BIPOLAR DISORDERS UPDATE

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OBJECTIVES

† Review the major developments and trends in diagnosis and management of bipolar disorders.
† Discuss and promote the role of the primary care physician in bipolar disorders.
† Review treatment strategies for bipolar disorders with a focus on the primary care setting.
SUMMARY OF MAJOR TRENDS

† Greater focus on BP depression
† Change in the status of antidepressants in BPAD
† Change in the status of second generation antipsychotics in BPAD
† Lithium “revival”
† Embedded psychiatry in primary care
† Increased emphasis on identifying and treating co-occurring medical disorders
BIPOLAR DISORDERS

Spectrum of disorders:
1. bipolar I
2. bipolar II
3. cyclothymic disorder
4. bipolar not otherwise specified (NOS)
Five criteria for validating psychiatric diagnoses (Feighner Criteria)

1. Clinical description - symptoms, signs, age of onset, precipitating factors
2. Laboratory studies (imaging)
3. Delimitation from other disorders – differential clinical features (e.g. treatments for BPAD not effective in SCZ or MDD)
4. Follow-up studies
5. Family studies
   ⇐ 60-80 % heritability

† Overdiagnosis?
BIPOLAR DISORDERS IN PRIMARY CARE

Need for treatment at the primary care level

†Common disorder with prevalence of ____
†Half of all mentally ill patients are treated at the primary care level
†Shortage of psychiatrists:
  †Long waiting periods for an initial consultation
  †Difficulty finding a psychiatrist that accepts low quality insurance.
†Community mental health centers are disappearing
ADVANTAGES OF PRIMARY CARE MGMT

†Earlier initiation of treatment
†Continuity of care
†Established therapeutic alliance
†Future trend towards embedded psychiatry
†Management of co-occurring medical ailments
†Alternative of non-medically trained prescribers
†BP patients have significantly higher rates of metabolic syndrome than the general population. 37%, according to a meta-analysis of 7000 pts.¹

†Multifactorial cause:
† Some attributable to certain SGAs, but CV risk factors present before the widespread use of SGAs and in treatment naïve pts.²
† Lifestyle: overeating, smoking, etoh, inactivity
† Possible genetic vulnerability independent of environmental/behavioral factors.
MEDICAL COMORBIDITIES

†BP patients have 1.5-2.5x higher CVD mortality risk
†With all cause mortality, die 8-9 years earlier
MEDICAL COMORBIDITIES

Metformin for SGA-induced weight gain
BP patients with high medical burden have:
†Greater number of lifetime mood episodes \(^5\)
†Longer duration of untreated illness \(^6\)
†A higher number of prescribed psychotropics \(^5\)
†Longer psychiatric IP stays \(^7\)
DIAGNOSIS
CHALLENGES IN DIAGNOSIS

Diagnosis is challenging with high rates of misdiagnosis

- 7 of 10 pts initially misdiagnosed

- 1 in 3 wait ten years before correct diagnosis

(Dx is longitudinal, however, majority of the misdiagnosis attributable to lack of understanding about the disorder.)
Major consequences of undiagnosed/untreated bipolar:
† Delaying correct treatment
† Risky behaviors
† High suicide rates (19 % die of completed suicide attempt!) 11
† High substance use disorder rates
† Unnecessary suffering
MAKING THE DIAGNOSIS

1. Use of DSM categorical diagnosis (with screening instruments)

2. Additional (non-DSM) features of the disorder
   † Exam findings, course of illness
   † Probabilistic approach (BP vs MDD)

3. Collateral information!
†Bipolar I: requires a manic episode

†Bipolar II: requires a hypomanic episode + major depressive episode
   †A less severe variant of bipolar I??
MAKING A DIAGNOSIS: BY DSM 5

Mania:
Criteria A: One week of elevated, expansive, irritable mood AND increased energy …
plus 3 of the following from B Criteria:
† Distractibility
† Indiscretion or Irresponsibility
† Grandiosity
† Flight of ideas
† Activity (increased goal-directed activity)
† Sleep (decreased need for sleep)
† Talkativeness (pressured speech)
DIAGNOSIS: DSM 5

†Hypomania:
  †Same criteria as mania
    †...but does NOT cause significant functional impairment
  †Shorter time requirement (4 days)
    †(In reality average hypomania is actually 2-3 days) 
  †Absence of psychosis
Rule out:

†Medical conditions such as Cushings, brain lesions

†Substance-induced (hypomania)
  †Psychostimulants, corticosteroids, thyroid hormone
  †Antidepressants*
  †DSM IV: AD-induced hypomania/mania‡  SIMD
  †DSM 5: AD-induced hypomania/mania‡  Bipolar disorder
**DIAGNOSIS: MIXED FEATURES**

† **What is it?:**
   † Transition state between poles, ultra rapid cycling, combined episode, just a severe manic state?

† **DSM IV:**
   † Mixed Episode - Full criteria for a MDE and a Manic Episode for one week
   † Too specific for dysphoric manic states

† **DSM 5:** Depressive Episode, Hypomanic Episode, or Manic Episode (with Mixed Features)
DIAGNOSIS: MIXED FEATURES

†To simplify:
†Manic symptoms with . . .
†prominent dysphoria, depressed mood, hopelessness, feeling of worthlessness/severe guilt, suicidality† urgent psychiatric consultation or send to the ED

High suicide risk
DIAGNOSIS: DSM 5 “WITH ANXIOUS DISTRESS”

- Tense, restless, worry, fear of losing control
- Adds to decreased sleep
- Less likely to respond to treatment

⚠️ High suicide risk
Mood Disorder Questionnaire (MDQ)

† 13 questions based off of DSM criteria
† Fairly sensitive
† Takes about 5 minutes
† Screen every patient with depression
† Self report version: http://www.dbsalliance.org/pdfs/MDQ.pdf
MISDIAGNOSIS RATES

† MDD (60%)
† Anxiety Disorders (26%)
† Schizophrenia (18%)
† Personality disorder (BPD, ASP) (17%)
† Substance use disorders (14%) \(^ {10} \)

Also: Anxiety disorders, PDs, and SUDs frequently co-occurring with BPAD
MISDIAGNOSIS: MDD

MDD **most common** misdiagnosis

† Up to 30% of patients who suffer from depression actually have a bipolar diagnosis

† 50% of the index mood episodes are depression

† More likely to seek help during a MDE

† BP patients spend most symptomatic days in depression (see next slide)
DIAGNOSIS: BIPOLAR VS MDD

Frequency of Symptoms in BP I

- Depression: 68%
- (Hypo)mania: 20%
- Mixed: 12%

[Diagram showing the distribution of symptoms]
# DIAGNOSIS: MDD VS. BP (SYMPTOMATOLOGY)

<table>
<thead>
<tr>
<th>BPAD</th>
<th>MDD</th>
</tr>
</thead>
<tbody>
<tr>
<td>†“Atypical” depressions:</td>
<td>†Insomnia</td>
</tr>
<tr>
<td>†Hyperphagia</td>
<td>†Decreased appetite</td>
</tr>
<tr>
<td>†Hypersomnia</td>
<td>†Psychomotor agitation</td>
</tr>
<tr>
<td>†Psychomotor retardation</td>
<td>†Somatic complaints</td>
</tr>
</tbody>
</table>
DIAGNOSIS: MDD VS. BP
(SYMPOTOMATOLOGY) 15,16

BP more likely to have:

† Psychotic features (delusions and hallucinations)

† Co-occurring SUDs, anxiety disorders, ADHD
  † SUDs 60% of BP I pts
  † 4x more likely to have a SUD in BP than MDD) 16

† Mood lability
DIAGNOSIS: MDD VS. BP (COURSE OF ILLNESS) 15,17

BPAD
† Early onset depression <25 years
 † The earlier, the likelier to be BP
† Multiple depressive episodes (>5)
 † 90% have recurrent MDEs
† MDEs vary in character (e.g. some episodes melancholic, some atypical)
† Seasonality (depressed late fall/ winter; manic spring)
† Index mood episode is postpartum

MDD
† Later onset depression >25 years
† Fewer episodes
 † 50% have recurrent MDEs
† MDEs similar in character
† Seasonal pattern less likely
<table>
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<th>BPAD</th>
<th>MDD</th>
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<tbody>
<tr>
<td>† Family history of bipolar disorder</td>
<td>† No bipolar history</td>
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Poor response to AD therapy

† Multiple trials failed
† Worsening symptoms (irritability, activation)
† Can be difficult to sort out from simple side effects
† Affective switch to hypomania, mania, mixed
**DIAGNOSIS: MDD VS. BP**

Biggest things to remember. . .

*BP diagnosis considered in *every* depressed patient

1. Family history of bipolar disorder
2. Antidepressants triggered (hypo)mania
3. Early onset
4. Recurrent pattern
DIAGNOSIS: OTHER DDX

† Borderline personality disorder
† Antisocial PD
† ADHD
† Anxiety disorder
† SUD
† Schizophrenia
† Schizoaffective
MANAGEMENT
† Decide your comfort level
  † Medications, level of acuity, risk assessment, BP knowledge base, ability/willingness to be available to pt and family.

† Know your referral options (substance treatment, psychotherapists, psychiatrists)

† Find psychiatrists that will see patients urgently and are highly available to their patients.

† Refer to psychiatry for comprehensive evaluation- any new bipolar diagnosis
TREATMENT: BASICS - MEDICATIONS

†“Mood stabilizers”
   †Lithium and the AEDs (VPA, lamotrigine, CBZ)
†Antipsychotics
†Antidepressants
†Adjunctive agents (benzos, omega 3, light therapy etc.)
Antidepressant in BPAD controversy:

† When to initiate?
  † Only with a mood stabilizing medication on board
  † Never with h/o mixed episodes, rapid cycling
  † SNRIs and TCAs most important to avoid
  † Bupropion probably the safest option
  † Strongly consider psychiatric consultation

† When to discontinue?
  † Acute mania
  † Possible or probable recent trigger of (hypo)mania

† When to continue?
  † Stopping AD causes relapse into depression
  † ADs are effective for co-occurring disorders
TREATMENT: MEDICATIONS (GENERAL CONCEPTS)

**BP depression**

† Lamotrigine (best)
† Quetiapine (best)
† Lithium
† Olanzapine, esp. in combo with fluoxetine
† Lurasidone (Latuda): new FDA indication

**Mania**

† Lithium (unless mixed/rapid cycling)
† Divalproex (when mixed/rapid cycling)
† Second-generation antipsychotics
TREATMENT: MEDICATIONS (GENERAL CONCEPTS)

† **Lifetime** mood stabilizers when there is history of two manias or one severe mania

† **Principles:** low threshold for dual therapy as only 20% are stabilized with monotherapy

† Don’t combine SGAs

† **Always remember interactions:**
  † Divalproex increases lamotrigine levels
  † Carbamazepine, major inducer
TREATMENT: SCREENING/MONITORING

1. All Patients: CVD risk factors, tobacco, alcohol, pregnancy status/birth control
2. Prior to initiation of any MS or SGAs: BMI, HCG, CMP, CBC, Lipid screening up-to-date
3. Additional drug-specific screening tests
4. Drug-specific monitoring schedule
TREATMENT CATEGORIES

1) Maintenance therapy to provide mood stabilization and prevent recurrence of mania or depression

2) Acute bipolar depression

3) Acute (hypo)mania
TREATMENT: MAINTENANCE PHASE

Step 1:
†Choose a core mood stabilizer
   1) Lithium 2) Lamotrigine 3) Divalproex
   Or
   • If already on a mood stabilizing agent(s) and stable‡ Continue current treatment unless side effects unacceptable
      Or
   †If history of stability on a certain agent(s) and well tolerated ‡ Restart
TREATMENT: MAINTENANCE PHASE

1) Lithium:
   † First line for maintenance
   † Best with h/o classic euphoric manias
   † Prevents both mania and depression (mania > depression)
   † Anti-suicide effect
   † Less effective in mixed episodes/rapid cycling
2) Lamotrigine
• Prevents both mania, rapid cycling, and depression
• Depression > mania
• Typically best option for BP II
• Approved for monotherapy, but use only in absence of severe, frequent, recent mania history
• Extraordinarily well-tolerated
TREATMENT: MAINTENANCE THERAPY

3) Divalproex
   † Second line
   † Less evidence for maintenance therapy
   † Less favorable SE profile
   † Prevents mania, not very effective for depression
   † Option for frequent manias, mixed episodes or rapid cycling
TREATMENT: MAINTENANCE THERAPY

Step 2: Consider addition of a second agent based on target symptoms

† Prevent depression
  † Add quetiapine
  † Add lamotrigine to lithium (best?)
  † Add lithium to lamotrigine (best?)

† Prevent Mania
  † Add another mood stabilizer or an SGA

† History of psychotic symptoms
  † Second generation antipsychotic
TREATMENT: ACUTE BIPOLAR DEPRESSION

† Step 1: If suicidal, agitated, psychotic, previous response to ECT‡ Urgent psychiatry consult or ED. If relatively stable, proceed. . .

† Step 2: Start (or add): quetiapine, lamotrigine, or lithium‡ maximize dose as needed.

† Step 3: If minimal response or partial response‡ add another agent (quetiapine, lithium, or lamotrigine)

* Note: usually a safer bet to add agent rather than switch

* Note: Lamotrigine not good option in severe acute depression (slow titration)

† Step 4: Still minimal response?‡ referral to psychiatry
TREATMENT: ACUTE (HYPO)MANIA

†Stop! Mixed features, suicidal, aggressive, agitated, dysphoric, significant decline in functional status? † send to ED

†Currently hypomanic with judgment preserved, absence of risky behaviors, SI absent, still getting at least a few hours of sleep per night, spouse/family supervision? † can often be managed as outpatient
Outpatient management:

† Step 1: Start lithium, divalproex, quetiapine, or another SGA you are comfortable with
† Step 2: Maximize dose as needed. Continue monotherapy if full response.
† Step 3:
  † If no response, add another agent from step 1 to a therapeutic dose‡ cross taper to another agent
  † If partial response‡ dual therapy with another agent from step 1
† Step 3: If no response or partial response refer to psychiatry.

*Where is lamotrigine?
ADJUNCTIVE TREATMENTS

†Benzos
†Omega 3 fatty acids: **All patients.** 1-2 grams daily. EPA:DHA > 2:1 ratio
†Bright Light Therapy: Caution in BPAD
†Folate/l-methylfolate (Deplin)
†N-acetylcysteine?
†Magnesium?
“ALTERNATIVE” TREATMENTS

†SAMe: avoid
†St. Johns Wort: avoid
†Lithium orotate: absolutely not
REFERENCES

9. DSM5
REFERENCES

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