

The Role of the Family in the Course and Treatment of Bipolar Disorder

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Senior Clinical Research

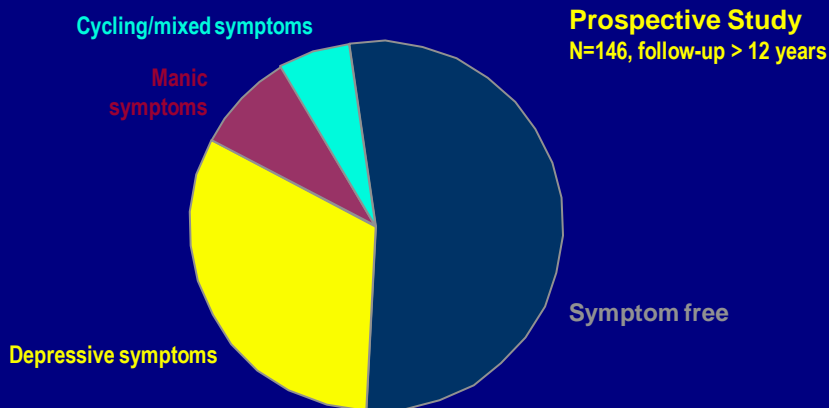
I cannot imagine leading a normal life without both taking lithium and having had the benefits of psychotherapy...ineffably, psychotherapy heals. It makes some sense of the confusion, reins in the terrifying thoughts and feelings, returns some control and hope and possibility of learning from it all...It is where I have believed – or have learned to believe – that I might someday be able to contend with all of this.”

-Kay Jamison, Ph.D., *An Unquiet Mind*, 1995

Bipolar Disorder From a Biopsychosocial Perspective

- Slow recoveries and high rates of recurrence despite drug treatment
- Significant symptoms (depression) between episodes
- Sixth leading cause of work disability worldwide
- High risk of suicide (15% lifetime)
- Significant rates of nonadherence with medications, often for psychological reasons
- Highly stress-generating and stress-sensitive

Bipolar Patients Spend Nearly Half of their Lives in States of Illness



Judd LL, et al. *Arch Gen Psychiatry* 59:530-537, 2002

Among the benefits of mania...



Questions Posed

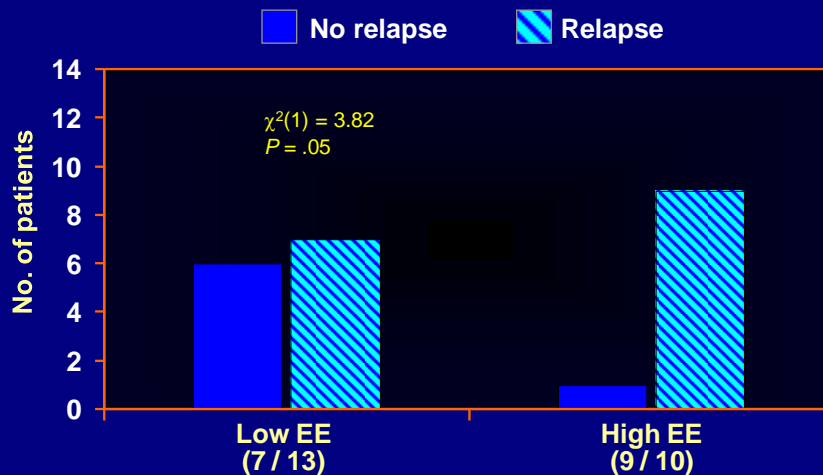
- Does stress within the family affect the course of bipolar disorder?
- Does a family psychosocial intervention augment medication management in managing the symptomatic course of BP?
- Are family interventions effective when tested in multiple-site effectiveness studies?
- Can family interventions be extended to younger bipolar populations?

How is Family Stress Measured? The Expressed Emotion Construct

- Refers to critical, hostile, or emotionally overinvolved/overprotective attitudes among caregiving relatives
- Families are classified as high-EE or low-EE based on face-to-face interviews of relatives by clinicians
- Interviews are conducted during the patient's acute illness episode, when family tension is highest

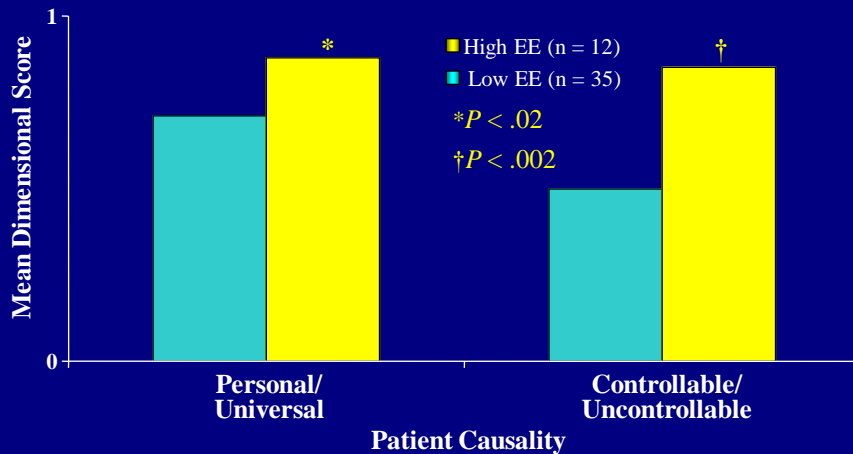
Source: Vaughn & Leff, 1976

Bipolar Disorder and Environmental Stress Family Expressed Emotion (EE) Predicts Relapse in a 9-Month Follow-Up of Adult Bipolar Patients



Miklowitz DJ, et al. *Arch Gen Psychiatry*. 1988;45(3):225-231.

EE and Relatives' Causal Beliefs About Patients' Roles in Negative Events



Wendel JS, Miklowitz et al. *J Abnorm Psychol.* 2000;109:792-796.

Family Focused Treatment (FFT)

of Bipolar Disorder

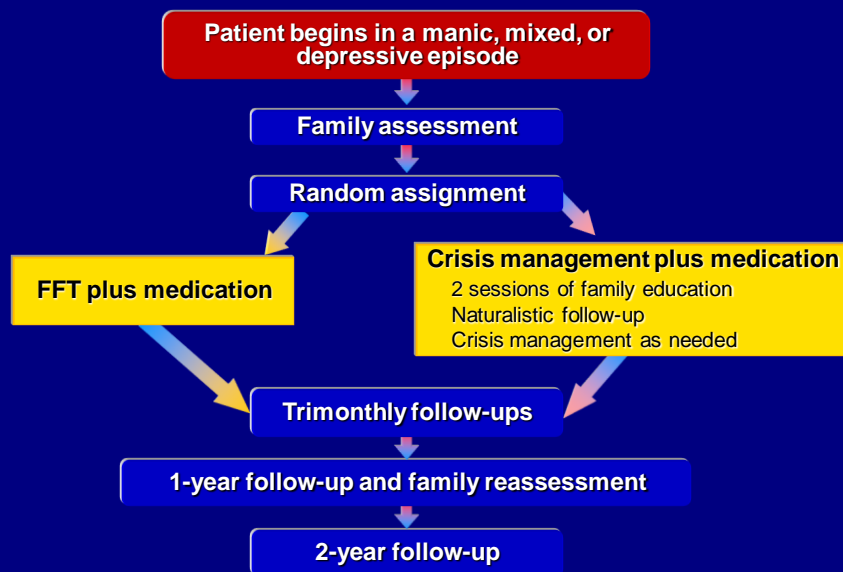
- ◆ Time-limited: 21 sessions over the 9 months following an acute episode
- ◆ Given in conjunction with pharmacotherapy
- ◆ Begins with assessment of family or couple
- ◆ Three component modules:
 - Psychoeducation about bipolar disorder (*symptoms, early recognition, etiology, treatment, self-management*)
 - Communication skills training (*behavioral rehearsal of effective speaking and listening strategies*)
 - Problem solving skills training

Miklowitz DJ and Goldstein MJ. *Bipolar Disorder: A Family-Focused Treatment Approach.* NY: Guilford Press, 1997

Is FFT Effective in Improving the Course of Bipolar Disorder?

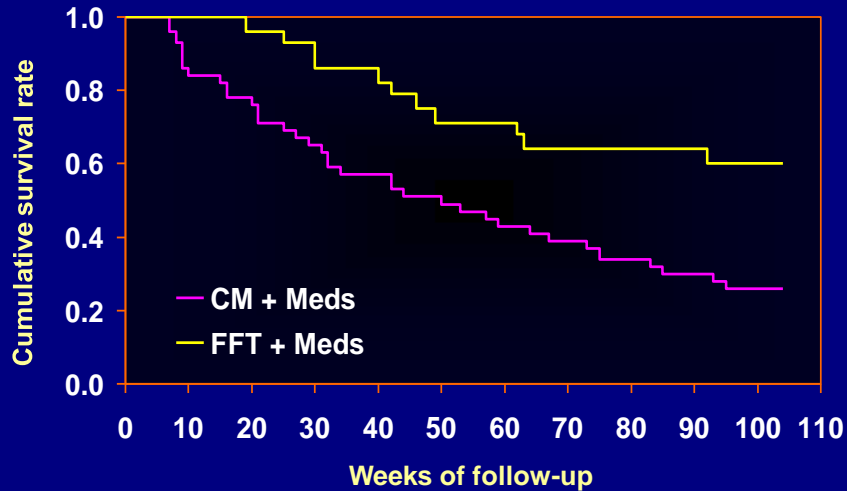
Results of Randomized Clinical Trials

The Colorado Treatment Outcome Study (N = 101)



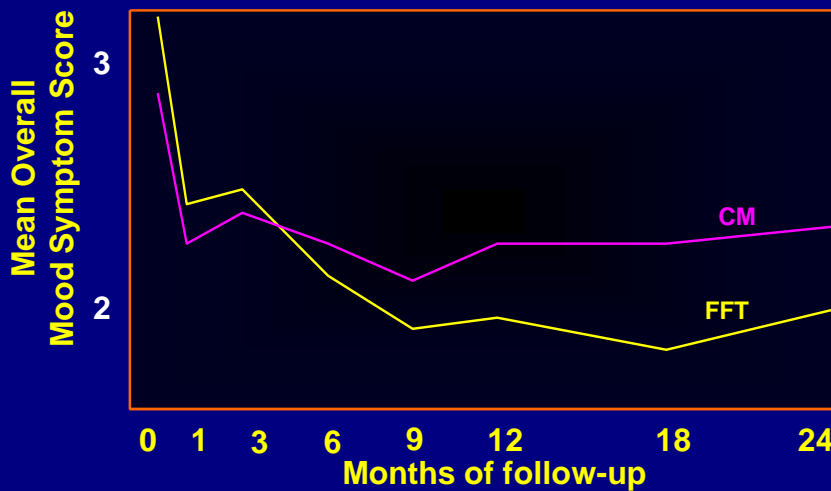
Miklowitz et al. *Arch Gen Psychiatry*. 2003;60:904-912. NIMH Grant MH43931

FFT + Medication Delays Relapse More than Crisis Management + Medication (N = 101)



CM vs. FFT $\chi^2 (1) = 8.71, p = .003$; FFT, mean survival = 73.5 weeks; CM, 53.2 weeks.
Miklowitz DJ, et al. *Arch Gen Psychiatry*. 2003; 60: 904-912

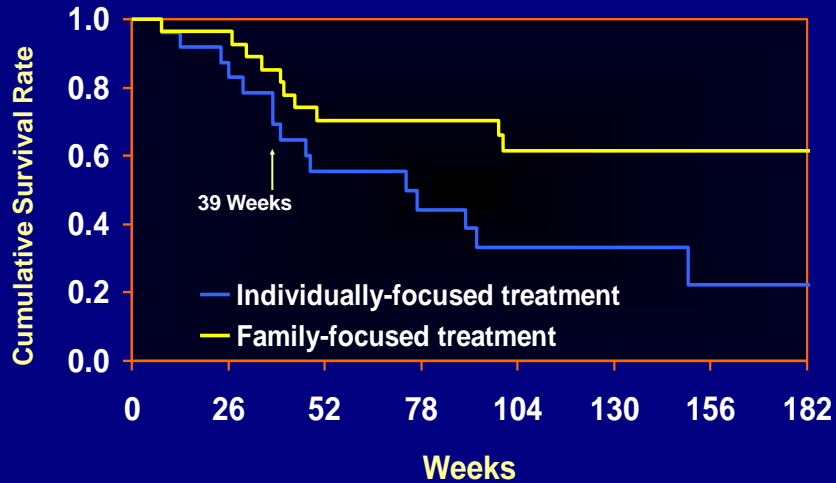
FFT & Medications Improve Mood Symptoms More Than Crisis Management and Medications: 2-Year Follow-Up



Treatment * Time $F(7,549) = 2.81, p = .007$
Miklowitz DJ, et al. *Arch Gen Psychiatry*. 2003; 60: 904-912.

Family vs. Individual Therapy: Time to Rehospitalization

UCLA FFT Study (N=53)



$\chi^2 (1) = 3.87, P < .05$

Rea, Tompson, Miklowitz et al. *J Consult Clin Psychol.* 2003; NIMH R01-MH55101

The Systematic Treatment Enhancement Program for Bipolar Disorder: A Multi-Center Study of Effectiveness and Treatment Dissemination

- NIMH-Funded, 15-22 sites
- 293 assigned to a randomized psychosocial study
- Follow-up over one year
- Outcomes: recovery from depression, likelihood of remaining well, functioning

Randomized Psychosocial Intervention for Bipolar Depression

3 Session Control Condition

“Collaborative Care”

(Education, Coping Strategies and Treatment Planning)

VS.

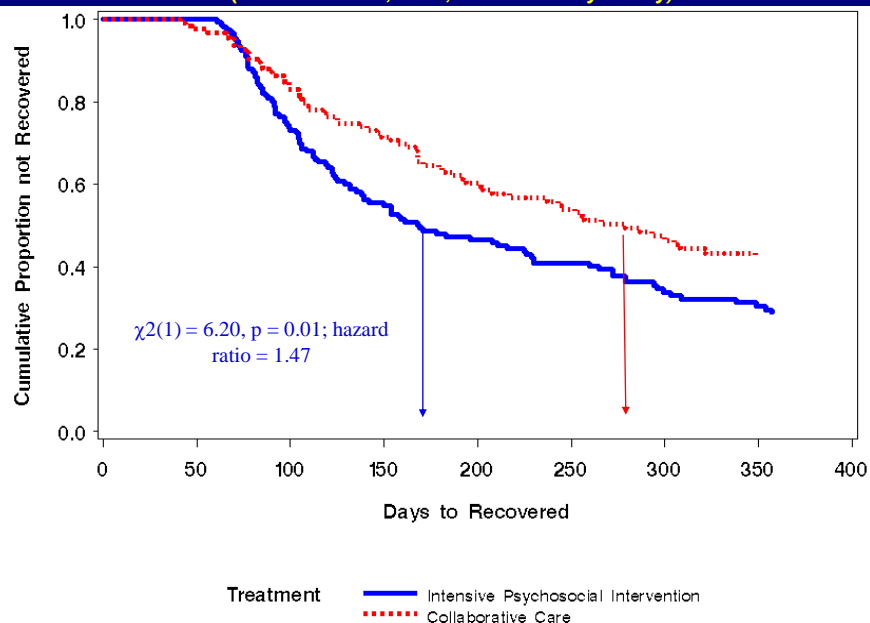
Intensive Interventions (up to 30 sessions)

Cognitive Behavioral Therapy (CBT)

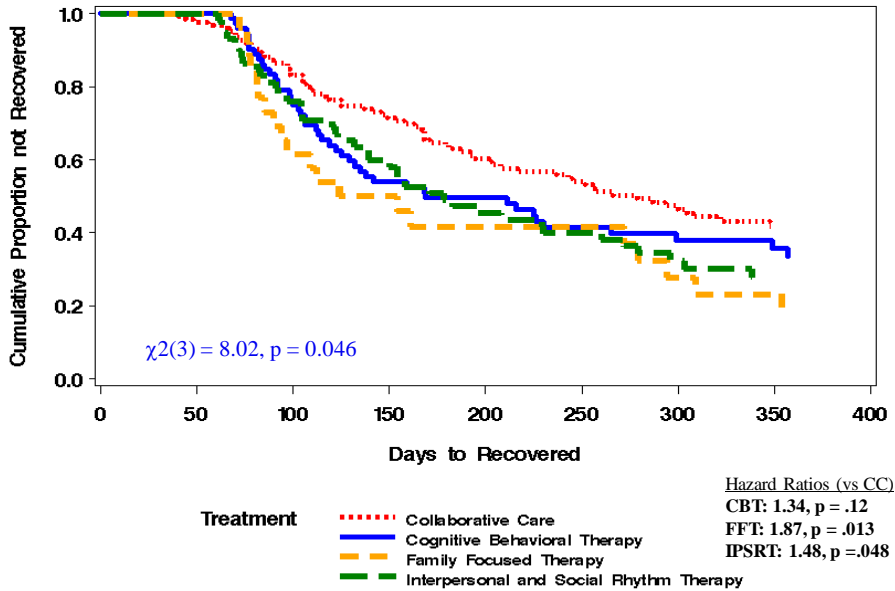
Interpersonal and Social Rhythm Therapy (IPSRT)

or Family Focused Therapy (FFT)

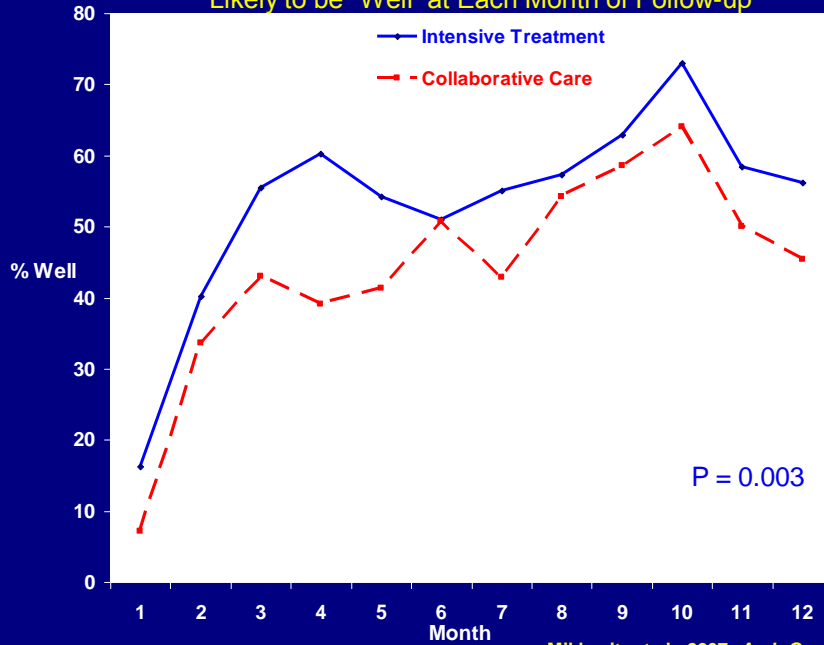
STEP-BD Study: 15 Sites, 293 Bipolar Patients in an Acute Episode of Depression
(Miklowitz et al., 2007; *Arch Gen Psychiatry*)



The STEP-BD Multisite Program (15 sites, N=293)
 (Miklowitz et al., 2007; Arch Gen Psychiatry)

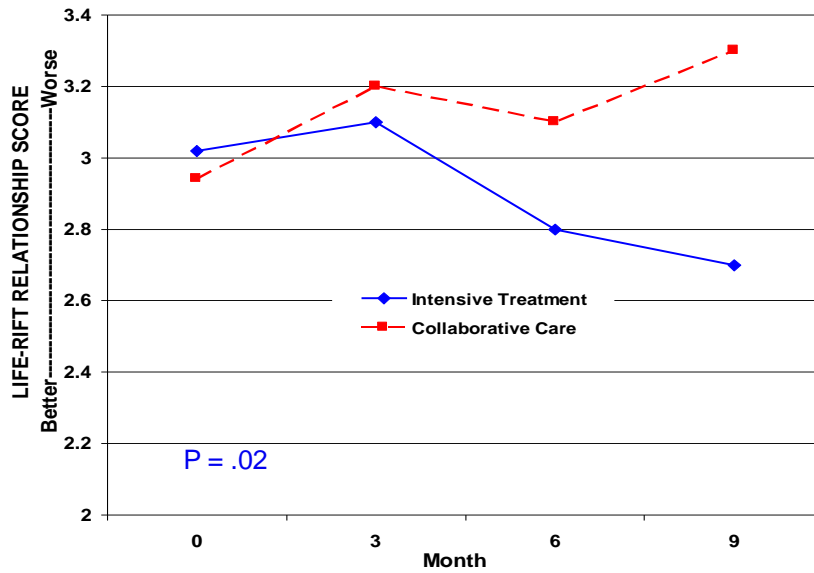


Patients in Intensive Therapy are 1.58 Times More Likely to be "Well" at Each Month of Follow-up



Miklowitz et al., 2007; Arch Gen Psychiatry

Psychosocial Treatment and Relational Functioning Scores

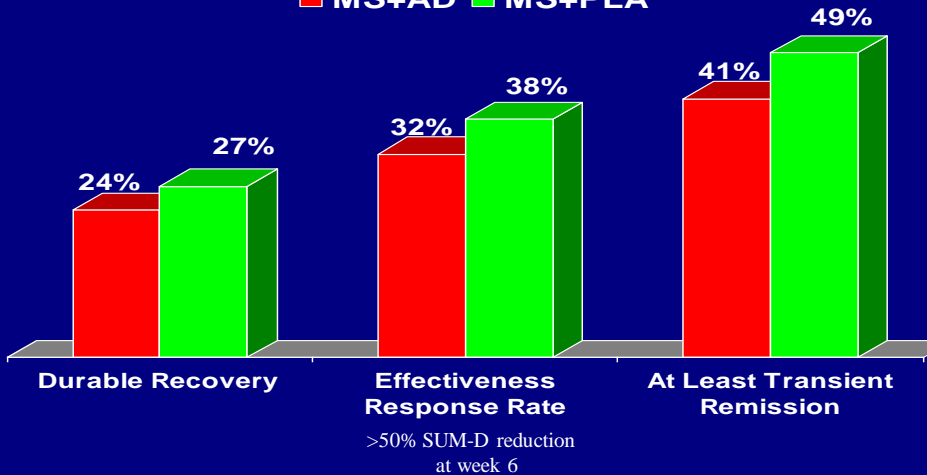


Miklowitz et al., *Am J Psychiatry*, 2007, 164, 1340-1347

Proportion Meeting Effectiveness and Efficacy Criteria: Mood Stabilizers with and without Antidepressants

No significant differences, All $p > .23$

■ MS+AD ■ MS+PLA



Sachs et al. 2007 *NFJM*

Conclusions from STEP

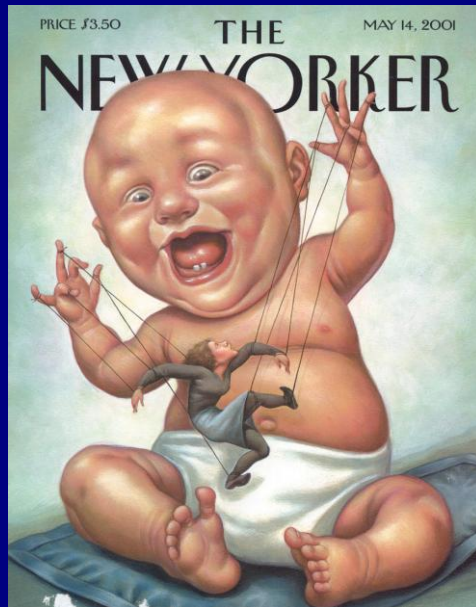
- Psychotherapy is a vital part of the effort to stabilize bipolar patients from an episode of depression
- Patients receiving intensive psychotherapy – FFT, IPSRT, or CBT – are more likely to remain well over a 1-year period
- Intensive psychotherapy is an important alternative to antidepressants

What do Modern Psychotherapies for Bipolar Disorder Have in Common?

- Psychoeducation (esp. about medications)
- Interpersonal problem-solving
- Relapse prevention planning
- Use of self-management strategies
- Enhancing coping with the stigma of BD
- Community advocacy

Miklowitz, Goodwin, Bauer, & Geddes, 2008; *J Psychiatric Practice*

Family-Focused Treatment for Bipolar Youth



Pediatric Bipolar Disorder is...

- Common (1-2% community, 6% clinical samples) - at least in U.S.
- Chronic mood instability, highly recurrent
- Socially and academically impairing
- Pharmacologically treatment-resistant
- Associated with significant family disruption

Modifying FFT to Address the Developmental Requirements of Adolescent Bipolar Patients

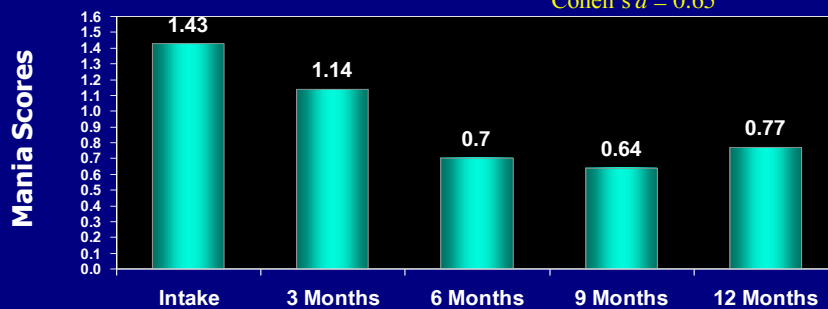
- *Episodes are often very short: focus on day-to-day mood fluctuations and “mood triggers” in the family and school settings*
- Identify triggers for family conflict - long-standing versus episode-specific
- *What’s bipolar disorder and what’s being a teenager? Help family distinguish age-appropriate moodiness from bipolar disorder*
- *Sleep/wake regularity*
- *Use of visuals: self-rated mood charts, educational videotapes*
- *Genetic vulnerability: address mood disturbances in parents and other family members*
- *High levels of family conflict: Support parents’ behavioral management efforts*

K-SADS Depression and Mania Scores During Treatment

(N = 20; Miklowitz et al., 2006; *Dev and Psychopathology*)



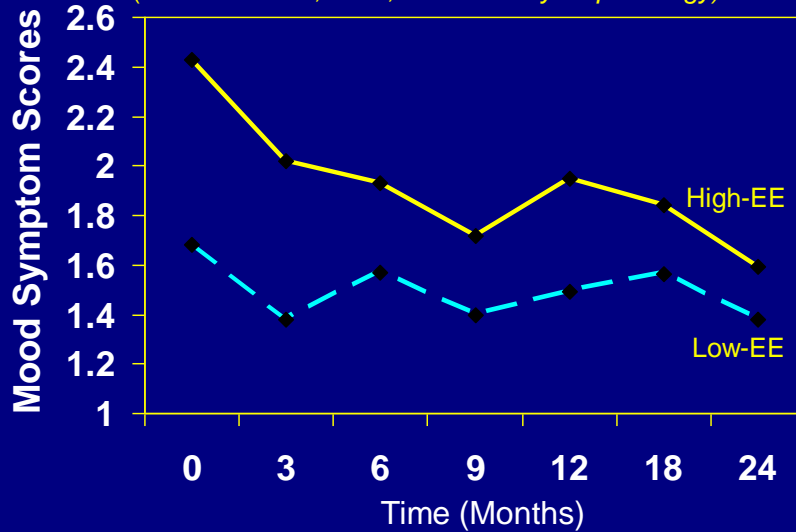
Cohen's $d = 0.65$



Cohen's $d = 0.79$

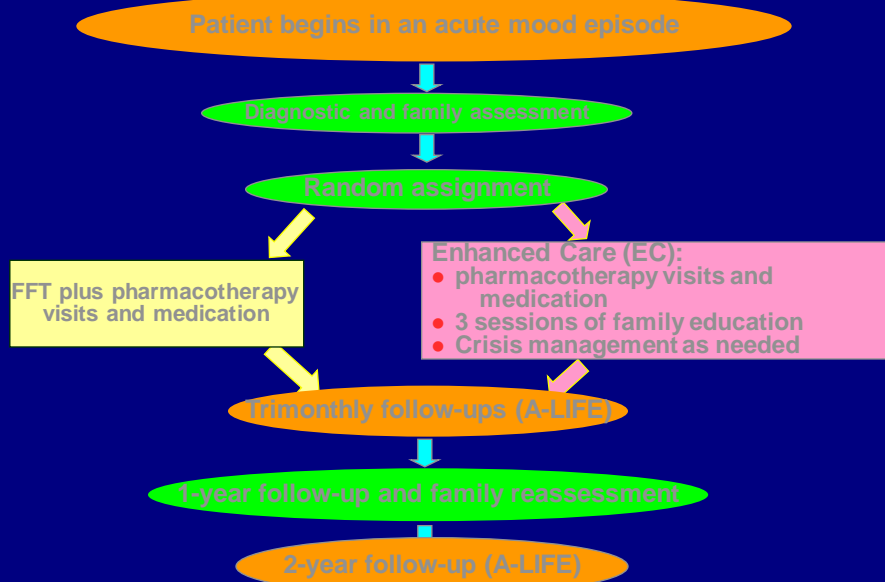
Does Expressed Emotion Predict Mood Symptom Scores Over 2 Years Among Adolescent Bipolar Patients (N=20)?

(Miklowitz et al., 2006; *Dev and Psychopathology*)



$F(1, 17) = 6.33, p = .02; \text{Cohen's } d = 0.98$

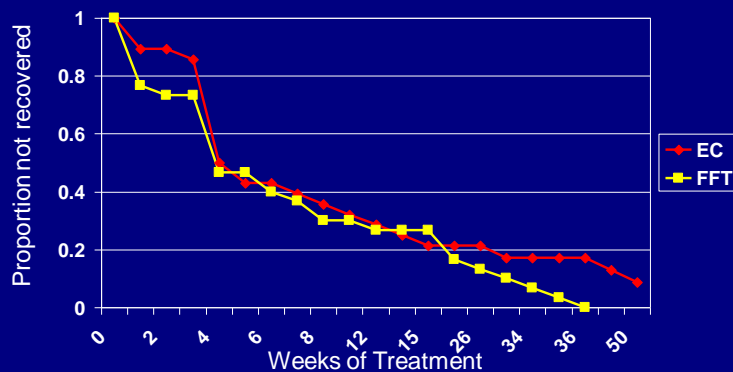
The Colorado/Pittsburgh Randomized Trial of FFT for Bipolar Adolescents (NIMH 62555) (N = 58)



Baseline Patient Characteristics

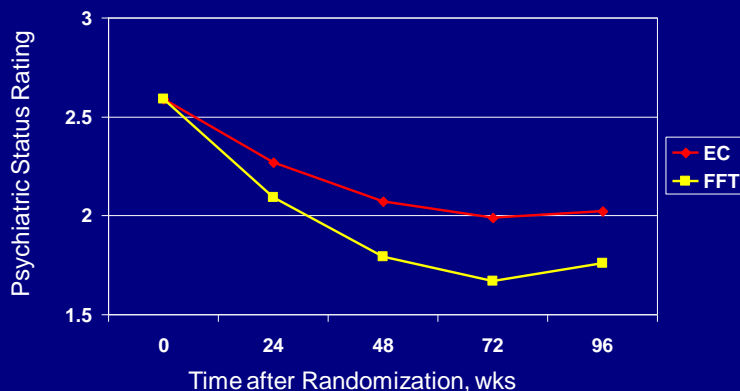
	FFT N=30	EC N=28	TOTAL N=58
Age, mean (sd)	14.5 (1.6)	14.4 (1.6)	14.5 (1.6)
Female (%)	56.7	57.1	56.9
Non-Hispanic White	80.0	92.9	86.2
Live with both bio. parents (%)	46.7	42.9	44.8
Bipolar I, %	66.7	64.3	65.5
Bipolar II, %	10.0	10.7	10.3
Bipolar NOS, %	23.3	25.0	24.1
Baseline Depression	28.8 (9.3)	28.3 (9.7)	28.6 (9.4)
Baseline Mania	24.5 (9.9)	24.0 (9.2)	24.3 (9.5)

Results of Survival Analysis: Time to Recovery from Depression at Intake



$\chi^2(1) = 4.36, p = 0.037, HR = 1.84$ (95% CI, 1.04 - 3.29)
Miklowitz et al., *Arch Gen Psychiatry*, 2008

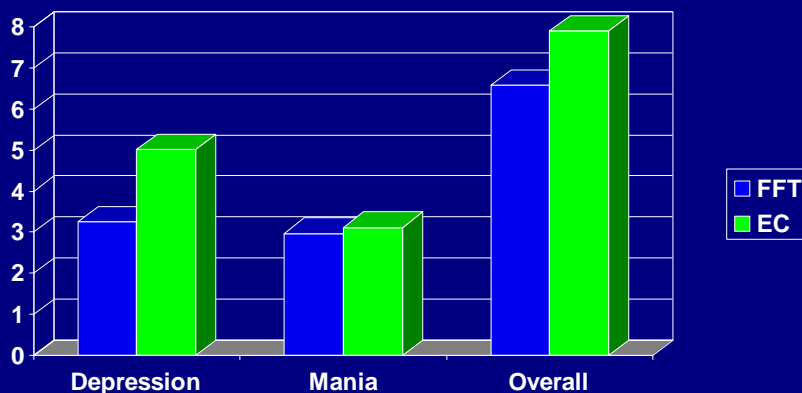
Results of Longitudinal Analysis: A-LIFE Depression Scores Over Time



Treatment x time interaction, $F [1, 5014] = 9.15, P = 0.0025$

Miklowitz et al., *Arch Gen Psychiatry*, 2008

Results from Poisson Regression: Time in Episode



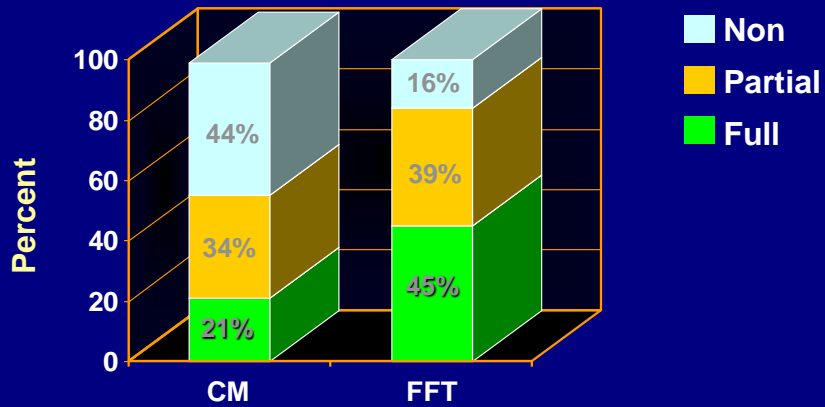
Depression: $\chi^2 = 13.03, p = .0003$; Mania: $\chi^2 = 0.1, p = .91$

Miklowitz et al., *Arch Gen Psychiatry*, 2008

Treatment Mechanisms: What is FFT Changing in the Patient or Family?

- **Hypothesis 1: Improvements in medication adherence mediate the effects of family intervention on mania symptoms only**
- **Hypothesis 2: Improvements in family risk indicators mediate the effects of family intervention on bipolar depression**
 - Reductions in familial criticism
 - Improvements in face-to-face interactional behavior

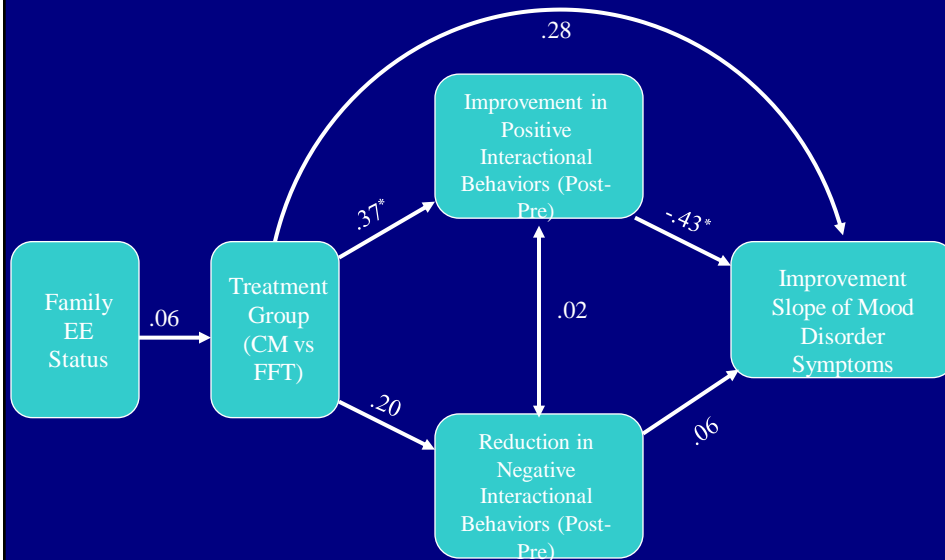
FFT is Associated with Better Drug Adherence than CM Over a 2-Year Follow-Up



$\chi^2(2)=9.1, P = .01.$

Miklowitz et al., *Archives of General Psychiatry* 2003; 60: 904-912.

Positive Family Interactional Behavior Mediates the Effects of FFT on Mood Disorder Outcomes



Path coefficients are standard Beta weights. * $p < .05$; Simoneau, Miklowitz et al., 1999; *J Abnormal Psychology*

Summary, I.

- **Family stress affects (and is affected by) the course of bipolar disorder**
- **Family and other psychosocial treatments should be key components of the outpatient management of bipolar disorder**

Summary, II.

- **FFT has shown effectiveness for hastening recovery, delaying relapse, and enhancing functioning**
- **Mechanisms may include enhancing family communication (for depression) and medication adherence (for mania)**
- **Results for bipolar adolescents are promising for depression as an outcome**

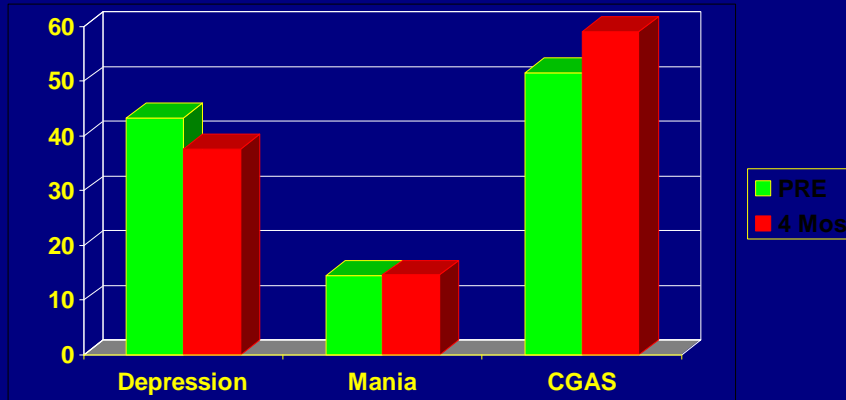
Future Directions

- Three-site (Colorado, Pittsburgh, Cincinnati) larger-scale randomized clinical trial of FFT for early-onset patients (collaborative R01, N = 150):
 - Examines moderators and mediators of treatment effects
 - treatment costs and benefits
 - the role of parental psychopathology

Children at Risk for Bipolar Disorder

- The role of family interventions in the prevention of bipolar disorder in at-risk youth
- Colorado and Stanford collaboration
- 12 sessions of FFT for children who have subsyndromal BP symptoms and who have a first-degree relative with BP I or II
- Status: Funded (NIMH R34-077856)

Children at Risk for Bipolar Disorder Treated with FFT: Changes From Pretreatment to 4 months



Where Else Has FFT Been Implemented?

Investigator-Initiated Trials, USA

- Emory University (E. Craighead)
- Univ of Pittsburgh Med Ctr. (D. Axelson)
- University of Cincinnati Children's Hospital (R. Kowatch)
- Beth Israel Hospital (D. Perlick)
- Univ of Massachusetts (J. Patel)
- Baylor College of Medicine (L. Marangell)
- Massachusetts General Hospital (G. Sachs)
- NY State Psych Institute (M. Oquendo, NIMH)
- Denver VA Medical Center (L. Adler and H. Nagamoto)
- Stanford Univ. Child Bipolar Clinic (K. Chang)
- Boston University (M. Tompson) and J. Asarnow (UCLA)

International

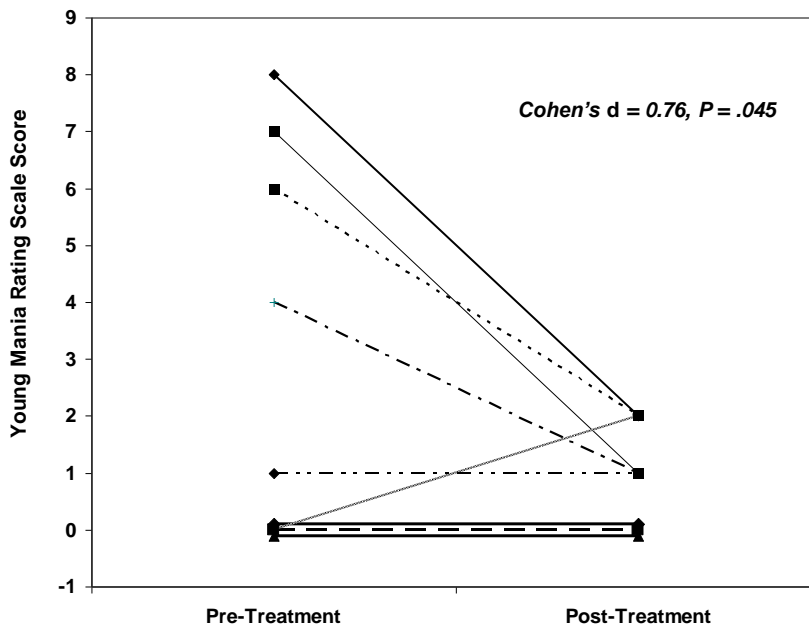
- Turkey (Dept Psychiatry, Izmir, A Ozerdem PI)

Colorado/Oxford Collaboration

Miklowitz, Alatiq, Geddes, Goodwin, Fennell, & Williams, 2008)

- Use of mindfulness-based CBT groups for bipolar patients in remission
- Small waitlist trial (N = 14) has been completed

Figure 2: Changes in Mania Scores After Mindfulness-Based Cognitive Therapy (N = 9)



Research Collaborators: 1989–2008

Colorado Family Project

Graduate Students

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Tina Goldstein
Kimberley Mullen
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Michael Bresznyak
Aparna Kalbag
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Kristin Powell
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Gary Sachs, M.D.

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Young Investigator
Award
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Univ. of Colorado