

Update on Bipolar Disorder
*Lessons from the STEP-BD
Study*

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Bipolar Disorder

- ❑ Prevalence is much more common than previously thought
- ❑ 4.5 % -1.0% Bipolar I
 - 1.1% Bipolar II
 - 2.4% Subclinical Bipolar D/O
- ❑ Often misdiagnosed as unipolar
- ❑ Future: cyclicity vs polarity

Merikangas, KR et al. *Arch Gen Psychiatry*. 2007, 64(5): 543-52.

Overview of the STEP- BD Study

STEP-BD

- ❑ NIMH funded study of treatment effectiveness
- ❑ Systematic Treatment Enhancement Program for Bipolar Disorder
- ❑ Gary Sachs, M.D. (MGH) Project PI
- ❑ 15 sites
- ❑ 8 years, 4361 patients
- ❑ Highly heterogeneous data base, multiple comorbidities, few exclusions, entered through normal referrals without recruitment, patients paid for treatment

Standard Care Pathways

- ❑ Acute Depression
- ❑ Refractory Depression
- ❑ Acute Mania
- ❑ Refractory Mania
- ❑ Rapid Cycling
- ❑ Relapse Prevention
- ❑ Pregnancy
- ❑ Substance Abuse
- ❑ Other Comorbidity

Randomized Care Pathways

- Acute Depression: mood stabilizers + antidepressants (paroxetine or bupropion) vs. mood stabilizers + placebo
- Acute Depression with Concurrent Manic Symptoms: mood stabilizers + antidepressants vs. mood stabilizers + placebo
- Impact of Bipolar Specific Psychotherapies:
 - CCP: Collaborative Care Program
 - CBT: Cognitive Behavioral Therapy
 - FFT: Family Focused Treatment
 - IPSRT: Interpersonal and Social Rhythm Therapy

Major Findings from the STEP-BD Study

Three Major Areas

- The STEP-BD study was designed to answer several broad areas of investigation.
- We focus today on three broad areas of findings: Comorbidity findings, Psychopharmacology findings, and Psychotherapy findings

Comorbidity Findings

Comorbidity Findings

- Comorbidity findings concern which psychiatric disorders commonly co-occur with a diagnosis of Bipolar Disorder

Comorbid Anxiety

- ❑ Bipolar I 52.8%
 Bipolar II 46.1%
- ❑ 2 to 3-fold increase in the history of suicide attempts
- ❑ Earlier age of onset of Bipolar Disorder (age 15.6 vs 19.4)
- ❑ Shortened duration of well intervals

Comorbid ADHD

- ❑ 5.9% current; 9.5% lifetime
- ❑ Bipolar I > Bipolar II
- ❑ More likely associated with with multiple comorbidities especially Anxiety Disorders and Substance Use Disorders
- ❑ More disabling course, earlier age of onset and higher rates of suicide attempts

Baldassano, CF. *J Clin Psychiatry*. 2006, 67 Suppl 11 :8-11.

Comorbid Substance and Alcohol Abuse

- ❑ 37% Substance Abuse or Dependence
- ❑ Alcohol abuse or Dependence
 - Bipolar I 46.2%
 - Bipolar II 39.2%
- ❑ Poorer outcome

Baldessano, CF. *J Clin Psychiatry*. 67 Suppl 11:8-11

Regional and Gender Differences

- ❑ Depression more prevalent in Northern sites
- ❑ Women had higher rates of Bipolar II (29.0% F vs 15.3% M)
- ❑ Men and Women had equal rates of depression and rapid cycling
- ❑ Women had higher rates of comorbid bulimia and thyroid disease

Baldassano, CF *J Clin Psychiatry*, 2006: 67 Suppl 11:8-11

Friedman, E et al. *Acta Psychiatr Scand*, 2006: 113(6):510-7

Psychopharmacology Findings

Psychopharmacology Findings

- Psychopharmacology findings concern which medications are most effective for Bipolar Disorder, which are least effective, whether there are associations between certain medications and undesirable effects such as switching and suicide, and the interaction between medications and psychotherapy.

Acute Depression

- ❑ Randomized N = 366
- ❑ Mood Stabilizer + Adjunctive Antidepressant (paroxetine or bupropion) vs Mood Stabilizer + Placebo
- ❑ Primary Outcome is Durable Recovery (≥ 8 weeks euthymia)
- ❑ No difference in outcome (24% with AD vs 27% Placebo)
- ❑ No difference in affective switch (10.1% AD vs 10.7% Placebo)

- Sachs,GS et al. *N Engl J Med.* 2007, 356(17):1711-22

Acute Depression with Concomitant Manic Symptoms

- ❑ Randomized N = 335
- ❑ Syndromal depression with 2 or more manic symptoms
- ❑ Mood stabilizer + AD vs mood stabilizer + placebo
- ❑ Primary outcome: time to recovery from depression
- ❑ No difference in time to recovery
- ❑ Higher manic severity levels at follow-up in AD vs placebo group

Goldberg, JF et al. *Am J Psychiatry*. 2007, 164(9): 1348-55

Psychotherapy Findings

Psychotherapy Findings

- Psychotherapy findings concern outcome studies comparing three “branded” Bipolar-Specific psychotherapies with a control condition for treating Bipolar Disorder, and the relative effectiveness of these Psychotherapies when compared to pharmacotherapy.

Psychotherapy Component to the STEP-BD

- “Branded” psychotherapies designed specifically to treat Bipolar Disorder have been developed in recent years
- These therapies have been developed in response to the fact that pharmacotherapy alone is often inadequate to fully treat Bipolar Disorder

Psychosocial Interventions for Bipolar Depression

- ❑ Randomized N = 293
- ❑ Primary Outcome is time to recovery and % patients well each of 12 months
- ❑ “Collaborative Care”: 3 session control condition (education, coping strategies, treatment planning)
- ❑ Intensive Interventions (up to 30 sessions)
 - ❑ -Cognitive Behavioral Therapy
 - ❑ -Interpersonal and Social Rhythm Therapy
 - ❑ -Family Focused Treatment
- ❑ Intensive Psychotherapies separate from Collaborative Care and do not separate from each other

Miklowitz, DJ et al. *Arch of Gen Psychiatry*. 2007, 64:419-427

Psychosocial Interventions and Functional Outcomes

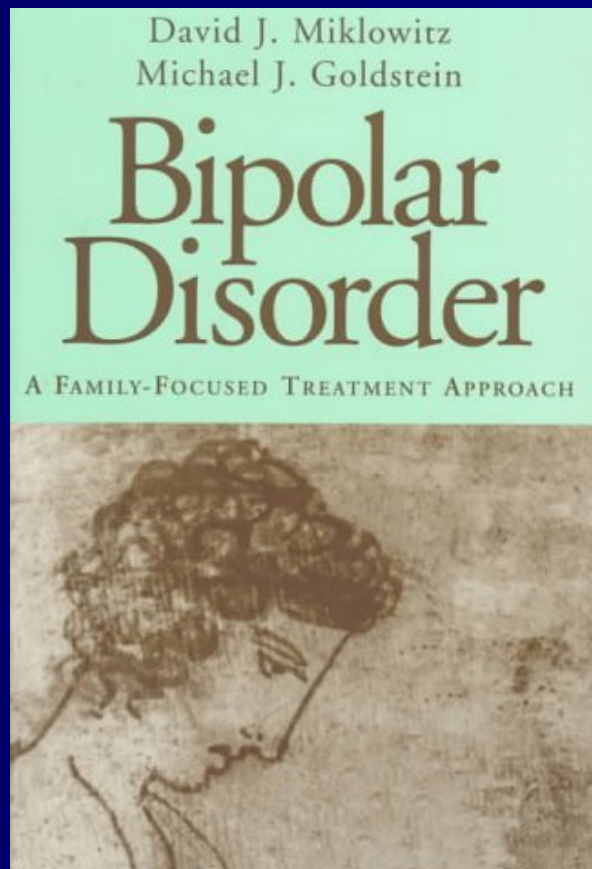
- ❑ Randomized N = 152
- ❑ Primary Outcome is score on functional assessment tool every 3 months for 9 months
- ❑ Collaborative Care vs Intensive Psychosocial Intervention (CBT, IPSRT or FFT)
- ❑ Intensive Psychosocial Treatment enhances relationship function and life satisfaction.
- ❑ No difference in work/role function or recreation scores
- ❑ No difference between Intensive Interventions

Miklowitz, DJ et al. *Am J Psychiatry*, 2007; 164(9): 1340-7.

Three Bipolar Psychotherapies

- Collaborators included 3 such Bipolar-specific psychotherapies in the STEP-BD Study:
 - Family-Focused Treatment
 - Interpersonal and Social Rhythm Therapy
 - CBT for Bipolar Disorder

Family Focused Treatment



- Family-Focused Treatment (FFT) was developed by Drs. David Miklowitz and Michael Goldstein at UCLA from research on Expressed Emotion (EE) and Affective Style (AS), two measures of the emotional climate in family members of Bipolar Patients

EE

- EE is a measure of family members' *attitudes* toward the patient assessed during an interview. High EE relatives express critical, hostile, and/or overinvolved attitudes. Low EE relatives do not express such attitudes
- Patients returning from hospital to home environments with High EE family members have much higher relapse rates than patients living with only Low EE family members

AS

- AS is a measure of *critical behavior* expressed by family members toward the patient in face-to-face interactions
- Patients returning from hospital to home environments with highly critical relatives, as measured by AS, have much higher relapse rates than patients with non-critical families

Rationale for FFT

- Patients from High EE/Critical AS homes also did not function as well in social and interpersonal relationships
- Moreover, coping with a family member with bipolar disorder is very stressful on family members
- Drawing from the extensive evidence-based EE family therapy literature in schizophrenia, the authors developed a Bipolar-specific family therapy, FFT

Treatment Structure

- Psychoeducation module
- Communication Enhancement Training module
- Problem-solving Skills module
- Maintenance Phase

Modules

- Psychoeducation Module: Similar to Psychoeducation in IPSRT and CBT
- CET: Teaching avoidance of High EE/Negative AS communication and new positive, adaptive communication skills, e.g. Expressing positive feelings, Active Listening, Making positive requests for change, Expressing negative feelings about specific behaviors rather than attacking character or global qualities

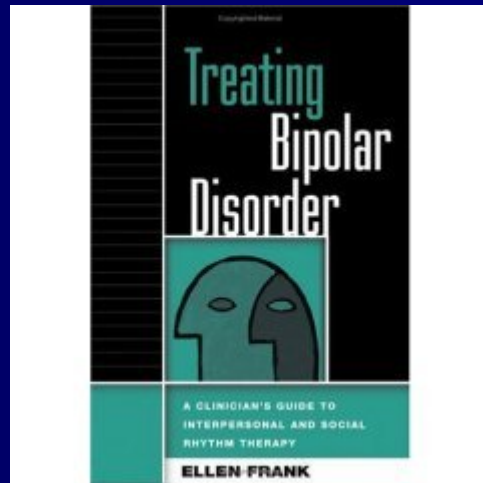
Modules Cont.

- Problem Solving: Skills such as agreement on the problem, generating possible solutions, discussing pros and cons as a family, planning and implementing best solutions, praising efforts and evaluating effectiveness

FFT Treats the System

- FFT is the only approach that is designed to treat the broader milieu within which the patient is functioning
- Although designed as a “stand alone” treatment, FFT is especially powerful when paired with concurrent individual therapy

Interpersonal and Social Rhythm Therapy (IPSRT)



- IPSRT was conceived in 1990 by Ellen Frank, Ph.D., at the University of Pittsburgh
- IPSRT is a highly effective psychosocial treatment for bipolar disorder

Overview of ISPRT

- ISPRT is a prophylactic treatment for a chronic, recurring condition
- *The primary purpose of ISPRT is relapse prevention*
- Relapse prevention is defined as preventing the recurrence of new episodes, or extending the time between subsequent episodes

3 Pathways to Relapse

- Even when patients are optimally medicated, three pathways are identified in ISPRT that may lead to relapse:
 - (1) Medication noncompliance
 - (2) Stressful life events, especially interpersonal events
 - (3) Disruptions in social rhythms

ISPRT Treats these 3 Pathways

- ISPRT treats these 3 pathways using a series of modules structured in an individualized treatment approach
- Assessment, Psychoeducation, different Interpersonal Problem Area modules have been developed for ISPRT, and Social Rhythm Regularization

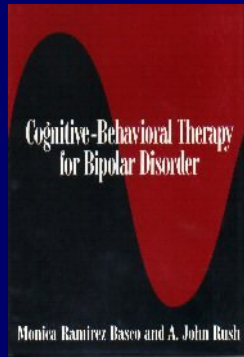
Interpersonal Modules

- In ISPRT, the Interpersonal Inventory will lead to the selection of an Interpersonal Module, done in conjunction with the patient.
- There are 5 Interpersonal Modules:
 1. Grief
 2. Grief for the Lost Healthy Self
 3. Interpersonal Role Disputes
 4. Role Transitions
 5. Interpersonal Deficits

Social Rhythm Module

- The patient completes the Social Rhythm Metric-II (SRM) for 2 weeks to determine timing of specified daily activities.
 - There is a 17 item version or a 5 item version; either can be used. The 5 item version is shown to the right:
 - For the first two weeks the patient notes the actual time each event occurred, 7 days a week
1. Out of bed
 2. First contact with another person
 3. Start work/school/volunteer/family care
 4. Dinner
 5. To bed

Cognitive-Behavioral Therapy (CBT) for Bipolar Disorder



- CBT has been reformulated by various clinicians for the treatment of BSD
- Modifications in CBT include length of treatment and where to intervene in the illness process

BSD are Chronic Disorders

- CBT for BSD (CBT-BSD) begins with the premise that BSD are longer-term in nature, and unlike unipolar depression and anxiety disorders
- Thus CBT-BSD can last several months or span a year or more, with follow-up contact suggested indefinitely, even over several years, given the high risk of relapse in this population
- *The primary goal of CBT-BSD is relapse prevention*

Intervening at the Patient's Current Need Level

- In CBT-BSD, therapeutic intervention is tailored to the patient's current needs and capacity to engage treatment, accept their illness, and the length of time that they have been living with the illness

Initial CBT Treatment

- Psychoeducation
- Patients are given tools to help them identify early warning signs so that they and their families can intervene before a full-blown manic or depressive episode is triggered
- Life Charts, Symptom Summary Worksheets, Mood Graphs, and lifestyle management skills are used to help the patient learn early detection skills

Behavioral Controls

- Patients are also taught specific behavioral controls to further regulate depressive and manic symptoms and manage stress triggers
- Examples include: Adding positive behaviors and stopping negative behaviors, improving sleep hygiene, increasing social contact, and managing excessive work commitments using an Activity Schedule

Cognitive Interventions

- Cognitive symptoms and distortions common to BSD are addressed, controlled, and corrected
- Examples include Cognitive Errors such as Tunnel Vision, Making Guesses rather than examining the evidence, Misperceptions rather than getting feedback, thinking in Absolutes rather than thinking across a continuum, and morbid thoughts about death and suicide

Stress Management

- Relaxation Training, learning Stimulus Reduction and Stimulus Enhancement techniques, Focusing on One Idea at a Time, Problem Solving and Decision Making Skills, and Schedule Management Skills all assist the patient in learning to control stress, which in turn can help manage BSD-PS symptoms

Interpersonal Communication

- Learning not to be oversensitive, addressing paranoid cognitions, challenging pessimistic cognitions, learning behavioral management of irritability, learning to recognize and slow pressured speech, and learning to recognize and adapt to cognitive impairment in social and occupational relationships can improve interpersonal functioning

Summary of CBT

- In summary, CBT is a highly structured, skills-oriented therapy that involves teaching the patient a set of tools to actively cope with many of the symptoms and challenges of BSD at various stages of illness with the goal of relapse prevention

Conclusions

- Bipolar Disorder has a high rate of psychiatric comorbidities especially anxiety disorders, substance abuse and ADHD
- Little evidence of antidepressant efficacy
- Intensive psychotherapies designed for Bipolar Disorder significantly improve symptomatic as well as functional outcome of depression

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