOS youth without familial BD (36).

Apart from early manic symptoms, the most reliable symptom complexes pre-dating mania are major depressive episodes or cyclothymic disorder. Rates of conversion from these states to BD I/II are highest in the first 4-5 years after initial onset, ranging from 15%-44% in 2 years to 20%-49% in 4 years (37-42).

A brief version of FFT for youth at high-risk for BD has been developed. This version consists of 12 sessions in 4 months after the high-risk youth has had a period of mood exacerbation (i.e., major depression or sub-threshold (hypo)mania). The focus is on skills relevant to managing the prodromal stages of BD – mood monitoring, reducing family conflict, improving problem-solving, and working toward stabilization of daily routines and sleep/wake cycles (43). The Colorado/Stanford High-Risk Trial is examining a cohort of 53 children and adolescents who meet criteria for BD-NOS, MDD, or cyclothymia (with active symptoms in the previous month) and have at least one parent with BD I or II. Results of a treatment development study (44), in which 13 youth (age 9-17, mean 13.4 yrs) were treated openly with FFT-HR over 4 months, indicated significant improvements over 1 year in (hypo)mania, depression, and psychosocial functioning, with Cohen's *d* effect size estimates ranging from .51 – 1.76. The results could not be attributed to participants' medication regimens at entry into the trial. Results of a recently completed RCT with high-risk youth (*N* = 40) will determine whether there are specific effects of FFT in bringing about symptom stabilization.

## CONCLUSIONS AND FUTURE DIRECTIONS

When combined with pharmacotherapy, FFT is an effective means of stabilizing youth and adults with BD. Recent research has examined the applicability of the approach to non-bipolar populations. A version of FFT for youth at risk for psychosis has recently been developed and is now being tested in an RCT (45). There is also an ongoing randomized trial of FFT for children (aged 6-14) with major depressive disorder, and promising open trial results (46).

There are significant gaps in the literature on FFT and other family interventions, notably the extension of these interventions into community settings. The difficulty with uptake of family interventions in community

settings may stem from several issues: the mistrust of family therapy approaches because of their association in many clinicians' minds with blaming parents for causing mental illness; a belief that family therapy is not cost-effective because too many people are involved; lack of training of clinicians in how to approach family members or conduct conjoint sessions; lack of reimbursement by insurance companies; and other issues which may not be related to treatment effectiveness. The primary responsibility for dissemination is on researchers, who need to 1) familiarize clinicians and administrators with the ways in which new forms of family psychoeducational treatment differ from traditional family system approaches; 2) conduct comparative cost-effectiveness studies; and 3) develop and test forms of family intervention that are economical and easily learned. Secondly, the responsibility lies with clinicians and administrators to familiarize themselves with treatment research relevant to family interventions and seek training when it is offered.

Most studies of family intervention consider only the behavioral pathways to change; future studies need to consider changes at the neural level as well. Bipolar adults and youth show increased amygdala activation and decreased prefrontal cortical activation (notably, the dorsolateral prefrontal cortex and the ventrolateral prefrontal cortex) on functional magnetic resonance imaging during affective challenge tasks (47-49). Studies that examine pre/post-treatment changes in neural markers may yield clues as to why family treatment, or more broadly, intensive psychosocial treatments have a positive impact on the course of BD. Our RCT of youth at high-risk for BD is examining neural activation during emotion challenge tasks that mirror the skills being taught in FFT, such as the ability to self-regulate one's emotions when in conflict with family members.

Long-term follow-up of high-risk samples will help determine whether the provision of brief, targeted interventions like FFT can prevent or delay the onset of BD I or II. More generally, psychosocial interventions designed to reduce stress, conflict, and affective arousal by enhancing communication, problem-solving, and emotion regulation skills may decrease the functional disabilities associated with this life-long disorder.

## References

1. Perlis RH, Miyahara S, Marangell LB, Wisniewski SR, Ostacher M, DelBello MP, et al. Long-term implications of early onset in bipolar disorder: Data from the first 1000 participants in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Biol Psychiatry* 2004;55:875-881.

2. Merikangas KR, Jin R, He JP, Kessler RC, Lee S, Sampson NA, et al. Prevalence and correlates of bipolar spectrum disorder in the world mental health survey initiative. *Arch Gen Psychiatry* 2011;68:241-251.
3. Shaw JA, Egeland JA, Endicott J, Allen CR, Hostetter AM. A 10-year prospective study of prodromal patterns for bipolar disorder among Amish youth. *J Am Acad Child Adolesc Psychiatry* 2005;44:1104-1111.
4. Youngstrom E, Van Meter A, Algorta GP. The bipolar spectrum: Myth or reality? *Curr Psychiatry Rep* 2010;12:479-489.
5. Youngstrom E, Youngstrom JK, Starr M. Bipolar diagnoses in community mental health: Achenbach Child Behavior Checklist profiles and patterns of comorbidity. *Biol Psychiatry* 2005;58:569-575.
6. Carlson GA, Findling RL, Post RM, Birmaher B, Blumberg HP, Correll C, et al. AACAP 2006 Research Forum - Advancing research in early-onset bipolar disorder: Barriers and suggestions. *J Child Adolesc Psychopharmacology* 2009;19:3-12.
7. Chang KD. Diagnosing bipolar disorder in children and adolescents. *J Clin Psychiatry* 2009;70:e41.
8. Kim EY, Miklowitz DJ. Childhood mania, attention deficit hyperactivity disorder, and conduct disorder: A critical review of diagnostic dilemmas. *Bipolar Disord* 2002;4:215-225.
9. Luby JL, Navsaria N. Pediatric bipolar disorder: Evidence for prodromal states and early markers. *J Child Psychol Psychiatry* 2010;51:459-471.
10. Axelson DA, Birmaher B, Strober M, Gill MK, Valeri S, Chiappetta L, et al. Phenomenology of children and adolescents with bipolar spectrum disorders. *Arch Gen Psychiatry* 2006;63:1139-1148.
11. Findling RL, Youngstrom EA, McNamara NK, Stansbrey RJ, Demeter C, Bedoya D, et al. Early symptoms of mania and the role of parental risk. *Bipolar Disord* 2005;7:623-634.
12. Post RM, Leverich GS. Early recognition and treatment of schizophrenia and bipolar disorder in children and adolescents. *Bipolar Network News* 1999;5:3-11.
13. Heru AM. Family psychiatry: From research to practice. *Am J Psychiatry* 2006;163:962-968.
14. Vaughn CE, Leff JP. The influence of family and social factors on the course of psychiatric illness: A comparison of schizophrenia and depressed neurotic patients. *Brit J Psychiatry* 1976;129:125-137.
15. Hooley JM. Expressed emotion and relapse of psychopathology. *Ann Rev Clin Psychology* 2007;3:329-352.
16. Miklowitz DJ, Goldstein MJ, Nuechterlein KH, Snyder KS, Mintz J. Family factors and the course of bipolar affective disorder. *Arch Gen Psychiatry* 1988;45:225-231.
17. Miklowitz DJ, Simoneau TL, George EL, Richards JA, Kalbag A, Sachs-Ericsson N, et al. Family-focused treatment of bipolar disorder: 1-year effects of a psychoeducational program in conjunction with pharmacotherapy. *Biol Psychiatry* 2000;48:582-592.
18. Yan LJ, Hammen C, Cohen AN, Daley SE, Henry RM. Expressed emotion versus relationship quality variables in the prediction of recurrence in bipolar patients. *J Affect Disorders* 2004;83:199-206.
19. O'Connell RA, Mayo JA, Flatow L, Cuthbertson B, O'Brien BE. Outcome of bipolar disorder on long-term treatment with lithium. *Brit J Psychiatry* 1991;159:132-129.
20. Priebe S, Wildgrube C, Muller-Oerlinghausen B. Lithium prophylaxis and expressed emotion. *Brit J Psychiatry* 1989;154:396-399.
21. Miklowitz DJ, Biuckians A, Richards JA. Early-onset bipolar disorder: A family treatment perspective. *Dev Psychopathol* 2006;18:1247-1265.
22. Wendel JS, Miklowitz DJ, Richards JA, George EL. Expressed emotion and attributions in the relatives of bipolar patients: An analysis of problem-solving interactions. *J Abnorm Psychol* 2000;109:792-796.
23. Scazufca M, Kuipers E. Coping strategies in relatives of people with schizophrenia before and after psychiatric admission. *Brit J Psychiatry* 1999;174:154-158.
24. Simoneau TL, Miklowitz DJ, Saleem R. Expressed emotion and interactional patterns in the families of bipolar patients. *J Abnorm Psychol* 1998;107:497-507.
25. Rosenfarb IS, Miklowitz DJ, Goldstein MJ, Harmon L, Nuechterlein KH, Rea MM. Family transactions and relapse in bipolar disorder. *Fam Process* 2001;40:5-14.
26. Miklowitz DJ, Goldstein MJ. Behavioral family treatment for patients with bipolar affective disorder. *Behav Modif* 1990;14:457-489.
27. Rea MM, Tompson M, Miklowitz DJ, Goldstein MJ, Hwang S, Mintz J. Family focused treatment vs. individual treatment for bipolar disorder: Results of a randomized clinical trial. *J Consult Clin Psychology* 2003;71:482-492.
28. Miklowitz DJ, George EL, Richards JA, Simoneau TL, Suddath RL. A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. *Arch Gen Psychiatry* 2003;60:904-912.
29. Miklowitz DJ. *Bipolar disorder: A family-focused treatment approach*. 2nd ed. New York, N.Y.: Guilford, 2008.
30. Miklowitz DJ, Otto MW, Frank E, Reilly-Harrington NA, Wisniewski SR, Kogan JN, et al. Psychosocial treatments for bipolar depression: A 1-year randomized trial from the Systematic Treatment Enhancement Program. *Arch Gen Psychiatry* 2007;64:419-427.
31. Miklowitz DJ, Otto MW, Frank E, Reilly-Harrington NA, Kogan JN, Sachs GS, et al. Intensive psychosocial intervention enhances functioning in patients with bipolar depression: Results from a 9-month randomized controlled trial. *Am J Psychiatry* 2007;164:1-8.
32. Goldstein BI, Goldstein T, Miklowitz DJ, Collinger KA, Bukstein O, Axelson D, Birmaher B. Family-focused treatment of adolescents with comorbid bipolar disorder and substance use disorders. Oral symposium presentation. American Academy of Child and Adolescent Psychiatry Annual Meeting; October 2009, Honolulu.
33. Miklowitz DJ, Axelson DA, Birmaher B, George EL, Taylor DO, Schneck CD, et al. Family-focused treatment for adolescents with bipolar disorder: Results of a 2-year randomized trial. *Arch Gen Psychiatry* 2008;65:1053-1061.
34. Miklowitz DJ, Axelson DA, George EL, Taylor DO, Schneck CD, Sullivan AE, et al. Expressed emotion moderates the effects of family-focused treatment for bipolar adolescents. *J Am Acad Child Adolesc Psychiatry* 2009;48:643-651.
35. Birmaher B, Axelson D, Goldstein B, Strober M, Gill MK, Hunt J, et al. Four-year longitudinal course of children and adolescents with bipolar spectrum disorders: The Course and Outcome of Bipolar Youth (COBY) study. *Am J Psychiatry* 2009;166:795-804.
36. Axelson DA, Birmaher B, Strober MA, Goldstein BI, Ha W, Gill MK, et al. Course of subthreshold bipolar disorder in youth: Diagnostic progression from bipolar disorder not otherwise specified. *J Am Acad Child Adolesc Psychiatry* 2011;50:1001-1016.
37. Angst J, Sellaro R, Stassen HH, Gamma A. Diagnostic conversion from depression to bipolar disorders: Results of a long-term prospective study of hospital admissions. *J Affective Disorders* 2005;84:149-157.
38. Duffy A, Alda M, Crawford L, Milin R, Grof P. The early manifestations of bipolar disorder: A longitudinal prospective study of the offspring of bipolar parents. *Bipolar Disord* 2007;9:828-838.
39. Geller B, Zimmerman B, Williams M, Bolhofner K, Craney JL. Bipolar disorder at prospective follow-up of adults who had prepubertal major depressive disorder. *Am J Psychiatry* 2001;158:125-127.
40. Kochman FJ, Hantouche EG, Ferrari P, Lancrenon S, Bayart D, Akiskal HS. Cyclothymic temperament as a prospective predictor of bipolarity and suicidality in children and adolescents with major depressive disorder. *J Affective Disord* 2005;85:181-189.
41. Nadkarni RB, Fristad MA. Clinical course of children with a depressive spectrum disorder and transient manic symptoms. *Bipolar Dis* 2010;12:494-503.
42. Strober M, Carlson G. Bipolar illness in adolescents with major depression: Clinical, genetic, and psychopharmacologic predictors in a 3-4 year prospective follow-up investigation. *Arch Gen Psychiatry*



- 1982;39:549-555.
43. Miklowitz DJ, Chang KD. Prevention of bipolar disorder in at-risk children: theoretical assumptions and empirical foundations. *Dev Psychopathol* 2008;20:881-897.
  44. Miklowitz DJ, Chang KD, Taylor DO, George EL, Singh MK, Schneck CD, et al. Early psychosocial intervention for youth at risk for bipolar disorder: A 1-year treatment development trial. *Bipolar Disord* 2011;13:67-75.
  45. Schlosser DA, Miklowitz DJ, O'Brien MP, De Silva S, Zinberg JL, Cannon TD. A randomized trial of family-focused treatment for adolescents and young adults at risk for psychosis: Study rationale, design, and methods. *Early Interv Psychiatry* 2011 Dec 20 doi. 10. 1111/j. 1751-7893. 2011. 00317. x[Epub ahead of print].
  46. Thompson MC, Pierre CB, Haber FM, Fogler JM, Groff AR, Asarnow JR. Family-focused treatment for childhood-onset depressive disorders: Results of an open trial. *Clin Child Psychol Psychiatry* 2007;12:403-420.
  47. Rich BA, Vinton DT, Roberson-Nay R, Hommer RE, Berghorst LH, McClure EB, et al. Limbic hyperactivation during processing of neutral facial expressions in children with bipolar disorder. *Proc Nat Acad Sciences* 2006;103:8900-8905.
  48. Yurgelun-Todd DA, Gruber SA, Kanayama G, Killgore WD, Baird AA, Young AD. fMRI during affect discrimination in bipolar affective disorder. *Bipolar Disord* 2000;2:237-248.
  49. Pavuluri M. Effects of early intervention on the course of bipolar disorder: theories and realities. *Curr Psychiatry Rep* 2010;12:490-498.
  50. Miklowitz DJ, Richards JA, George EL, Suddath RL, Frank E, Powell K, et al. Integrated family and individual therapy for bipolar disorder: Results of a treatment development study. *J Clin Psychiatry* 2003;64:182-191.
  51. Perlick D, Miklowitz DJ, Lopez N, Chou J, Calvin C, Adzhiashvili V, et al. Family-focused treatment for caregivers of patients with bipolar disorder. *Bipolar Disord* 2010;12:627-637.
  52. Miklowitz DJ, Axelson DA, Kowatch R. Effectiveness of family-focused treatment plus pharmacotherapy for bipolar disorder in adolescents. [www.ClinicalTrialsGov](http://www.ClinicalTrialsGov). 2009;NIMH Grant MH073871, ClinTrials ID: NCT00332098.
  53. Miklowitz DJ, Chang KD. Early intervention for youth at risk for bipolar disorder. *Bipolar Disord* 2010;12 :37.