Bipolar Disorder in Children and Adolescents

Molly Faulkner, PhD, CFNP, LISW
University of New Mexico
Department of Psychiatry

Child Bipolar I Disorder is a contentious diagnosis.

Barbara Geller, MD

Objectives

1. Cite Incidence of Bipolar Disorder in Children

2. Describe 3 Criteria of Disruptive Mood Disregulation Disorder in the new DSM 5

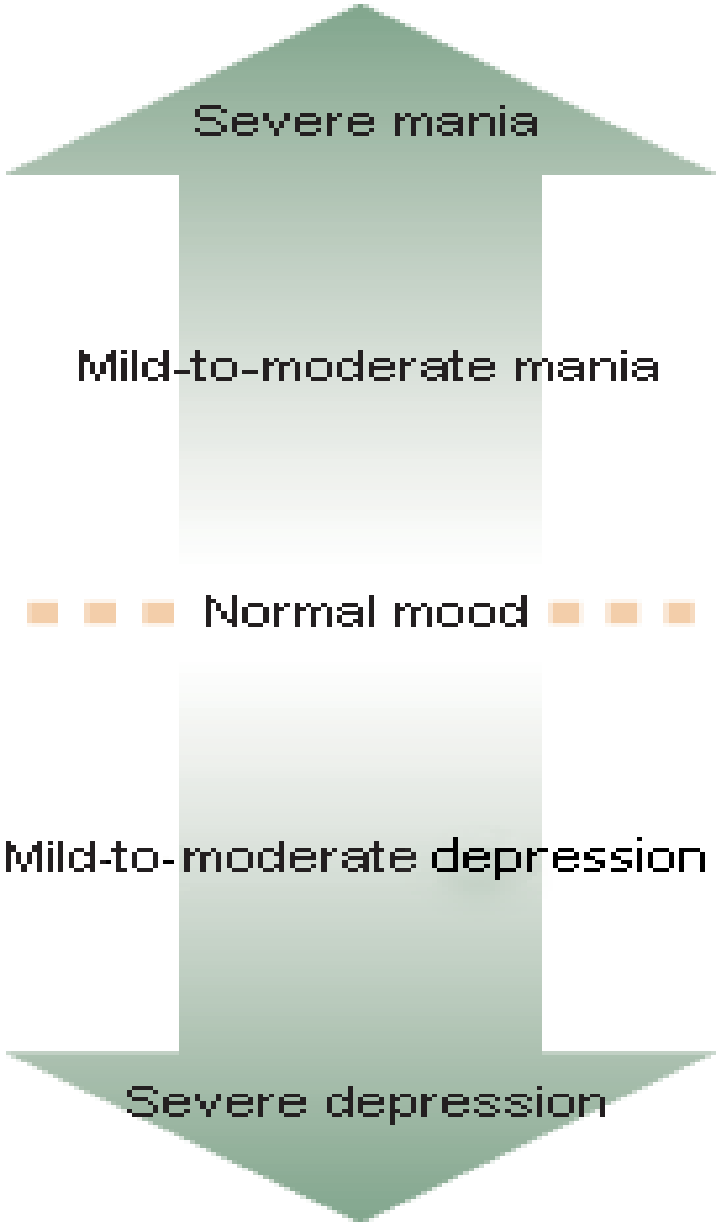
3. Identify 2 Comorbidities with Childhood Bipolar Disorder

4. Explain 2 Criteria that Differentiate Bipolar Disorder from ADHD or DMDD

Agenda

- Bipolar disorder
- Epidemiology
- Definitions
- Genetics,
- Bipolar vs ADHD vs DMDD
- Bipolar vs Schizophrenia
- Psychopharmacological Treatment
- Assessment, Triage and Treatment
-

- What Is Bipolar Disorder?



Epidemiology

- Problems with obtaining good data
- Prevalence and validity of the dx in children remains controversial.
- Onset prior to age 10 occurs in only 0.3% to 0.5% of bipolar patients
- 0.8% to 1% was thought to be incidence but new data of meta analysis estimates it to be higher.

Epidemiology: Meta-Analysis

Van Meter, Moreira, Youngstrom (2011)

- Studies from 1985-2007 16,222 youths between ages of 7 and 21
- 6 Samples from US and 6 from Netherlands, United Kingdom, Spain, Mexico, Ireland, and New Zealand
- No significant difference in the mean rates between US & non-US studies
- US studies had a wider range of rates, highest BPAD NOS.
- **Overall prevalence of bipolar disorder was 1.8%** (95% CI, 1.1%-3.0%), higher than the previous studies

- Symptoms may be present since infancy or early childhood, or may suddenly emerge in adolescence or adulthood.

- Some studies indicate 59% of adults with bipolar disorder had first symptoms in childhood

Only been in past 6 yrs or so that clinicians generally accept that bipolar disorder is a childhood onset disorder…

- "The thought that a child can be too happy, too cocky, too exuberant, is anathema to many people. But when we're talking about childhood bipolar I disorder, we are talking about children who are so silly and giddy that families are asked not to bring them to church; who are so cocky, expansive, and grandiose that they go to the principal's office and tell them to fire teachers they don't like; bright kids who fail classes because they are fully convinced they know it all and don't study," Geller.

Pediatric bipolar disorder

Narrow phenotype: Classic presentation of bipolar disorder (grandiosity, hypersexuality, elation)

Broad phenotype: irritability, not necessarily episodic - non episodic severe irritability coupled with symptoms of hyperarousal a developmental presentation of BPAD?

Child Bipolar I Disorder

Prospective Continuity With Adult Bipolar I Disorder; Predictors of 8-Year Outcome

October 2008 Barbara Geller,
Archives of General Psychiatry

- Prospective, longitudinal study of 115 children, mean age 11 years dx 1st episode of child bpad from 1995 to 1998 & followed for 8 yrs.

- **60.2%** of weeks with *any mood* episodes &
- **39.6%** of weeks with *mania* episodes, during 8-year follow-up

- 87.8% recovered from mania

  BUT

- 73.3% relapsed to mania

18 yrs+

- 44.4% had manic episodes
- 35.2% had substance use disorders

- Supports childhood onset hypothesis
- Chronic, unremitting nature of this illness in children into adulthood
- Longer episodes with ultra rapid cycling

Family History

Genetics-offspring of parents with bipolar disorder were 2.7 times higher risk for developing a psychiatric

disorder & fourfold higher risk (14–50%) for developing a mood disorder (Chang, Steiner, & Ketter, 2000).

- Degree of familiarity increased in early-onset cases
- Lifetime rates of BPAD approx 15% in first degree relatives
- Monozygotic twins 60% concordance rate

Characteristics

- turbulent, dysfunctional lives
- poor academic performance
- impaired peer and family relationships
- alcohol and substance abuse in fam hx
- suicidal behavior

Gender Issues

- BPAD affects both sexes equally.
- Early-onset cases, males > females
- Especially w/onset before age of 13 years
- Depressive disorders females > males

Intelligence

- Over 90% of youth with bipolar disorder have normal IQs which positively influences prognosis
- BPAD- including rapid cycling, found in patients w/moderate to severe mental retardation, autism, and trisomy 21

BPAD Criteria DSM 5

DSM-IV-TR Classification and Definitions for Mood Disorders

Bipolar I Manic episodes with or without depression, w/ mixed features specifier
Bipolar II Major depression with hypomania
Bipolar disorder-not elsewhere defined (NED)
Criteria not met for bipolar I, bipolar II, cyclothymia or have too few manic symptoms

Manic and depressive symptoms lasting at least 1 week
Mania An abnormally and persistently elevated, expansive, or irritable mood, lasting at least a week
Hypomania A persistently elevated, expansive, or irritable mood, lasting at least 4 days, that is clearly different from the usual nondepressed mood
Cyclothymia Chronic fluctuating mood disturbances hypomania and minor depressive symptoms 2 yrs for adults and 1 yr for children

Rapid cycling Four or more episodes per year
Ultrarapid cycling Five to 364 episodes per year
Ultraradian cycling Mania is present for more than 4 hr/day

Bipolar Disorder DSM 5 Conceptual Changes

- Bridge btwn psychotic disorders & depressive disorders
- BPAD I essentially unchanged
- BPAD II
  - no longer considered a milder form of BPAD I due to the severity of their depressions and severity of work & social impairment

- During the period of mood disturbance, 3 (or more) of the following symptoms have persisted (4 if the mood is only irritable) and have been present to a significant degree:

  - Inflated self-esteem or grandiosity
  - Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)
  - More talkative than usual or pressure to keep talking
  - Flight of ideas or subjective experience that thoughts are racing
  - Distractibility (i.e., attention too easily drawn to unimportant or irrelevant external stimuli)
  - Increase in goal-directed activity (either socially, at work or school, or sexually) or psychomotor agitation)
  - Excessive involvement in pleasurable activities that have a high potential for painful consequences (e.g., engaging in unrestrained buying sprees, sexual indiscretions, or foolish business investments

Specifiers

- **With anxious distress**
- **With mixed features**
- **With rapid cycling**
- **With mood-congruent psychotic features**
- **With catatonia. Coding note: Use additional code 293.89 (F06.1).**
- **With peripartum onset**
- **With seasonal pattern**

Specifiers

- **With anxious distress:** The presence of at least 2 of the following symptoms during the majority of days of the current or most recent episode of mania, hypomania, or depression:
  - Feeling keyed up or tense.
  - Feeling unusually restless.
  - Difficulty concentrating because of worry.
  - Fear that something awful may happen.
  - Feeling that the individual might lose control of himself or herself.

Bipolar

Manic/Hypomanic

- Add to Criterion A:

  “and abnormally and persistently increased goal-directed activity or energy.”

Bipolar and Related Disorders

No “Mixed Episodes”

- (was: full Manic + MDD nearly every day/ 1 week)
- Now a specifier:
- “with mixed features”

Hypomanic Manic + 3/6 MDD symptoms

or MDD + 3/7 Manic symptoms

“With Mixed Features” Specifier

- New specifier "with mixed features" can be applied to bipolar I disorder, bipolar II disorder, bipolar disorder NED (previously called "NOS") and MDD
- Recognition that "mixed" mood states that do not meet full criteria for a mixed episode of bipolar I disorder are common
- In DSM 5, the predominant mood can either be depression, mania, or hypomania
- The secondary mood can be "subclinical“
-

Subtypes

- Manic symptoms in youth- freq not long enough to meet the 1-week duration criteria for manic episode & esp true for children.
- Youth more likely to have Bipolar II or Cyclothymic disorder, rather than Bipolar I disorder.
- Children & adolescents may also be more likely than adults to present with rapid-cycling aka *ultradian* episodes (Geller et al. 2004)~ euthymia, depression, mania within a day
- Geller et al. (1995) found that in 26 patients with early-onset bipolar disorder (ages 7 to 18 years), 81% had a rapid-cycling course.

Why BPAD Diagnosed More?

- Late 1990s and into 2000s, increased number of children being diagnosed with bpad
- No criteria for children with bpad ever established
- Researchers developed own criteria that replaced manic/hypomanic episodes with irritability and anger

BPAD Dx More (cont'd)

- Atypical antipsychotics were developed
- Prescribers diagnosed bpad in children with criteria of irritability and anger
- AAs prescribed more frequently
- Led to 40 fold increase in past 10 years of bpad dx in children

Pediatric bipolar disorder

- Between 1996 and 2004 – rates of children with a hospital discharge diagnosis of bipolar disorder rose from 1.3 to 7.3 per 10000

- Discharges of adolescents with BPAD increased 400%

Disruptive Mood Dysregulation Disorder

A. Severe recurrent temper outbursts grossly out of proportion in intensity of duration

- Temper Outbursts

verbally (rages) and/or behaviorally (physical aggression people or property)

Inconsistent with Developmental Level

Disruptive Mood Dysregulation Disorder

B. Frequency: temper outbursts on average 3 or more x per week

C. Mood between temper outbursts:

1. Nearly every day, most of day, mood between persistently irritable or angry

2. Irritable or angry mood observable by others (parents, teachers, peers)

D. Duration:

Criteria A-C present 12 or more months. During this time person has not had 3 or more consecutive months when without symptoms of Criteria A-C.

Present in 2 or more settings

Ages 6 and 10

DMDD

- Some symptoms present in other child psychiatric disorders
  depression, bipolar disorder
  oppositional defiant disorder.

- Some children also have a second disorder, such as problems with attention or anxiety.
- important to get a comprehensive evaluation by a trained & qualified mental health professional.

DMDD--continued

- Captures children with frequent temper tantrums and irritability
- Less research is available on DMDD than on most other DSM 5 diagnoses
- Placed in DSM 5 due to concerns about overdiagnosis of BPAD - prepubertal onset of these symptoms
- Natural history -children at risk for MDD and anxiety disorders as adults rather than bipolar disorder
- Treatment: SSRIs might be indicated, given developmental outcome
- Concerns: validity and specificity still unclear, will it result in over diagnosis of normal children?

Comorbid Conditions

- ADHD
- Conduct Disorder
- Substance abuse disorders

Comorbidities with BPAD

- ADHD-60-90%
- 69% rate of conduct disorder (Kovacs & Pollack, 2005) Substance abuse
- Depression
- Anxiety disorders
- Tourette syndrome
- Bulimia Nervosa
- PDD
- (Birmaher et al., 2002; Lewinsohn
- et al., 1995; West et al., 1996; Wozniak et al., 1997,
- 1999, 2001).

ADHD as Comorbidity – Present in 60 to 90% of Bipolar Pts Biederman et al. (2004),

Three overlapping sx

1. Excessive talking
2. Increased activity
3. Distractibility

But these sx are unlikely to be present every day in child with BPAD.

ADHD as Comorbidity

- ADHD alone does not have persistent mood instability with explosive outbursts as seen in bipolar disorder.

- BPAD Children Three common symptoms not usually
- observed in children with ADHD:

1. Elevated mood,
2. Grandiosity
3. Flight of ideas (Geller et al., 2002).

Is it BPAD or ADHD or BOTH?

- Strong family history of bipolar disorder
- "Mean" & hurtful style of social interaction which is typically not seen with kids with ADHD
- Sexualized to a worrying extent, but no history of sexual abuse.
- Grandiose statements regarding their strengths & abilities
- Comments & actions might make adults in their environment feel uncomfortable.

Jason

14 year old boy, raised by single mother, has younger brother with whom he fights.

C/O moodiness, fastidiousness, ‘emo’, persistently irritable mood, angry, disrespectful to mother, adults at school, extremely poor judgment, thinks adults overreact to his delinquency. Cognitively above average

Mania

- ✓Behavior
  - ✓Agitation
  - ✓Decreased need for sleep
  - ✓Energy increase
  - ✓Goal directed activity increased
  - ✓Talkative, rapid, speech
- ✓Cognition
  - ✓Distractibility
  - ✓Flight of ideas
  - ✓Racing thoughts
  - ✓Grandiosity
  - ✓Self-esteem increased
- ✓Interpersonal
  - ✓High-risk pleasurable behavior
  - ✓More talkative
  - ✓Recklessness
  - ✓Sexual behavior increased
  - ✓Social disinhibition

Depression

✓ Behavior

- Agitation
- Appetite decrease/weight decrease
- Appetite increase/weight gain
- Energy reduction
- Excessive sleep
- Insomnia
- Psychomotor retardation

✓ Cognition

-Anhedonia

-Confidence diminished

-Concentration reduced

-Indecisiveness

-Morbid ideation

✓ Emotional Distress

-Blunting of emotions

-Guilt/self-reproach

-Hopelessness

-Self esteem reduced

-Suicidal plans, acts, ideation

-Thoughts of death

Symptoms (that could be) Unique to Children

- Severely negative, petulant mood
- Frequent almost constant, mood shifts
- Unpredictable triggers
- Family “walking on eggshells” to avoid outbursts
- Interferes with their functioning
- Extended, excessive tantrums and acts of physical & verbal aggression
- Better stronger, smarter & more capable than any peer or adult

Symptoms (that could be) Unique to Children

- Direct and order peers rather than play
- Tell adults how to do their jobs
- Believe they have special abilities or talents
- Rules of nature do not apply to them, can jump off roofs, out of moving cars
- Decreased need for sleep without daytime fatigue or restorative sleep.
- Rapid pressured speech
- Self stimulation, touching of others,
- Psychotic features appear in the context of affective sx as opposed to schizophrenia where psychotic symptoms are independent of them.
-

Adolescents w/Mania

Complicated presentations:

- psychotic symptoms, including mood-incongruent hallucinations, paranoia, and marked thought disorder;
- markedly labile moods, with mixed manic and depressive features; and
- severe deterioration in their behavior

Differential Diagnosis

- Schizophrenia
- Schizoaffective
- Agitated Depression
- Post-traumatic Stress Disorder
- Borderline Personality Disorder
- Childhood Disruptive Behavioral DO
- Cross-Cultural Issues and Culture-Bound Syndromes
- Mood Disorder Due to a Medical Condition
- Substance Use Disorder

This has led to….

- Underdiagnosis in teenagers
- Misdiagnosis of schizophrenia

BPAD or Schizophrenia?

Features	Pediatric schizophrenia	Pediatric bipolar disorder
Delusions	>Mood incongruent[a,b,c,d]	>Mood congruent[g,h]
Grandiose delusions	11%[d]	50%[h]
Hallucinations	80%[d]	23%[l]
Thought Disorder	>Loosening of associations[a,b,c,d]	Pressure of speech[h]
Non psychotic	7%[e]	25%[e]
Mood symptoms	Depression in prodromal and residual phase[f]	Prominent irritability, elated mood depression, and mixed[i,h,j]
Family history	Less homotypic[f]	More homotypic[f]
Chronic impairment	>90%[e]	25–40%[g,h,k]
Episodic	Not episodic[e]	AO-BD*: 20–50%[e,g] PEA-BD**: 0–16%[h,l]

Course and Prognosis

- Early course of bipolar disorder in adolescents often more chronic and refractory to treatment
- Long-term prognosis is probably similar to that of adults
- Presence of comorbid behavioral disorders and/or substance abuse negatively influences prognosis and treatment response

Adolescent Course vs. Adult Course

- Prolonged early course
- Less responsiveness to treatment
- Increased risk for completed suicides
- In one study 20% of adolescent patients made at least one medically significant suicide attempt

Highest risk of suicide

- Male or
- Depressed phase of illness

Pharmacology

- Lithium

Starting dose: 150mg to 300mg daily, increase 150mg q 3 to 5 days

Tx Blood level: 0.8-1.2meq/L

Initiation Labs:

CBC w/diff, LFTs, TSH, FT4, UDM, UA (creatinine), EKG

Follow up labs: CBC w/diff, Chem7 and LFTs and Lithium level q 5 days after initiation and q 5 days after change in dose & every 6 months after stabilization.

Side Effects-

- ✓ increased urination
- ✓ polyuria
- ✓ polydipsia
- ✓ lethargy
- ✓ stumbling
- ✓ visual disturbances
- ✓ tremor
- ✓ hair loss
- ✓ hypothyroidism

Lithium-
Mechanisms of Action

- Exerts multiple neurotransmitter effects, including enhancing serotonergic transmission, increasing
- norepinephrine synthesis, blocking postsynaptic dopamine, & increasing GABA activity (Beschor et al.,2003).
- Produces alterations in ion channels of cell membranes & affects the intracellular signaling processes (Manji & Lenox, 1999).

Valproic acid

Starting Dose: 250mg q hs or BID

Tx Blood Level 50-125ug/mL

Initial Labs: CBC w/diff, LFTs, Chem7, TSH, FT4, UA

Follow Up Labs: q 5 days draw CBC w/diff, Chem 7, Valp level as titrating, then q 2 wks, then q month, then q 3 months

SE-Wt gain, sedation, nausea/anorexia, tremor, inhibits metabolism of other medications

Rare SE- pancreatitis, hepatoxicity, Stevens-Johnson syndrome

Carbamazepine

Starting Dose: 200mg BID

Tx Blood Level: 4-12ug/mL

Initial Labs: same as Valp + ECG

Follow Up Labs: q 5 days draw CBC w/diff, Chem 7, Tegretol level as titrating, may be lower second blood draw as auto induction; then q 2 wks, then q month, then q 3 months

SE: nausea/anorexia, rash sedation, dizziness/ataxia

Induces hepatic metab of other meds

Rare SE: hyponatremia, agranulocytosis, Stevens-Johnson syndrome

Anticonvulsants- Mechanism of Action

- Prolong the inactivation of voltage-sensitive sodium and calcium channels.
- This decreases the release of catecholamines, which neutralize neurotransmitters such as dopamine,

  serotonin, and norepinephrine.
- Also increase the inhibitory neurotransmitter GABA (White, 2003).

- Divalproex sodium- linked to the development of polycystic ovarian syndrome in women (Joffe et al., 2006).

- Provide adolescent females and their families with informed consent, including warnings about menstrual irregularities, hirsutism, acne, male pattern hair loss, and elevated testosterone before staring divalproex sodium.
- Oral Contraceptives less effective with Carbamazepine.

Valproate > Lithium

- Rapid-cycling
- Dysphoric
- Mixed mania
- Comorbid substance abuse (Bowden, 2001).
- Preferred treatment for children and adolescents with BD because they frequently present with mixed states.
- Mixed states at all ages are difficult to treat and may require treatment with more than one mood stabilizer.

Atypical Antipsychotics

- Monotherapy or augmentation
  - Ziprasidone-13 to 17 for schiz, 10 to 17 for bipolar/mixed
  - Aripiprazole- 13 to 17 for schiz, 10 to 17 for bipolar/mixed and 6 to 10 autistic disorder, irritability,
  - Risperidone 13 to 17 for schiz, 10 to 17 for bipolar/mixed & 5 to 16 autistic disorder, irritability
  - Quetiapine, 13 to 17 for schiz, 10 to 17 for bipolar/mixed
- Olanzapine- 13 to 17 for schiz, 13 to 17 for bipolar/mixed
- Quetiapine- greater efficacy w/ Quetiapine & Divalproex sodium-(87% response) than with Divalproex sodium alone (53% response rate)
- SE- wt gain, dyslipedmia, possible diabetes
- Guideline-prior to starting do wt, lipid profile, HgA1c, measure abdominal girth, BMI

Atypical Antipsychotics-Mechanism of Action

- Combine dopaminergic & serotonergic properties to provide mood stabilization.
- The studies evaluating monotherapy using the atypical antipsychotics are either open label or chart reviews

Disruptive Mood Dysregulation Disorder (DMDD)
Symptoms

- Severe temper outbursts at least 3 x per week
- Sad, irritable or angry mood almost every day
- Reaction is bigger than expected
- Child must be at least 6 years old
- Symptoms begin before age 10
- Symptoms present for at least a year
- Child has trouble functioning in more than one place (e.g., home, school and/or friends.

Combination Pharmacotherapy

- Kowatch and colleagues (2003) studied the effectiveness of combination pharmacotherapy for children and adolescents with BD & more promising for long term remission.
- Small study n=35 rec'd 6-8 wks w/single lithium, divalproex or carbamazepine.
- 58% of the participants required treatment with one or two mood stabilizers and either a stimulant, an atypical antipsychotic agent or an antidepressant.
- Response rate increased to 80% w/addition of concurrent therapy,

References

Hamer, A. (2004). Update on Children and Adolescents With Bipolar Disorder. *Bipolar Disorder and Impulsive Spectrum Disorder Letter. May. Accessed online August 24, 2004. http://www.psychiatrictimes.com/bp0405update.html*

Clinical correlates of therapeutic response in bipolar disorder. J Affect Disord 67(1-3):257-265. Bowden CL (2001),

Evins AE (2003), Efficacy of newer anticonvulsant medications in bipolar spectrum mood disorders. J Clin Psychiatry 64(suppl 8):9-14.

Ketter TA, Wang PW, Becker OV et al. (2003), The diverse roles of anticonvulsants in bipolar disorders. Ann Clin Psychiatry 15(2):95-108.

Wang PW, Ketter TA, Becker OV, Nowakowska C (2003), New anticonvulsant medication uses in bipolar disorder. CNS Spectr 8(12):930-932, 941-947.

Carandang CG, Maxwell DJ, Robbins DR (2003), Lamotrigine in adolescent mood disorders. J Am Acad Child Adolesc Psychiatry 42(7):750 [letter].

References

Van Meter AR, Moreira AL, Youngstrom EA, **Meta-analysis of epidemiologic studies of pediatric bipolar disorder.**
J Clin Psychiatry. 2011 Sep;72(9):1250-6. doi: 10.4088/JCP.10m06290. Epub 2011 May 31.

. Danielyan A, Pathak S, Kowatch RA, Arszman SP, Johns ES. Clinical characteristics of bipolar disorder in very young children. J Affect Disord. 2006 Jul 3; [Epub ahead of print].

- Kyte ZA, Carlson GA, Goodyer IM. Clinical and neuropsychological characteristics of child and adolescent bipolar disorder. Psychol Med. 2006;36:1197-1211.
- Nierenberg AA, Miyahara S, Spencer T, et al. Clinical and diagnostic implications of lifetime attention-deficit/hyperactivity disorder comorbidity in adults with bipolar disorder: data from the first 1000 STEP-BD participants. Biol Psychiatry. 2005;57:1467-1473.
- Grohl, J. M. (2012). What is Disruptive Mood Dysregulation Disorder? http://psychcentral.com/blog/archives/2012/05/16/what-is-disruptive-mood-dysregulation-disorder/
- Stetka, B. & Correll, C. (2013). A guide to DSM-5. Disruptive Mood Dysregulation Disorder (DMDD). http://www.medscape.com/viewarticle/803884_6