

Diagnosing Mood Disorders: Why Do We Still Get It Wrong

Scott T. Aaronson, MD
Director, Clinical Research Program
Sheppard Pratt Health System
Clinical Associate Professor
University of Maryland Medical School

Disclosures

- Research Support
 - Neuronetics
- Consulting and Advisory Boards
 - LivaNova
 - Neuronetics
 - Genomind
- Speaker's Bureaus
 - Sunovion
 - Neurocrine

THE PROBLEMS WITH PSYCHIATRIC DIAGNOSES OF MOOD DISORDERS

Biology of Mood Disorders

- Over 100 different genes may contribute to the development of a mood disorder.
- Any one patient may have a handful of single nucleotide polymorphisms (SNPs)
- As we understand the underpinnings of these illnesses there may be less to distinguish one illness for another but may account for the myriad presentations of mood disorder we see

What We Do Know

- Mood disorders are chronic, recurrent and progressive diseases of the nervous system
- Mood disorders are associated with functional and structural changes in the brain and in physical health
- They are associated with changes in neuroplasticity, neurogenesis and neural resilience
- Residual symptoms greatly increase the risk of future episodes

Current Concerns in Diagnosis

- Poor recognition of bipolar disorder
- Under recognition of psychotic symptoms especially in major depression
- Reliance on clinical presentation in the absence of biological understanding
- Poor understanding of conditions not represented in DSM--highly recurrent major depression, bipolar spectrum disorder

Current Problems in Treatment

- Lack of evidence base for treatment resistant depression
- Confusion over use of antidepressants in bipolar depression
- Where do TMS and VNS belong in the treatment paradigm
- What represents valuable vs. profitable additions to the armamentarium

Mood Disorder Diagnosis

- Mood disorders still go undiagnosed about half the time
- Even when diagnosed it is often:
 - Incorrect (miss the diagnosis for bipolar disorder)
 - Inadequate (overestimate the adequacy of previous treatment)
 - Incomplete (not focused on the chief problem— substance abuse, eating disorder, PTSD or psychosis)

WHAT GOES INTO A PSYCHIATRIC DIAGNOSIS

Elements of Psychiatric Diagnosis

- **Presentation** (often way overvalued in the total assessment, causes missed symptoms). Make sure to assess functioning in all domains—sleeping, eating, concentration, mood and consider changes over time
- **Collateral information** (critical when patient lacks insight into disorder, especially bipolar and psychotic disorders, too often undervalued)
- **Psychiatric history** (be careful when an illness is still evolving with new presentations or young folks, bipolar may have several depressive episodes before a mixed or manic one)

Elements of Psychiatric Diagnosis 2

- **Family history** (often more critical that we give credit to and highlights at times arbitrary distinctions between schizophrenia and mood disorders)
- **Medical history and relevant lab work** (do neuroimaging and/or genetic testing help?)
- **Mental status exam**
- **Psychological and environmental formulation** (is this where PTSD fits in?)

BIPOLAR DISORDER DIAGNOSIS

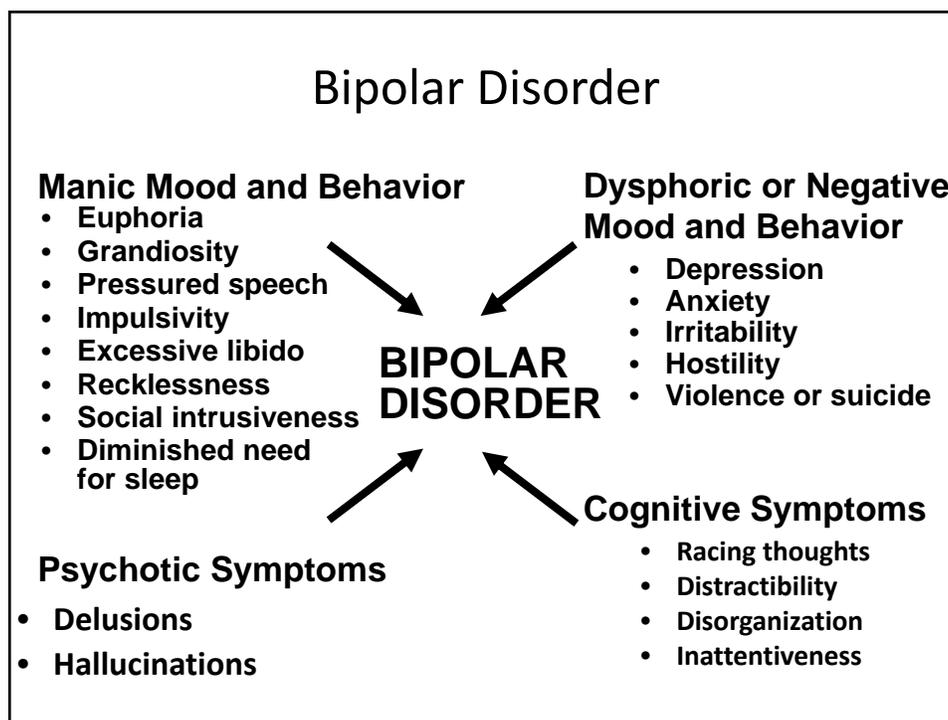
Bipolar Disorder – Difficult Diagnosis

- 7 out of 10 people with Bipolar Disorder are initially misdiagnosed in specialty mental health sector¹
 - Psychiatrists correctly diagnosed 48% of bipolar sufferers²
 - PCPs correctly diagnosed 23% of bipolar sufferers²
- More than 1/3 sought help for more than 10 years before an accurate diagnosis¹
- **30% of patients with a diagnosis of depression or anxiety may have bipolar disorder³**

¹National Survey DMDA, 2000.

²Calabrese JR, et al. Presented at 155th APA Annual Meeting; May 18-23, 2002; Philadelphia, PA.

³Manning JS, et al. *Compr Psychiatry*. 1997;31(2):102-108.



The Bipolar Diagnostic Star

Age of onset

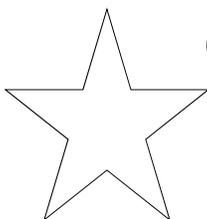
Early age (< 25) with high episode rates

Family history

“Loaded” family history

Course of symptoms

Depression with abrupt onset and termination or seasonal pattern



Response to treatment

Antidepressant “misadventures”

- Treatment emergent hypomania or agitation
- Erratic or uneven antidepressant responses
- Multiple antidepressant failures

Current symptoms

Hypomania/Mania

Risk of Misdiagnosis

- Most confusion is around bipolar depression vs unipolar and agitated depression vs. mixed bipolar state
- Better to err on the side of overdiagnosis of bipolar disorder due to risk of therapeutic “misadventures”

Diagnostic Considerations

- Depression+anxiety/agitation, be suspicious
- Depression+bipolar family hx
- Abuse substance of choice is cocaine, crack, methamphetamine or other stimulant
- History of multiple marriages, multiple jobs
- Two clearly different depressive presentations-retarded depression cycling into an agitated depression

Diagnostic Considerations II

- Hx of family drama or violence
- Rapid response to antidepressants or agitation in response to antidepressants
- Rapid onset or offset of sx
- Criminal history
- Multiple affairs or judgment errors

Bipolar Comorbidities: Substance Abuse

- Substance abuse-single best predictor of poor outcome. Long term rates may approach 60%, baseline rates 30-40%
- Substance abusers are more likely to be rapid cyclers, be lithium non-responsive, have higher suicide rates, more functional disability, and have more depressive features
- Substance abusers likely excluded from clinical trials, so data set is limited

Bipolar Comorbidities: Anxiety Disorders

- No controlled studies of anxiety and bipolar disorder
- Higher rates of treatment non-response, substance abuse and suicide
- Comorbid frequency in bipolar population may be 50%

Bipolar Comorbidities: ADHD

- Common diagnostic concern in pediatric population
- All bipolar patients will meet most of the criteria for ADHD but fewer of the ADHD patients will meet the bipolar criteria
- Differentiate the cyclical from the constant courses of the illnesses
- Care in using stimulants

DIAGNOSING DEPRESSION

Five of Nine Symptoms Over Two Weeks

- Depressed mood
- Anhedonia
- Weight or appetite change
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Worthlessness and/or guilt
- Poor concentration
- Thoughts of death or suicide

Many Different Presentations Possible

- Better to think of it as depressive disorders rather than a single illness
- The myriad of different presentations may suggest different interventions
- Be careful to rule out other causes, other illnesses and comorbidities

Evaluating the Depressed Patient

- Diagnostic Considerations
 - Bipolar disorder
 - Psychosis (subtle guilty delusions, suicidal conviction)
 - Anxiety
 - Dysthymia
 - Substance Abuse (suspicion over stimulant abuse)
 - PTSD
 - Personality Disorder
- Family History
- Past Treatment History
- Course of illness

Looking for Relevant Comorbidities in Depression

- General Medical disorders
 - thyroid and other endocrine diseases
 - dementia, Parkinson's disease, and other CNS disorders
 - autoimmune diseases (inflammatory markers may also be increased in depression)
 - malignancies
- Psychiatric disorders
 - anxiety (symptoms and syndromes)
 - substance abuse
 - personality disorders

DIAGNOSING TREATMENT RESISTANT DEPRESSION

What is Treatment Resistance?

- Failure to respond to two or more agents to treat a carefully diagnosed condition
- But.....

What Treatment Resistance is Not

- Does not count if the diagnosis is wrong (more common than you realize)
- Inadequate treatment by dose or duration (how should this be determined)
- Non compliance
- Substance abuse makes all psychiatric illness non responsive
- PTSD is often missed and diagnosed as a mood or psychotic disorder (can present as almost any psychiatric condition)

Are you sure it is not bipolar?

- More than three episodes a year (even if only depressive) may represent a cyclical mood disorder subtype
- Anger episodes that seem explosive
- Differentiate between insomnia and decreased need for sleep
- Periods of very high energy or productivity
- Pressure of speech
- Intense irritability (getting into verbal or physical fights)

When to Consider PTSD

- Often there is no report of childhood abuse
- Can present as a disconnect between content and affect
- Are there periods of dissociation, do they lose time?
- Sense of emotional numbing or hypervigilance
- Presents with more anxiety or irritability than depression

Chronicity

- The longer an episode persists the harder it is to treat
 - At 6 months—50% recovered
 - At 12 months—16% recovered
 - At 5 years—1% recovered
- Once an episode exceeds 12 weeks, chance of recovery drops 37%

TRD Overview: Levels of Resistance

Stage	Treatment Response
0	No single adequate trial of medication
1	Failure to respond to an adequate trial of 1 medication
2	Failure to respond to 2 different monotherapy trials of medications with different pharmacologic profiles
3	Stage 2 plus failure to respond to augmentation of 1 of the monotherapies
4	Stage 3 plus failure of a second augmentation strategy
5	Stage 4 plus failure to respond to ECT

Thase ME, Rush AJ. Treatment-resistant depression. In: Bloom FE, Kupfer DJ, eds. *Psychopharmacology: The Fourth Generation of Progress*. New York, NY: Raven Press, Ltd.; 1995:1082-1097.

33

Definitions

- Nonresponse--<25% reduction on depression rating scale
- Partial response—25-50% reduction
- Treatment response-->50% reduction
- Remission—no dysfunction or minimal sx remain
- N.B.—response is not remission
- Most clinical trial give statistics for response, not remission
- Responders at least three times as likely to experience a relapse in 12 months than remitters

Treatment Resistant Depression (TRD)

- Single episode vs. recurrent
- Verifying adequate trials by pharmacy records—check on dose and duration
- Some folks will respond to another medication from the same class (which just underscores that our medications in the same class are not equivalent)

TRD

- Is there anything that gives a clue as to where to grasp onto this illness?
- Has the patient ever responded to anything ever? This includes any medications from any class (including opiates, stimulants, benzos) and neurostimulation (ECT and TMS and VNS)
- Does exercise help? Has the pt ever been an obligate exerciser?
- Has the patient ever had an eating disorder? Anorexia can give a sense of well being.
- Any self harm? Does it help the depression or just distract?

Final Words

- Be thoughtful when evaluating patients with mood disorders.
- Don't be as concerned with fitting patients into a limited diagnostic box, look to establish a sense of shared target symptoms. There are no clear lines between diagnostic categories
- In general, you are better off erring on the side of treating possible bipolar or psychotic symptoms